

FIRST EDITION • 2026

Pēpi Whānau Wawe Nutrition Guideline

A national nutrition guideline for preterm babies
in Aotearoa New Zealand

Poipoia te kākano kia puāwai

Nurture the seed and it will bloom

Guideline Development Group
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Waipapa
Taumata Rau
University
of Auckland



About this guideline

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AUTHORSHIP

This guideline was developed by the Pēpi Whānau Wawe Nutrition Guideline Steering Group and Guideline Development Groups. For membership and terms of reference see Appendix A.

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REVISION OF THE GUIDELINE

The guideline is intended to be a living document; therefore, the Liggins Institute will continue to monitor new publications, reports and resources and identify anything relevant. Available evidence will be reviewed on a 3–5 yearly basis, from 2029, to decide if the entire guideline or selected topics need to be updated. New topics will be addressed in future versions where appropriate.

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Foreword

Poipoia te kākano kia puāwai

Nurture the seed and it will bloom

We are pleased to present the Pēpi Whānau Wawe Nutrition Guideline, a national nutrition guideline for preterm babies.

Providing nutrition care for preterm infants is complex. These infants have diverse clinical needs, and nutrition practices vary between neonatal units. These differences may affect short-term health, whānau wellbeing and longer-term growth and neurodevelopment. This guideline has been developed to reduce unwarranted variation in practice and to support healthcare professionals, parents and families with clear, evidence-informed recommendations.

Consistent and equitable use of this guideline across all healthcare settings has the potential to improve outcomes for preterm infants and reduce health inequities. By following the same evidence-based recommendations, regardless of location or circumstance, healthcare teams can work together to ensure all preterm infants receive a high standard of nutrition care. In line with national policy and best-practice guideline standards, this guideline recognises the responsibility of healthcare services and professionals to uphold Te Tiriti o Waitangi and to support Māori health equity and wellbeing.

This guideline was developed by a multidisciplinary group of 25 clinicians and researchers and people with lived experience of preterm birth from across Aotearoa New Zealand who systematically reviewed and summarised the evidence that underpins the recommendations. We thank all contributors who shared their time, expertise and experience alongside busy clinical and personal commitments. We are especially grateful to whānau who shared their experiences of preterm care; their voices have informed the development of the guideline and are reflected throughout.

We hope it will help ensure that every preterm infant in Aotearoa New Zealand has the healthiest possible start in life.

Dr Barbara Cormack
Principal Investigator

Endorsements



The Paediatric Society of New Zealand
Te Kāhui Mātai Arotamariki o Aotearoa

The Paediatric Society of New Zealand | Te Kāhui Mātai Arotamariki o Aotearoa endorses this guideline as a national evidence-based resource, developed with the involvement of Paediatric Society of NZ members.



The Perinatal Society of New Zealand



New Zealand
College of Midwives
Te Kāreti o ngā Kaiwhakawhānau ki Aotearoa

The New Zealand College of Midwives | Te Kāreti o ngā Kaiwhakawhānau ki Aotearoa

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We are grateful to Dr Peter Bloomfield for undertaking the majority of the literature searches and to Dr Julie Brown, a systematic review specialist, for leading the development of the Evidence-to-Decision documents. We especially thank our methodologist Associate Professor Vanessa Jordan for her expert methodological advice, education in Evidence-to-Decision processes and guidance throughout the project.

We acknowledge Professor Frank Bloomfield for his skilled leadership in chairing the Guideline Development Group to achieve the consensus required to deliver this guideline and Catherine Belfield Haines our Project Manager whose organisation persistence and attention to detail ensured the project remained on track.

We also thank those who contributed lived experience perspectives including whānau and consumers whose insights grounded the guideline in real-world care. We acknowledge the contributions of Māori and Pacific Guideline Development Group members whose knowledge values and guidance strengthened the equity focus, cultural relevance and responsiveness of this guideline and we recognise Haunui Royal, our Kaiārahi, for his leadership, cultural guidance and wisdom throughout the guideline development process.

About the design

The guideline was designed by Tuatahi Creatives. The cover and topic dividers combine pūhoro, mangōpare and koiri.

Pūhoro represents flow and movement, reflecting the journey of pēpi whānau wawe and their growth over time. Mangōpare represents strength, courage, determination and leadership across all who are involved. Koiri, derived from the koru, represents nurturing, protection and the continual growth of both the kaupapa and the people within it.

Koiri is also used separately along the footer of each page, carrying these themes throughout the guideline.

Design and typesetting: Tuatahi Creatives.

Pēpi Whānau Wawe Nutrition Guideline

A National Nutrition Guideline for Preterm Babies

Breastfeeding, Whānau & Monitoring

Breastmilk and Breastfeeding

Expressing: Mothers should be supported to express early (<6 hours post birth), frequently (≥8 times/day) and by double pumping their breastmilk throughout their neonatal unit stay.

First feed: Babies should receive only mother's own milk for the infant's first feed whenever possible, to support the continuation of breastmilk expressing and breastfeeding.

Lactation consultants: Specialist neonatal lactation consultants should be embedded within the multidisciplinary neonatal care team.

Skin-to-skin care (ongoing and prolonged) should be initiated as early and as often as possible, prioritising mother–baby contact to support lactation, while actively encouraging fathers or partners to provide skin-to-skin care when the mother is unavailable or in addition to maternal contact.

Staff-led support: Provide timely, proactive, specialised staff-led breastfeeding support, additional targeted staff training and involvement of all NICU staff in lactation and breastfeeding support as an addition to standard care to improve breastfeeding outcomes.

Early education on breastfeeding should be part of routine postnatal care, given the benefits of breastfeeding for babies and mothers. Breastfeeding information, discussion and advice should also be included in routine antenatal care.

Mana-enhancing tikanga practices that support whānau Māori breastfeeding and Te Ao Māori values (e.g. whanaungatanga, manaakitanga) should be incorporated as part of good clinical care to support breastfeeding. Māmā Māori would like to have a whānau approach (e.g. include kuia, sisters, partner) to support breastfeeding.

Monitoring of Nutrition and Growth

Growth measurement: Measure weight, length and head circumference at least weekly. Use calibrated digital scales (to nearest 5 g) for weight, a neonatometer for length (to nearest mm) and non-stretch tape for head circumference. Apply Fenton 2025 growth charts from birth to 50 weeks postmenstrual age, then switch to WHO standards. Correct for gestational age up to 2 years.

Faltering growth: Assess after 2–3 weeks of age, and once birthweight is regained. Use these recommendations to screen for and intervene to resolve faltering growth – weight z-score change from birth. To calculate z-score, use the NeoGrowth Fenton 2025 mobile phone application. Babies with mild malnutrition (loss of >0.8 z-score) may require a higher feed volume/nutrient intake. Babies with moderate malnutrition (loss of >1.2 z-score) should be referred to a neonatal dietitian for individual assessment of their growth and intervention if needed.

Fetal growth restriction: Nutritional management and growth assessment for babies born with fetal growth restriction and/or SGA should be the same as those born AGA, although initial weight loss is often less.

Neonatal dietitians who meet the Australasian Neonatal Dietitians Network skill requirements for the level of neonatal care should be embedded within the multidisciplinary neonatal care team.

Whānau Education and Involvement

Whānau Māori should be included and are essential members of the team caring for their pēpi. Healthcare professionals need to communicate in a culturally safe way, as determined by whānau Māori. Incorporating Māori values (e.g. whanaungatanga (connectedness) and manaakitanga (kindness and hospitality)) when providing healthcare will contribute to increasing health equity for whānau Māori.

Pacific families should be regarded and therefore included as essential members of the team in nutrition care discussions for their pēpi. Healthcare professionals should communicate as determined by Pacific families and include relationship-centred, culturally safe communication that nurtures and recognises this value, Teu Le Vā, respects and supports expressions of faith and spirituality, and actively includes extended family members who are central to decision-making.

Whānau-led tikanga around food should be integrated into supporting whānau Māori in the nutritional care of pēpi Māori. Kai is an important aspect of tikanga Māori. It is important that manaakitanga is extended to both pēpi and whānau Māori; therefore, ensure whānau have access to an area to prepare and share kai. When possible, if there is more than one whānau member in NICU, offer more than one meal to the whānau.

Involve parents in tube feeding (feeding, changing tubes and using feeding pumps if needed) and preparing supplements (fortification and similar supplements) for their babies, as this may enhance parental confidence, engagement and satisfaction with care.

Education delivery: Alongside standard care, additional education for parents should be through a mix of delivery methods (face-to-face, written, online) and tailored to cultural and contextual needs.

“Poipoia
te kākano
kia puāwai

*Nurture the seed
and it will bloom.”*

Parenteral Nutrition

Who needs parenteral nutrition: For babies born $<31^{+0}$ weeks, start neonatal parenteral nutrition. For babies born $\geq 31^{+0}$ weeks, start parenteral nutrition if sufficient progress is not made with enteral feeding in the first 72 hours after birth.

For babies on enteral feeds, start parenteral nutrition if:

- enteral feeds need to be stopped and it is unlikely they will be restarted within 48 hours.
- enteral feeds have been stopped for more than 24 hours and there is unlikely to be sufficient progress with enteral feeding within a further 48 hours.

Use 10% glucose instead of parenteral nutrition for moderate-to-late (32^{+0} to <37 weeks' gestation) preterm babies whose mother's own breastmilk is not available after birth, while waiting for mother's breastmilk. Parenteral nutrition should be reserved for babies with a specific clinical indication.

How soon: When a preterm baby meets the indications for parenteral nutrition, start it as soon as possible, and within 8 hours at the latest.

How much fluid: Either lower or higher parenteral fluid volumes may be used, guided by the infant's condition, humidity settings, local protocols and biochemical results.

Iodine: Routine additional iodine supplementation is not recommended. Iodine supplementation may be considered for babies who are at risk of iodine deficiency and reliant on parenteral or low-iodine enteral nutrition.

Minimum glucose load to maintain metabolic homeostasis or prevent hypoglycaemia is 4 to 8 mg/Kg/minute.

Hyperglycaemia: Either insulin or glucose reduction may be used for managing hyperglycaemia. The choice should be guided by clinical judgement, local protocols and the availability of close monitoring, as the evidence does not favour one approach over the other.

Lipid in sepsis: The reduction of lipid emulsion during episodes of sepsis is not recommended. When a baby is at risk of hypertriglyceridaemia, e.g. has a lipaemic blood sample, triglycerides should be monitored.

Fish oil-only-based lipid should not be used for preventing liver disease but may be useful as rescue therapy in babies with established or evolving intestinal failure-associated liver disease.

When to stop: Parenteral nutrition should continue until an enteral feed volume of ≥ 120 mL/Kg/day has been reached. Ceasing parenteral nutrition at a lower volume of enteral feed (e.g. 60 to 100 mL/Kg/day) is not recommended.

Hang time (standard solutions): Aqueous phase – at least 48 hours and up to 96 hours. Lipid emulsion – up to 48 hours.

Initiate Parenteral Nutrition on Day 1 – Adjust for Tolerance and Clinical Condition

Component	Recommendation
Energy	• Give a starting range of 40 to 60 kcal/Kg/day • Gradually increase to a maintenance range of 75 to 120 kcal/Kg/day • If starting parenteral nutrition more than 4 days after birth give 75 to 120 kcal/Kg/day
Carbohydrate	• Give a starting range of 6 to 9 g/Kg/day (~4 to 6 mg/Kg/min) glucose • Gradually increase to a maintenance range of 9 to 16 g/Kg/day (6 to 11 mg/Kg/min) • If starting parenteral nutrition more than 4 days after birth give 9 to 16 g/Kg/day (6 to 11 mg/Kg/min)
Protein	• Give a starting range of 1.5 to 2 g/Kg/day amino acid • Increase to a maintenance range of 3 to 4 g/Kg/day • If starting parenteral nutrition more than 4 days after birth give 3 to 4 g/Kg/day
Protein: energy ratio	• Ensure protein: energy ratio is 23 to 34 kcal of total energy per g amino acid
Lipid	• Give a starting range of 1 to 2 g/Kg/day and gradually increase to 3 to 4 g/Kg/day • To prevent essential fatty acid deficiency a lipid emulsion dose providing a minimum linoleic acid intake of 0.25 g/Kg/day should be given (~1.5 g/Kg/day SMOFLipid) • Parenteral LC-PUFA supplementation is recommended where LC-PUFA-containing lipid emulsion products are available and cost-effective, e.g. SMOFLipid

Electrolytes, minerals, trace elements and vitamins: Provide parenteral electrolytes, minerals, trace elements and vitamins in accordance with ESPGHAN 2018 recommendations for preterm babies. As Aotearoa NZ soil is deficient in iodine, selenium and zinc, use the mid to upper half of the recommended intake.

Nutrient	Intake/Kg/day
Sodium	2 to 7 mmol (<1500 g); 2 to 5 mmol (>1500 g)
Potassium	2 to 3 mmol
Chloride	2 to 5 mmol
Calcium	1.6 to 3.5 mmol
Phosphorus	1.6 to 3.5 mmol
Magnesium	0.2 to 0.3 mmol
Iron	200 to 500 µg
Zinc	400 to 500 µg
Copper	40 µg
Iodine	1 to 10 µg
Selenium	7 µg
Manganese	≤ 1 µg
Molybdenum	1 µg

Vitamin	Intake/Kg/day
Vitamin A	227 to 455 µg (700–1500 IU)
Vitamin D	2 to 10 µg (80–400 IU)
Vitamin E	2.8 to 3.5 mg
Vitamin K	10 µg
Vitamin C	15 to 25 mg
Thiamin	350 to 500 µg
Riboflavin	150 to 200 µg
Pyridoxine	150 to 200 µg
Vitamin B12	0.3 µg
Niacin	4 to 6.8 mg
Folic acid	56 µg
Pantothenic acid	2500 µg

Biochemical Monitoring

Biochemical Monitoring – Parenteral Nutrition

Investigation	Neonatal Reference Range	Before Clinical & Metabolic Stabilisation		Once Clinically & Metabolically Stable		
		Every 1–2 Days	As required*	Every 1–2 Weeks	After 1 Month on Parenteral Nutrition, Then Monthly	As required*
Glucose	2.6–6.5 mmol/L	X		X		
Blood gases (capillary)	pH 7.35–7.45, PCO ₂ 4.7–6.0 kPa, HCO ₃ 22–26 mmol/L	X		X		
Sodium	134–148 mmol/L	X		X		
Potassium	4.5–6.0 mmol/L	X		X		
Chloride	90–114 mmol/L	X				X
Calcium	Total 1.8–2.1 mmol/L, Ionised 1.15–1.45 mmol/L	X			X	
Phosphorus	1.4–2.5 mmol/L (see footnote for frequency)	X			X	
Magnesium	0.7–1.0 mmol/L		X			X
Zinc	9–17 µmol/L		X			X
Total protein	45–75 g/L		X			X
Albumin	25–40 g/L		X			X
Urea	1.0–4.0 mmol/L		X			X
Creatinine	<95 µmol/L		X			X
Triglycerides	<3 mmol/L		X			X
Bilirubin (conjugated)	<20 µmol/L		X		X	
AST	<80 U/L		X		X	
ALT	<45 U/L		X		X	
GGT	<150 U/L		X		X	
ALP	80–600 U/L (up to 1000 U/L in growth phase)		X		X	
PTH	1.7–7.3 pmol/L		X		X	
Vitamin A	0.7–1.5 µmol/L (200–430 µg/L)		X		X	
Vitamin B12	170–800 pmol/L		X		X	
Vitamin D	50–150 nmol/L		X		X	
Vitamin E	11–46 µmol/L Auckland 5–50 µmol/L Waikato 23–70 µmol/L Christchurch		X		X	
INR	Lab-dependent norm		X		X	
Trace elements: Se, Zn, Cu	Lab-dependent norms					X
C-reactive protein	0–5 mg/L		X			X
Iron	10–31 µmol/L		X			X
Ferritin	15–400 µg/L		X			X
Urine electrolytes	Urinary Na >30 mmol/L adequate for growth					X

AST aspartate aminotransferase · ALT alanine aminotransferase · GGT gamma-glutamyl transferase · ALP alkaline phosphatase · INR international normalised ratio (an elevated INR may indicate vitamin K deficiency) · PTH parathyroid hormone. Neonatal reference ranges are those of the reporting laboratories. *No routine monitoring is recommended. Individualised monitoring may be needed based on the clinical situation.

Monitoring for refeeding syndrome: For babies with a birthweight <1500 g or <10th centile, monitor serum phosphate and calcium on days 3, 5 and 7 and then on alternate days until commenced on fortified breastmilk or preterm formula.

Urea: Limiting amino acid intake based on serum urea alone is not warranted. Urea levels up to 14 mmol/L may be considered acceptable in babies on parenteral nutrition provided there are no other parameters to suggest protein intolerance (e.g. hyperammonaemia >122 µmol/L).

Triglycerides: The routine monitoring of plasma triglyceride concentrations is not recommended.

Biochemical Monitoring – Enteral Nutrition

Zinc: Consider measuring serum zinc in babies with faltering growth and low serum alkaline phosphatase, especially if they have excessive gastrointestinal fluid losses.

Urea: Plasma urea concentration can be used to indicate whether standard breastmilk fortification is sufficient to support appropriate growth. More protein may be needed if a baby has faltering growth and their serum urea is <2.0 mmol/L.

Urinary sodium: Consider measuring urinary sodium in infants with faltering growth and normal serum sodium.

Bone mineral status: Phosphorus, calcium, ALP and parathyroid hormone status should be monitored regularly – as above.

Vitamin D: Serum Vitamin D (25-hydroxyvitamin D) should be measured at one month of age in babies born before 32 weeks' gestation or birthweight <1500 g. If low, adjust dose and monitor every 10–14 days until well inside the reference range.

Enteral Nutrition

Initiate enteral feeding within 24 hours of birth. Use mother's own milk where possible, followed by donor human milk and then preterm formula if no human milk is available. Use the gastric route and intermittent bolus feeding. Start with 10–20 mL/kg/day and increase by at least 24 mL/kg/day depending on tolerance.

Moderate-to-late preterm: In moderate-to-late preterm babies wait as long as is clinically feasible for mother's own milk. This may be at least 3 days from birth. Give 10% IV glucose while waiting for mother's own milk. Donor milk or infant formula is not recommended unless there is a specific clinical indication.

Donor breastmilk (unpasteurised from a screened donor, or pasteurised) is preferred over infant formula for all preterm babies with insufficient mother's own expressed breastmilk. Very low birthweight and extremely preterm babies benefit most.

Smell and taste of breastmilk or infant formula should be provided before all enteral tube feeds.

Fortify expressed breastmilk for babies who are born at <32 weeks or <2000 g birthweight.

Fortification of breastmilk at full strength should begin at around 75–100 mL/Kg/day of enteral feeds, or once a feed volume of at least 5 mL is reached, rather than at lower volumes.

Preterm formula rather than term formula should be used for babies born at <32 weeks or birthweight <2000 g when breastmilk is not available or is insufficient.

Full enteral feeds of 180 mL/Kg/day should be used for extremely low birthweight babies (birthweight <1000 g). Higher enteral volume may be needed if growth is faltering. For other babies, give the fluid intake that is needed for appropriate growth (more details below).

Continue fortifier / preterm formula until preparing for discharge or until weight gain is excessive. Stopping breastmilk fortifier or preterm formula at a specific weight or gestational age is not recommended.

Continuous feeds should not be used routinely.

Standardised fortification should be used over routine individualised fortification of expressed breastmilk. Human milk-based fortifier is not recommended to fortify expressed breastmilk.

Osmolality: Enteral feeds should be selected based on factors other than osmolality. However, if the osmolality is very high (>600 mOsm/Kg), consider practical steps to lower it, such as divided medication doses.

Zinc: Routine enteral zinc supplementation (5 to 10 mg/day) should be used for all preterm babies while in neonatal care.

Vitamin D: Routine enteral vitamin D supplementation is recommended. The suggested dose is 2 drops (800 IU) cholecalciferol per day for all preterm babies, reducing to 1 drop (400 IU) cholecalciferol at discharge or 40 weeks gestational age. Routine supplementation of other vitamins is not supported by the evidence.

Enteral nutrient intakes (ESPGHAN 2022): Provide enteral nutrient intakes for preterm babies according to ESPGHAN 2022 guidance. Use individualised plans considering gestational age, tolerance and clinical status. Monitor growth (more details below) and biochemical markers routinely. As Aotearoa NZ soil is deficient in iodine, selenium and zinc, use the mid to upper half of the recommended intake.

Enteral Nutrient	Recommended Intake/Kg/day
Energy	115 to 140–160 kcal
Protein	3.5 to 4.0–4.5 g
Carbohydrates	11 to 15–17 g
Lipids	4.8 to 8.1 g
Sodium	3.0 to 5.0–8.0 mmol
Chloride	3.0 to 5.0–8.0 mmol
Potassium	2.3 to 4.6 mmol
Calcium	3.0 to 5.0 mmol
Phosphorus	2.2 to 3.7 mmol
Magnesium	0.4 to 0.5 mmol
Iron	2.0 to 3.0–6.0 mg
Copper	120 to 230 µg
Selenium	7 to 10 µg
Manganese	1 to 15 µg
Iodine	11 to 55 µg
Zinc	2 to 3 mg

Enteral Nutrient	Recommended Intake/Kg/day
Chromium	0.03 to 2.25 µg
Molybdenum	0.3 to 5.0 µg
Thiamine (B1)	140 to 290 µg
Pantothenic acid	0.6 to 2.2 mg
Biotin	3.5 to 15 µg
Niacin	1100 to 5700 µg
Vitamin C	17 to 43 mg
Riboflavin (B2)	200 to 430 µg
Pyridoxine	70 to 290 µg
Folic acid	23 to 100 µg
Cobalamin (B12)	0.1 to 0.6 µg
Vitamin A	400 to 1000 µg (1332 to 3330 IU)
Vitamin D	10 to 25 µg (400 to 1000 IU)
Vitamin E	2.2 to 11 mg
Vitamin K	4.4 to 28 µg

Not Recommended

- Routine measurement of gastric aspiration volumes before enteral feeds to monitor feed tolerance.
- Withholding feeds for transfusion, extubation or eye screening examinations – continue providing feeds unless there is a clinical indication to do otherwise.
- Routine enteral protein supplementation (in addition to breastmilk fortification). Aim for the ESPGHAN recommended enteral protein intake of 3.5 to 4.0 g/Kg/day, which may be increased to 4.5 g/Kg/day where growth is too slow.
- Routine enteral supplementation of breastmilk with glucose polymer powder.
- Routine enteral fat supplementation. Enteral fat supplementation may be beneficial when there is a high energy requirement and faltering growth, but should not be used where there is insufficient feed volume and an inadequate intake of other nutrients, such as protein, vitamins and minerals.

Introduction

Every year approximately 4,600 infants are born preterm in Aotearoa New Zealand [1]. Preterm birth brings a higher risk of death, neonatal illnesses, 20–50% higher risk of neurodisability and increased healthcare costs [2]. Variation in feeding preterm infants across our neonatal intensive care units is associated with differences in survival, morbidity [3], growth [4] and neurodisability. For example, pēpi Māori are more likely to receive infant formula earlier and are less likely to be breastfed at discharge [5] than infants of other ethnicities. This variability and subsequent systematic inequity in health outcomes for whānau Māori means there is a need to optimise neonatal nutrition care based on the best available evidence and to ensure this care is implemented equitably.

We have produced this guideline because currently available international guidelines are inconsistent, incomplete and lack relevance for our population. The overall objective of the guideline is to provide evidence-based, consensus guidance that standardises optimal nutritional care for preterm infants across Aotearoa New Zealand to improve health, growth and long-term outcomes while reducing unwarranted variation and inequities in practice and outcomes.

Cultural responsiveness for pēpi and whānau Māori

“In Māoridom, you stay close to your baby and the parents being there is helping his wairua and it's helping our wairua too, so that's another thing that we've noticed, being here is helping him.”

Whānau Māori want the very best health outcomes for their pēpi, want to be there for pēpi, advocate for pēpi and desire a good experience of the healthcare system. Healthcare professionals play an important role in contributing to achieving these goals and supporting whānau, where their actions can have a direct impact on health equity.

Foundations to guide care with preterm pēpi and whānau Māori

Te Hā o Whānau (whānau voices leading maternity care in Aotearoa New Zealand) is a culturally responsive healthcare framework developed specifically for the maternal-infant healthcare system in Aotearoa, providing practice points and guidelines aligned with three tikanga Māori: manaakitanga (hospitality and care), rangatiratanga (self-determination), and whakawhanaunga (building relationships) [6]. This framework offers a practical approach to making neonatal and maternity services more accessible and culturally safe for whānau Māori, with the broader aim and impact of achieving health equity.

He Tamariki Kokoti Tau (Babies Born Prematurely) research identified that preterm birth was experienced as an emotional roller coaster that disrupted whānau birth plans and placed them in healthcare environments that were often not culturally safe [7]. Whānau expressed the fundamental desire to be close to their pēpi, to hold, love, nurture them, and to connect them within whakapapa networks through cultural practices such as naming, karakia (blessings), and whenua ki te whenua (returning placenta to the earth). When healthcare practitioners or hospital policies create barriers to this intimacy by isolating, excluding, or discriminating, whānau Māori experienced frustration and trauma [7]. Healthcare professionals who provided empathetic, culturally safe care, involved whānau Māori as knowledge holders, and respected tikanga Māori. The healthcare professionals became like whānau to whānau Māori and were identified as champions [7].

As citizens of Aotearoa, it is everyone's responsibility to uphold He Whakaputanga o te Rangatiratanga o Nu Tirenī (The Declaration of Independence of New Zealand, 1835) and Te Tiriti o Waitangi (The Treaty of Waitangi, 1840), as they are foundational documents. Since the signing of Te Tiriti in 1840, there have been ongoing breaches of this agreement, by the Crown, resulting in Pākehā privileges, including health privileges, and health inequities for Māori. To contribute to increasing equity, Manatū Hauora (Ministry of Health) has set goals of mana whakahaere (stewardship), mana motuhake (self-determination), mana tangata (equity across life course), and mana Māori (rights), by applying principles of tino rangatiratanga (leadership), equity, active protection, options, and partnership.

Alongside this, Māori health data sovereignty and governance is essential for upholding Māori rights and mana motuhake self-determination, enabling iwi/hapū/whānau to control the collection, use, and protection of their data for their health benefit [8].

Whānau Māori lived experience

“... three times I had spoken (to lactation consultant) and they would give me tips and pointers ... that was very helpful. They were very helpful.”

Whānau Māori who have shared their lived experience of hauora (health), provide the whānau led solutions to healthcare. Additionally, healthcare professionals need to understand and reflect on their own biases and stereotype 'shortcuts' which directly influence clinical practice and health outcomes [9]. Critical self-reflection is an important step for healthcare professionals to take to help break down these biases and stereotypes, and therefore enable inclusive clinical practice [10]. Also, recognition and consideration of the power imbalance during communication with whānau Māori is important as not all whānau feel empowered to ask questions [11].

"I wouldn't ask many questions ... Oh, I don't know. I don't like asking questions."

Healthcare professionals may recognise that some whānau Māori find asking questions difficult, and the first step in supporting them is via connection and communication with whānau Māori. Acknowledging previous experiences that may be less positive and the resulting impact on whānau Māori to continue to engage with the health system, provides an opportunity for health professionals to reflect and navigate discussions and support for whānau Māori.

Workforce development

"Yeah, it's cool having a Māori (midwife). I've never had one. Yeah, it's rare, eh?"

Having Māori health professionals within the health system provides opportunities to support whānau Māori. For example, kaimahi (staff) Māori within the health system can support whānau Māori, ask questions and support access to health services using a relational approach and understanding. This includes a workforce in all aspects of healthcare and within the system embedding in opportunities to support, value and develop this workforce.

Quotes are from participants in our qualitative study.

Application of the Guideline

Purpose

A clinical guideline recommends courses of action judged most likely to maximise desirable health outcomes for a defined population and setting, based on evidence evaluated through a structured and transparent process [12].

Incorporating clinical guidelines into practice is associated with improved patient outcomes [13].

This guideline provides an evidence-based summary of best practice for nutritional care of preterm infants in Aotearoa New Zealand neonatal services. Its purpose is to standardise nutritional management across care settings to improve outcomes for infants and their families. The guideline offers nationally consistent recommendations to optimise nutritional care and positively influence short- and long-term health outcomes, including nutrition-related morbidity, growth and neurodevelopment, while reducing unwarranted variation and inequities in care.

Our specific aims were to:

- Give effect to Te Tiriti o Waitangi, including the interests and needs of tangata whenua.
- Improve consistency, standardisation, cost effectiveness and evidence-based nutritional practice.
- Promote equity for preterm infants and their whānau.
- Support the transition to exclusive breastmilk feeding.
- Promote nutritional practice that supports the health and wellbeing for infants and their whānau.
- Support open and effective communication between health practitioners and the infants' whānau.

The guideline covers recommendations for parenteral (intravenous) nutrition, enteral nutrition, breastmilk and breastfeeding, monitoring nutrition and growth, and parent and whānau education.

Scope

The target population for this guideline is all preterm infants while in neonatal care in Aotearoa New Zealand from birth to discharge from neonatal care. Preterm birth is defined as infants born alive before 37 weeks of pregnancy are completed. Sub-categories of preterm birth, may be based on gestational age [14]:

- Extremely preterm (less than 28 completed weeks of gestation).
- Very preterm (28 to less than 32 completed weeks of gestation).
- Moderate-to-late preterm (32 to 37 completed weeks of gestation) [14].

or on birthweight

- Extremely low birthweight (<1,000 g).
- Very low birthweight (<1,500 g).
- Low birthweight (<2,500 g).

The guideline does not cover infants with specific clinical (e.g. congenital chylothorax) or inherited metabolic (e.g. phenylketonuria) conditions that require very specific specialised nutritional management.

Target audience

The guideline is intended for use by all neonatal healthcare workers, defined here as any professional person working in a neonatal healthcare system (including voluntary workers). The guideline will be of particular interest to neonatologists, nurses, neonatal dietitians, paediatric dietitians working in neonatal care, lactation consultants, pharmacists, parents and families. It may also be used by healthcare policy makers.

Terminology

We acknowledge and respect gender diversity within the birthing population of Aotearoa New Zealand, including trans and non-binary people. In this guideline, we use the terms 'mother' and 'women' due to their prevalence in the literature reviewed to ensure clarity about the specific individuals to whom the health practitioner is providing clinical care, and to ensure clarity about the biological benefits of breastfeeding and skin to skin contact between a mother and infant. Using alternative terms may introduce confusion about the meaning of the findings and conclusions being communicated.

The terms “infant, pēpi or baby” rather than “neonate” are used as this term is more parent-centred, which is an intended audience for the guideline. Culturally safe practice includes health practitioners respecting and engaging with each individual receiving care and adapting their use of language accordingly in practice.

Appendix B provides definitions of Māori and Pacific peoples words used in the guideline.

Appendix C provides a glossary of clinical and technical terms.

Appendix D provides a list of abbreviations and their meanings.

We acknowledge that language and terminology is evolving, therefore influencing the need to update future editions of the guideline.

Methods and Development of the Guideline

Framework

The guideline was developed by a Guideline Development Group (GDG) and Steering Group and informed by the National Health and Medical Research Council Standards for Guidelines and the National Institute for Health and Care Excellence (NICE) Appendix A. Aotearoa New Zealand is a bicultural nation under Te Tiriti o Waitangi; therefore, the expertise and views of Māori health practitioners and people with lived experience of preterm birth have played a central role in the guideline development.

Inclusion of diverse ethnic perspectives

In addition to people of European and Māori ethnicities, people of Pacific and Asian ethnicity form the largest ethnic groups in Aotearoa. We sought their views through qualitative research at Auckland City and Middlemore Hospitals.

Contributors to the Guideline

Steering Group

Steering Group member selection was a carefully considered process to ensure the group had necessary expertise and diversity of perspectives to develop a high-quality, evidence-based guide that would adhere to international standards. All Steering Group members were also appointed to the Guideline Development Group Appendix A.

Steering Group Terms of Reference

The Steering Group developed and approved terms of reference at the project initiation to ensure the principles of Te Tiriti o Waitangi and other key obligations were applied at all stages. The terms of reference were to:

- Provide advice, expertise, and direction on the development of the Aotearoa Nutrition Guideline for Preterm Babies.
- Ensure that the Steering Group and the Guideline Development Group uphold the five principles in Te Tiriti o Waitangi and both groups work towards achieving health equity for Māori (Tino rangatiratanga, Equity, Active protection, Options and Partnership).
- Ensure the guideline is developed in accordance with best practice in guideline methodology, including the AGREE II standard.
- Identify and invite members to join the Guideline Development Group.
- Provide administrative support for the Guideline Development Group, including preparation of papers and organisation of meetings.
- Oversee all aspects of development of the guideline, including review of the evidence, drafting the guideline including recommendations, consultation with stakeholders, publication, dissemination, implementation and evaluation.
- Consult widely to develop an evidence-based guideline that will function as a useful resource for health professionals and will be of interest and relevance to the whānau of preterm babies in all Aotearoa healthcare contexts.
- Ensure that the Guideline recommendations will help meet the health needs for Māori.
- Produce a plan for the dissemination, implementation and ongoing monitoring of clinical uptake of the guideline recommendations.

The Steering Group met on a two to four-monthly basis or as required.

Guideline Development Group

Invitations to join the GDG were sent by the Steering Group to a diverse group of organisations, experts, including clinicians, researchers and lived experience of preterm birth groups. Additional considerations when selecting GDG members included geographic representation, cultural diversity, different stakeholder group representation, balance of clinical and research expertise, and experience in research and guideline development Appendix A.

The voices of people with lived experience of preterm birth were incorporated through direct participation in the Guideline Development Group, which included three representatives: a mother of a preterm baby, an adult who was born preterm, and a person nominated by The Little Miracles Trust, a consumer support organisation for parents of preterm infants. This approach enabled patient and family perspectives to be embedded throughout the guideline development process rather than consulted separately. These members contributed their views through active involvement in meetings, discussion of key topics, review of draft recommendations and shared decision-making. Insights gathered included priorities around clear communication, emotional and practical support for families, the importance of breastmilk provision and the need for consistent, family-centred care across services. This information directly informed the scope of the guideline, the framing of recommendations and the emphasis on supporting parents, promoting equity and improving the consistency of nutritional care for preterm infants, ensuring the guideline reflects both clinical evidence and lived experience.

The Clinical Director from each of the six Aotearoa New Zealand Level 3 neonatal units was asked for their support for the project and to nominate a neonatologist from their team who would participate. The New Zealand College of Midwives were asked to nominate midwives. Three neonatal lactation consultants were invited to join and two were appointed. After consultation with the Māori Steering Group members, the Liggins Institute Kaiārahi, Haunui Royal joined.

GDG members were also selected for their diversity of perspectives to ensure the guideline reflects the views of a wide range of stakeholders and it is relevant to the needs of the population it is intended to serve.

Guideline Development Group Terms of Reference

The GDG Members (Appendix A) participated in the development, review and revision of the Pēpi Whānau Wawe Nutrition Guideline. The role of the GDG Members included:

- Upholding the principles of Te Tiriti o Waitangi and addressing health equity.
- Providing advice, expertise and direction in relation to the Guideline.
- Confirming key clinical questions and outcomes.
- Reviewing evidence and formulating recommendations.
- Signing off recommendations and disseminating for consultation among the related organisations.
- Disseminating the finalised Guideline to ensure clinical uptake of the Guideline.

The GDG met approximately three-monthly, as well as an in-person meeting on the 18 August 2023 to agree key outcomes, scope, topics and working groups for the guideline questions.

Declaration of interests

All GDG members were asked to declare all relevant interests using forms which included specific questions under the headings of financial, organisational and intellectual interests. The time period of disclosure was the last five years. The Conflict of Interest Policy and Register can be found in Appendix E.

Research evidence synthesis team

This team was comprised of GDG members, Liggins interns and medical students Chloe Bell and Sarah Latus and neonatologists Professor Nick Embleton and Dr Chris van den Akker. Dr Meiliana Meiliana conducted a systematic review of existing guidelines that might be suitable for adopting or adapting (adoption). Dr Adrienne Lynn and Lilia Delgado Paramo and Dr Anja Bronnert searched for literature relevant to each of the guideline questions and identified suitable existing systematic reviews and other high-quality evidence. They also identified the questions that would require new systematic reviews. Dr Julie Brown, a systematic review specialist, and Solene Bertrand were contracted to undertake systematic reviews and EtD development for which the GDG had insufficient capacity due to high clinical workloads.

Methodology expertise

We collaborated with Associate Professor Vanessa Jordan from the University of Auckland Medical School who provided the GDG with guideline methodology expertise. Vanessa attended the 2-day meeting to assist with application of the guideline development process to ensure we met GRADE standards and to assist with contentious issues and clarifications in EtD evidence. Training sessions by Vanessa Jordan for GDG members took place between July and November 2024 and covered Evidence review, Risk of Bias and the use of GRADEpro.

Dr Julie Brown provided Covidence software training for the GDG members. Dr Luling Lin from the Liggins Institute also provided systematic review expertise for the GDG members who did systematic reviews and developed Evidence-to-Decision documents.

Stages in Development of Recommendations

Identifying priority questions and outcomes

GDG members identified the key clinical outcomes for the overall guideline which were rated as a) critical for making a decision, b) important but not critical, or c) of limited importance Appendix F. Consensus was reached on the minimum effect size that would support recommending using or not using a particular intervention for each outcome. The standard way of presenting an effect size is in numbers of infants who would benefit or be harmed per thousand infants receiving the intervention, also known as the absolute risk difference. Draft thresholds for each outcome were provided to GDG members.

The GDG drafted 100 key clinical questions covering 5 topics. The number of questions was then reduced to 60 via an online survey to reach consensus on the most important questions that should be prioritised for each topic.

Where necessary, the categorisation of the key clinical outcomes (critical for making a decision vs. important but not critical etc.) was modified by the principal investigator or systematic reviewers to be appropriate for each of the 60 questions. Specific additional outcomes were added for a small number of the questions. The 60 questions and the associated key clinical outcome ratings and thresholds were finalised at a virtual GDG meeting in July 2024, Appendix F.

Evidence Search and Synthesis

Systematic reviews

Systematic methods were used to identify and appraise the evidence underpinning the guideline, including structured searches of relevant electronic databases and review of key international guidelines and reference lists. Clear inclusion and exclusion criteria were applied to select evidence based on relevance to preterm infant nutrition, study design, population and clinical applicability.

Systematic searches for the questions were undertaken by Dr Peter Bloomfield, Lilia Delgado Paramo, Chloe Bell with assistance from Dawn Carlile from the Philson Library, University of Auckland. The searches were conducted from August 2024 to November 2024 and addressed the key clinical questions, each of which was framed as one or more questions and where possible in (Population, Intervention, Comparison, Outcome) PICO format by the Steering Group, ([Link to Questions document](#)). No date restriction was set for the literature searches (except for Question 11 which was limited to studies in the past 25 years due to changes in the parenteral nutrition solutions available). Databases searched included Cochrane Central Register of Controlled Trials (CENTRAL), Embase (Excerpta Medica Database), Medical Literature Analysis and Retrieval System Online (MEDLINE) (via Ovid), Cumulative Index to Nursing and Allied Health Literature (CINAHL) (via EBSCO), ClinicalTrials.gov, The WHO International Clinical Trials Registry Platform (ICTRP), and The Australian and New Zealand Clinical Trials Registry. The search protocol and search strategies can be found at ([Link to Search Protocol](#)) and the published systematic reviews Appendix G.

When up-to-date systematic reviews could address a question, data was extracted from the review. Where possible, the most recent data was added to those included in a systematic review and findings re-analysed. Where no relevant systematic review was identified but suitable data was available, a new systematic review was undertaken. Covidence software was used to screen articles. When the question or the evidence was not in an appropriate format for a systematic review, this was summarised in narrative form with summary tables.

Evidence to decision frameworks

GRADEpro is an online tool used to prepare Evidence to Decision documents (EtDs) and develop clinical recommendations. EtDs were prepared for each question by the team via this tool. EtDs provided a framework for summarising the evidence, organised by topics including desirable effects, undesirable effects, certainty of the evidence of effects, values, balance of effects, resources required, certainty of required resources, cost effectiveness of required resources, equity, acceptability, and feasibility sections.

When reviewing the evidence for each EtD, consideration was given to the evidence (or lack thereof) for Māori and non-Māori babies and their whānau. Consideration was also given to the evidence (or lack thereof) for extremely preterm or extremely low birthweight (birthweight <1,000 g), very low birthweight (<1,500 g), low birthweight (<2,500 g) and moderate-to late-preterm subgroups. A summary of equity issues was included in every EtD equity section and two additional subsections: considerations for Māori, considerations for Pacific peoples and their families and underrepresented groups.

Review of evidence

Forty-seven EtDs were prepared using GRADEpro Appendix H. For each of the questions, the strengths and limitations of the body of evidence were assessed, with consideration given to study quality, consistency of findings and applicability to the Aotearoa New Zealand context.

Voting methods used to formulate the recommendations

The methods used to formulate the recommendations were predefined, transparent, and consistent with AGREE II standards. Following completion of the systematic reviews and development of the Evidence to Decision frameworks, all GDG members undertook training in the use of Grading of Recommendations Assessment, Development and Evaluation methodology. GDG members were then asked to independently review each Evidence to Decision framework and record their judgements within the GRADEpro platform across all domains, including the balance of benefits and harms, certainty of the evidence, values and preferences, resource use, equity, acceptability, and feasibility. This initial round of voting enabled assessment of the degree of agreement within the GDG prior to face-to-face deliberation.

A two-day face-to-face GDG meeting (10–11 April 2025, Auckland) was convened to review each EtD in detail. For every question, the evidence summary and EtD were presented, followed by structured discussion and anonymous voting online via the GRADEpro platform or Zoom voting tool. Consensus was defined a priori. Where a clear consensus was reached, this informed the final judgement for each Evidence to Decision domain and the direction of the recommendation. Where consensus was not achieved, further discussion was undertaken to explore areas of disagreement, including consideration of differences in interpretation of the evidence, clinical experience and contextual factors. A second round of voting was conducted where required. If consensus could not be reached after further deliberation, a majority vote was used to determine the final judgement.

Following the face-to-face meeting, seven additional virtual GDG meetings were conducted using the same structured processes and anonymous voting via the Zoom voting tool to complete the remaining EtDs. Finalisation of clinical recommendations and approval of the guideline were undertaken via iterative electronic review and email consensus, ensuring full GDG agreement prior to dissemination. All judgements, including areas of agreement and disagreement, were documented within the Evidence to Decision frameworks, alongside the rationale for decisions and relevant implementation considerations. This ensured a clear and transparent link between the evidence and the final recommendations.

Adolopment (Adopt or adapt existing guidelines)

For the remaining 13 questions, we used the structured adolopment approach described by the WHO to integrate existing high-quality guidance while ensuring relevance to the New Zealand context [15]. A systematic search identified international neonatal nutrition guidelines that met pre-specified quality criteria. Eligible guidelines were appraised using AGREE II and only those assessed as high quality (scored $\geq 60\%$ in at least three of six domains, including domain 3 (rigour of development) were considered for adoption or adaptation [16].

An Adolopment EtD template was created, and existing recommendations were considered for each of the 13 questions using the template to consider explicitly the benefits and harms, certainty of evidence, values and preferences, resource use, feasibility and equity. Where search strategies were available, the original searches were updated on 6 August 2025, screened using Covidence and any appropriate new evidence added to the Adolopment EtDs.

A draft Adolopment EtD document drafted by the principal investigator was then circulated to the GDG for review and feedback which was then incorporated into the recommendations. Recommendations were adopted unchanged where they were directly applicable and supported by up-to-date evidence. Where contextual differences existed, including models of care, available products, equity implications or cultural considerations the recommendations were adapted to fit the Aotearoa New Zealand context. Consensus on adoption or adaptation was reached through online review and email discussion to ensuring transparency consistency and alignment with local practice Appendix I.

Wording of recommendations

Recommendations are worded according to the GRADE handbook as follows:

Strong recommendation: The GDG is very confident that the desirable consequences of the proposed course of action clearly outweigh the undesirable consequences or vice versa.

Conditional recommendation. There is:

- a close balance between benefits and downsides (including adverse effects and burden of treatment), or.
- uncertainty regarding magnitude of benefits and downsides, or.
- uncertainty or important variability in the value consumers place on the treatment outcomes, or.
- the cost or burden of the proposed intervention may not be justified.

Conditional recommendation for either option. The GDG feels strongly that:

- the pros and cons of the intervention and the comparison are very closely balanced, or
- there is so much uncertainty that a recommendation for or against the intervention would be speculative.

Wording of conditional recommendations

Conditional recommendations are usually worded as “suggest” or “consider” or similar, rather than “should” or “recommend”. However, in consultation with the methodologist, the GDG considered the stronger wording was appropriate for some conditional recommendations in situations where:

- The recommendation is aligned with established national guideline or guidance, or.
- The recommendation is grounded in widely accepted principles, norms and standards of practice, or variability in practice would be undesirable, particularly in areas where specific thresholds, targets or screening criteria are outlined. Although some uncertainty may exist regarding the precise details of the recommendation, it is clear that adherence is crucial for effective and consistent clinical practice, or.
- While the overarching recommendation could have been framed as 'strong,' a conditional recommendation was chosen to provide greater specificity and practicality.

Drafting of recommendations

Draft recommendations based on the GDG decisions addressing each of the key clinical questions were prepared by the principal investigator. The draft recommendations and the guideline were then circulated again for final feedback and sign-off by the Steering Group and GDG. An online survey was conducted to create a list of the research gaps that the GDG members recommend should be prioritised, Appendix J.

Independent review process

An independent external review process was undertaken to ensure the methodological rigour, transparency and credibility of the guideline.

A formal methodological review of the guideline development process and supporting evidence was conducted by Associate Professor Vanessa Jordan (methodologist). This review focused on the appropriateness and application of systematic review methods, risk of bias assessment, use of Grading of Recommendations Assessment, Development and Evaluation methodology, and the structure and completeness of the Evidence to Decision frameworks. Feedback from this review led to refinement of the Evidence to Decision documents.

An independent appraisal of the guideline using the Appraisal of Guidelines for Research and Evaluation II (AGREEII) tool was undertaken by Dr Meiliana Meiliana.

This appraisal assessed the guideline across all domains, including scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability, and editorial independence. In response to this review, the description of the Guideline Development Group consensus and voting processes was expanded to improve transparency and reproducibility.

Following these revisions, the guideline was reviewed by two external clinical experts to ensure clinical relevance, feasibility and alignment with international practice. Their feedback informed final refinements to the recommendations and supporting text prior to approval.

Stakeholder consultation

The draft guideline was circulated to stakeholders for feedback. All feedback was collated, and a summary document prepared that included all responses (Appendix K). The draft was revised in response to feedback, and final recommendations were circulated to the GDG for final approval via email and a zoom meeting.

Dissemination and Implementation

Pre-Implementation needs assessment

A pre-implementation needs assessment will be conducted to identify gaps between current practice and Guideline recommendations. The audit will be repeated post-implementation to monitor change in practice.

Dissemination

Resources will be prepared for dissemination of the Pēpi Whānau Wawe Nutrition Guideline to hospitals and clinicians to raise awareness and provide key information. These resources include the complete version of the guideline and recommendations, a nutshell summary of the guidelines for practice. All resources will be available online and for downloading.

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Clinical Questions Prioritised by the Guideline Development Group

Topic 1 – Parenteral Nutrition	Method	EtD Number
1. In moderate-to-late preterm infants, while we wait for mothers' breastmilk what method of nutrition (IV nutrition vs. 10% glucose vs. infant formula vs. donor milk), is best?	Existing high-quality evidence	Recommendation 1 EtD1
2. Which infants (by birthweight or gestational age) should receive intravenous (IV) nutrition?	Adolopment	Recommendation 2 AA2
3. How many hours should pass before starting IV nutrition in extremely preterm infants? When mothers' breastmilk is not available at birth for very preterm infants: how many days should pass without sufficient enteral nutrition before starting IV nutrition?	Existing high-quality evidence and Adolopment	Recommendation 3 EtD1 AA3
4. What is the recommended IV fluid intake by postnatal age (e.g. for reducing bronchopulmonary dysplasia, patent ductus arteriosus and necrotising enterocolitis)?	New systematic review	Recommendation 4 EtD4
5. What is the recommended IV iodine intake by postnatal age?	Existing high-quality evidence and Adolopment	Recommendation 5 EtD5 AA17
6. In preterm infants what is the minimum glucose load (mg/kg/min) administered via IV infusion needed for maintenance of metabolic homeostasis or prevention of hypoglycaemia?	Adolopment	Recommendation 6 AA6
7. Is there evidence that reduced glucose load or insulin is better for the management of hyperglycaemia for clinical outcomes in preterm babies?	New systematic review	Recommendation 7 EtD7
8. Are there any indications (e.g. high triglycerides, sepsis) to wean, reduce or restrict lipid administration?	Adolopment	Recommendation 8 AA8
9. Are there benefits for using fish oil only based lipids (for prevention or rescue therapy for preterm infants with (any cause) liver disease? If so, what is the criteria?	Existing high-quality evidence	Recommendation 9 EtD9
10. Is there evidence for addition of specific fatty acids in lipid emulsions?	Adolopment	Recommendation 10 AA10
11. What is the recommended hang time for aqueous IV nutrition and lipid solutions?	New systematic review	Recommendation 11 EtD11
12. What is the enteral nutrition criterion (volume) to stop IV nutrition?	New systematic review	Recommendation 12 EtD12
13. What is the recommended parenteral energy and macronutrient intake by postnatal age?	Adolopment	Recommendation 13 AA13
14. Should higher parenteral protein (>4 g/kg/day) vs. lower parenteral protein be used for preterm infants and what is the recommended protein intake by postnatal age?	Existing high-quality evidence and Adolopment	Recommendation 14 EtD14 AA13

15. What is the recommended IV vitamin intake by postnatal age? Fat-soluble vitamins (vitamin A, E, D, K), Water soluble vitamins (B vitamins, vitamin C, choline)	New systematic review Adolopment	Recommendation 15 EtD15 AA16
16. What is the recommended IV intake of sodium, potassium, chloride and acetate, calcium, phosphorus and magnesium, iron, zinc, selenium, chromium, copper, manganese, molybdenum, fluoride, and vitamins?	Adolopment	Recommendation 16 AA16
Topic 2 – Enteral Nutrition	Method	EtD Number
17. When to start enteral feeding after birth, recommended type (breastmilk, formula etc.), route, method, starting feed volume and frequency of enteral feeding	Adolopment	Recommendation 17 AA17
18. In preterm infants for whom there is insufficient mother's own breastmilk, does waiting X days before starting a breastmilk substitute improve outcomes (NEC, neurodevelopment, time to full enteral feeds, time to discharge, breastmilk feeding at discharge, excessive weight loss)?	Existing high-quality evidence	Recommendation 18 EtD18
19. In moderate-to-late preterm infants whose mothers' breastmilk is not available at birth, for how long should we wait for mother's own breastmilk?	Existing high-quality evidence	Recommendation 19 EtD18
20. In preterm infants for whom there is insufficient mother's own breastmilk, does donor breastmilk vs. infant formula improve outcomes (NEC, neurodevelopment, time to full enteral feeds, time to discharge, breastmilk feeding at discharge, growth)?	Existing high-quality evidence	Recommendation 20 EtD20
21. In preterm infants who require enteral feeding, does faster feed advancement compared with slower advancement of feeds reduce the incidence of gastrointestinal complications (e.g. feed intolerance, necrotising enterocolitis) or decrease the number of days to full enteral feeds or discharge from neonatal care?	Existing high-quality evidence	Recommendation 21 EtD21
22. In preterm infants who require enteral feeding, does routine gastric aspiration before feeds compared with the absence of regular gastric aspiration reduce the early identification or incidence of necrotising enterocolitis or increase days to full enteral feeds or discharge from neonatal care?	Existing high-quality evidence	Recommendation 22 EtD22
23. In preterm infants who require enteral feeding, do continuous feeds compared with bolus feeds reduce the incidence of necrotising enterocolitis or decrease the number of days to full enteral feeds or discharge from neonatal care? In preterm infants who require enteral feeding, do "compressed" (bolus feed given over a longer time) feeds compared with continuous or bolus feeds reduce the incidence of respiratory issues, spills, necrotising enterocolitis or decrease the number of days to full enteral feeds or discharge from neonatal care?	New systematic review	Recommendation 23 EtD23
24. In preterm babies does fortified EBM vs. unfortified EBM lead to improved growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?	Existing high-quality evidence	Recommendation 24 EtD24
25. In preterm babies does commencing less than full strength fortified EBM compared with full fortified enteral feeds lead to shorter time to full enteral feeds improve growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?	New systematic review	Recommendation 25 EtD25
26. In preterm babies does individualised fortification of EBM compared with standard fortified enteral feeds using commercially available fortifiers lead to shorter time to full enteral feeds improve growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?	New systematic review	Recommendation 26 EtD26
27. In preterm babies does fortified EBM commenced before full enteral feeds are reached vs. once full enteral feeds are reached lead to shorter time to full enteral feeds improve growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?	Existing high-quality evidence	Recommendation 27 EtD27

28. In preterm babies does human based fortifier vs. bovine-based fortifier lead to shorter time to full enteral feeds improve growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?	New systematic review	Recommendation 28 EtD28
29. In preterm babies does a preterm formula compared with a term formula lead to improved growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?	Existing high-quality evidence	Recommendation 29 EtD29
30. Pasteurised donor milk vs. unpasteurised donor milk: In preterm infants for whom there is insufficient mother's own breastmilk, does screened pasteurised donor milk vs. screened unpasteurised donor milk improve outcomes (infection, NEC, neurodevelopment, time to full enteral feeds, time to discharge, breastmilk feeding at discharge, growth)?	New systematic review	Recommendation 30 EtD30
31. In preterm infants does higher feed osmolality (e.g. >450 mOsm/kg) compared with lower feed osmolality reduce feeding tolerance and/or increase necrotising enterocolitis? If so, what is the minimum breastmilk volume for dilution of medication in feeds of breastmilk?	New systematic review	Recommendation 31 EtD31
32. In preterm infants requiring a blood transfusion does withholding enteral feeds compared with not withholding enteral feeds improve outcomes for NEC, and aspiration (for extubation)? In preterm infants requiring extubation or an eye examination, does withholding enteral feeds compared with not withholding enteral feeds improve outcomes for NEC, and aspiration (for extubation)?	New systematic review	Recommendation 32 EtD32
33. What is the recommended enteral fluid intake by postnatal age?	New systematic review	Recommendation 33 EtD33
34. Recommended enteral nutritional intake by postnatal age (macro/micronutrients): Energy, protein, carbohydrates, lipids Sodium, potassium and chloride, calcium, phosphorus and magnesium, iron, selenium, iodine, chromium, copper, manganese, molybdenum, fluoride	Adolopment	Recommendation 34 AA34
35. In preterm babies receiving enteral feeds does routine additional protein intake improve neurodevelopment, growth, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?	Existing high-quality evidence	Recommendation 35 EtD35
36. In preterm babies receiving enteral feeds does routine additional carbohydrate supplementation compared with no supplementation improve growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer renal or gastrointestinal complications?	Existing high-quality evidence	Recommendation 36 EtD36
37. In preterm babies receiving enteral feeds does routine additional fat supplementation compared with no supplementation improve growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?	Existing high-quality evidence	Recommendation 37 EtD37
38. In preterm babies receiving enteral feeds does routine additional vitamin A, vitamin D or folic acid supplementation compared with no supplementation improve growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?	New systematic review Adolopment	Recommendation 38 EtD15
39. In preterm infants who are enterally fed does routine zinc supplementation and monitoring compared with routine no supplementation and zinc monitoring reduce the incidence of zinc deficiency faltering growth, reduced immune function and impaired neurodevelopment?	Existing high-quality evidence	Recommendation 39 EtD39
40. In preterm babies receiving preterm formula, does switching to term formula at discharge/term vs. earlier lengthen the time to discharge or compromise growth or neurodevelopment?	New systematic review	Recommendation 40 EtD40
41. Should exposure to the smell or taste (or both) of breastmilk or formula administered with tube feeds vs. no exposure be used for preterm infants who are fed via an orogastric or nasogastric tube?	New systematic review	Recommendation 41 EtD41

Topic 3 – Breastmilk and Breastfeeding

42. Does breastmilk expression within six hours of birth increase expressed milk volumes and breastfeeding/breastmilk feeding at discharge? Does the frequent expression of breastmilk (minimum of 8 times in 24 hours) after preterm birth reduce the risk of low lactation for the mother? Does double pumping increase mothers' milk supply compared to single/consecutive breast pumping?	3 New systematic reviews	Recommendation 42 EtD42a EtD42b EtD42c
43. Are preterm infants who have a first feed of infant formula or donor breastmilk at greater risk of their mothers discontinuing optimal expressing or breastfeeding compared with infants who have a first feed of mother's own expressed milk?	New systematic review	Recommendation 43 EtD43
44. Does referral to lactation consultant services within 48 hrs of birth improve breastfeeding outcomes for preterm babies in NICU compared to no referral to lactation consultant services? OR referral to lactation consultant services after 48hrs of age? Does having access to dedicated NICU neonatal lactation consultant services support mothers with optimal expression of breastmilk, establishment and maintenance of breastfeeding, and breastfeeding on NICU discharge compared to mothers who do not have access to dedicated NICU neonatal lactation consultant services? NB. Due to a lack of evidence, the question was revised to: Should mothers of preterm infants have access to lactation consultant services vs. no access to lactation consultant services?	New systematic review	Recommendation 44 EtD44
45. Does skin to skin care (initiated within 24 hours of birth and continued through all levels of the NICU) improve milk supply and the initiation, establishment, and maintenance of breastfeeding (including readiness to breastfeed, sucking bursts, competent sucking and establishment of breastfeeding prior to discharge) for mothers of preterm babies in NICU? Does skin to skin care improve milk supply and the initiation, establishment, and maintenance of breastfeeding for mothers of preterm babies in NICU? Does skin to skin care initiated at least 30 minutes prior to a scheduled feed time increase preterm infant responsiveness and readiness to feed compared to no skin to skin prior to feed? N.B This question was simplified to: Should skin-to-skin care vs. no skin-to-skin care be used for mothers of preterm infants to improve breastfeeding and clinical and growth outcomes?	Existing high-quality evidence	Recommendation 45 EtD45
46. Do external factors support improved breastmilk expression and milk supply for mothers of preterm infants in NICU? External factors include but are not limited to: information availability, 24/7 consistent ongoing skilled support, galactagogues, expressing packs, limited or no whānau support. Do internal factors (e.g. mother's medical history, birth experience, postnatal health status) have a negative impact on expressing frequency and maintaining milk supply? NB. Due to an overabundance of evidence, the question was narrowed to: Should additional staff-related interventions vs. standard care be used for improving breastfeeding outcomes in whānau of preterm infants in NICU?	New systematic review	Recommendation 46 EtD46
47. What are mana enhancing tikanga practices that support whānau Māori breastfeeding?	New systematic review	Recommendation 47 EtD47

Topic 4 – Monitoring Nutrition and Growth

48. What equipment/tools are recommended for accurately measuring and monitoring the growth of neonates? (refers to both measuring tools as well as monitoring tools i.e. growth charts)	Adolopment	Recommendation 48 AA48
49. What specific growth parameters (e.g. weight, length, head circumference, BMI) should be included in growth monitoring, and how frequently should they be monitored? At what age should chronological age be used for growth assessment (as opposed to corrected age) in babies born preterm?	Adolopment	Recommendation 49
50. What are acceptable growth goals for AGA and SGA infants? What is the recommended growth target for small-for-gestational-age infants, and should it aim for them to reach or exceed the 50th percentile?	Adolopment	Recommendation 50 AA50

51. What is the definition of faltering growth that requires attention or nutrition intervention?	New systematic review	Recommendation 51 EtD51
52. What biochemical monitoring is recommended to monitor parenteral nutritional adequacy and tolerance? What are the reference ranges for the neonatal population? ◦ Sodium · Triglycerides · Alkaline phosphatase ◦ Calcium · Blood urea nitrogen · Parathyroid hormone ◦ Phosphate · Bicarbonate · Liver function tests ◦ Magnesium · Creatinine · Trace elements ◦ Potassium · Haemoglobin · Fat-soluble vitamins ◦ Blood gases · Ferritin · Transaminases ◦ Blood glucose · Full blood count (including reticulocytes) ◦ Urinary sodium and phosphate · Blood pH ◦ Urinary glucose · Albumin and protein ◦ Ammonia	Adolopment	Recommendation 52 AA52
53. What biochemical monitoring is recommended to monitor enteral nutritional adequacy and tolerance: Who should be monitored and when (gestational age, birthweight, prolonged IV nutrition, steroids, short gut syndrome) ◦ Zinc, Ferritin ◦ Vitamins ◦ Sodium, Potassium, Phosphate ◦ Blood glucose ◦ Full blood count ◦ Blood urea nitrogen ◦ Bilirubin, conjugated ◦ Prealbumin and albumin ◦ Bone mineral status (alkaline phosphatase, calcium, phosphate, Vitamin D, parathyroid hormone)	Adolopment	Recommendation 53 AA53
54. Does access to a specialist neonatal dietitian vs. no access improve outcomes for preterm infants?	New narrative review	Recommendation 54 EtD54
Topic 5 – Whānau Education and Involvement		
55. How do Māori whānau prefer to engage in discussions and receive information when making shared decisions about the care of their preterm pēpi?	New systematic review	Recommendation 55 EtD55
56. How do Pacific peoples and their families prefer to engage in discussions and receive information when making shared decisions about the care of their preterm pēpi?	New systematic review	Recommendation 56 EtD56
57. What are the benefits of integrating whānau-led tikanga around food into the care of Māori preterm pēpi?	New systematic review	Recommendation 57 EtD57
58. How do early education and communication about a preterm infant's nutrition plan, mode of feeding and growth impact parents' understanding and engagement in their child's care? In the NICU, how does early education (prior to birth or just after) on the importance of breastmilk, fortification, and nutritional supplements influence parents' approach to feeding, breastfeeding practices and overall outcomes for preterm babies?	New systematic review	Recommendation 58 EtD58
59. Should additional education around the nutrition and/or care of their preterm infants throughout their NICU stay be delivered through different methods (face-to-face, written, online) vs. standard care be used for families of preterm infants?	New systematic review	Recommendation 59 EtD59
60. How does encouraging parents to be involved in tube feeding (feeding, changing tubes and using feeding pumps if needed) and preparing supplements (fortification and similar supplements) of their infants affect EBM expression and initiation/establishment of breastfeeding and their confidence, participation, and overall care experience, as well as the health and development of their infants?	New systematic review	Recommendation 60 EtD60

01

TOPIC 1

Parenteral Nutrition

Who needs intravenous nutrition, when to start and stop it, fluid volumes, macronutrients, micronutrients and lipid management.

“I kind of just felt a little bit comfortable that he was here, that he was in good hands, that he had the support that he needed to, I guess, keep surviving as a baby that’s quite premature.”

“I actually thought my journey would be easier in the NICU. I made an assumption. It was not, and here I am now”

“There’s a great clash in your understanding that you are a mum, this is your child, this is what we do at home, this taking care business, this illness business, this is something that mum and baby will handle at home. When you’re in a NICU situation, you come to a work environment. I guess when a person rationalises that now this is a business, my [baby] is on somebody’s charted notes who has things to get done, formulas to fulfil, I have to re-manage my life and come to help my kid or be a present witness for my kid, for all these professionals. [...] Because I have only one precious thing. I don’t have 120 staff who are my precious things.”

“They were explaining what they’re going to do to her, put her in a bag. I won’t be able to hold her. I won’t be able to do anything with her until she’s up at NICU, which kind of broke my heart. It tore me apart when they said I couldn’t touch her, couldn’t do anything. And then it kind of felt like I had, I turned into real bad mother that I wasn’t good enough for her. I had so many emotions that day, so many thoughts running through my mind, like, what if I did this? What if I had done that? Or is it my fault?”

The quotes throughout this guideline are drawn from qualitative interviews with mothers of preterm babies.

1 In moderate-to-late preterm infants, while we wait for mothers' breastmilk what method of nutrition (parenteral nutrition vs. 10% glucose vs. infant formula vs. donor milk), is best?

RECOMMENDATION

CONDITIONAL
EtD 1

Use 10% glucose instead of parenteral nutrition for moderate-to-late preterm infants whose mother's own breastmilk is not available after birth, while waiting for mother's breastmilk. Parenteral nutrition should be reserved for infants with a specific clinical indication.

Justification

There is no evidence of benefit for key clinical outcomes such as mortality, sepsis, necrotising enterocolitis, length of hospital stay or breastfeeding at discharge when parenteral nutrition is used instead of 10% glucose in this population. Parenteral nutrition is invasive, increases resource use and costs and may negatively influence the transition to exclusive maternal breastmilk, particularly in pēpi Māori. The evidence does not support the routine use of parenteral nutrition in this population without clear clinical indication. In contrast, 10% glucose is inexpensive, widely available and safer for short-term use while awaiting maternal milk. Standardising the use of 10% glucose and delaying formula or parenteral nutrition unless clinically necessary may reduce variation and support equitable outcomes. A consistent approach using 10% glucose while actively supporting lactation may protect maternal milk feeding and improve equity for whānau Māori. Supporting early breastmilk expression and timely transition to enteral feeds should remain the priority.

Subgroup considerations

Families from under-represented backgrounds may struggle with the complexity of early feeding decisions. Clear, culturally responsive communication about the temporary use of IV fluids, the benefits of maternal breastmilk and plans to transition to enteral feeding can help ensure informed parental involvement and support equitable care.

Implementation considerations

Ensure that all infants have prompt access to IV glucose if needed. Consider initiating parenteral nutrition if breastfeeding is contraindicated or has not commenced by 96 hours after birth. Prioritise culturally safe, whānau-led lactation support to reduce early use of formula, particularly for pēpi Māori.

Monitoring and evaluation

Track use of 10% glucose and parenteral nutrition by ethnicity, gestation and birthweight. Evaluate equity impacts by ethnicity in feeding transitions, exposure to alternative nutrition and discharge feeding outcomes.

Research priorities

- Culturally responsive strategies to optimise early lactation and reduce time to mother's milk availability.
- Long-term outcomes associated with early 10% glucose vs. parenteral nutrition in moderate-to-late preterm infants.
- Impact of early nutritional decisions on exclusive breastmilk feeding at discharge across ethnic groups.

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2 Which infants (by birthweight or gestational age) should receive parenteral nutrition?

RECOMMENDATION

ADOPTED

CONDITIONAL

AA 2

For preterm babies born $<31^{+0}$ weeks, start neonatal parenteral nutrition.

For preterm babies born $\geq 31^{+0}$ weeks, start parenteral nutrition if sufficient progress is not made with enteral feeding in the first 72 hours after birth.

For preterm babies on enteral feeds, start parenteral nutrition if:

- enteral feeds need to be stopped and it is unlikely they will be restarted within 48 hours.
- enteral feeds have been stopped for more than 24 hours and there is unlikely to be sufficient progress with enteral feeding within a further 48 hours.

Implementation considerations

Requires streamlined processes to ensure vascular access is secured and parenteral nutrition can be started within 6–8 hours of birth.

Monitoring and evaluation

Track time from birth to initiation of parenteral nutrition.

Research priorities

- Early vs. delayed parenteral nutrition initiation stratified by gestation and birthweight.

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3 How many hours should pass before starting parenteral nutrition in extremely preterm infants?

RECOMMENDATION

ADOPTED**CONDITIONAL**

EtD 1

AA 3

When a preterm baby meets the indications for parenteral nutrition, start it as soon as possible, and within 8 hours at the latest.

Subgroup considerations

Particularly relevant to infants born <28 weeks or <1,000 g who may have a prolonged transition to full enteral feeding.

Implementation considerations

Ensure availability of early vascular access protocols, standard parenteral nutrition solutions, education for staff on timing targets and coordination between clinical teams.

Monitoring and evaluation

Audit timing of parenteral nutrition initiation and correlate with short-term metabolic outcomes and infection rates.

Research priorities

- Research comparing parenteral nutrition initiation at <8 hours vs. 8–12 hours in extremely preterm infants.

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4 Should lower parenteral fluid vs. higher parenteral fluid be used for preterm infants receiving parenteral nutrition?

RECOMMENDATION

CONDITIONAL**EtD 4**

Either lower or higher parenteral fluid volumes may be used, guided by the infant's condition, humidity settings, local protocols and biochemical results.

Justification

While some older studies suggest that lower parenteral fluid volumes may reduce the risk of patent ductus arteriosus and necrotising enterocolitis (NEC), these findings come from small, pre-surfactant era trials and observational studies with potential confounding. The overall certainty of the evidence is very low, and no significant benefit has been demonstrated for mortality, bronchopulmonary dysplasia or neurodevelopment. In contrast, lower fluid volumes were associated with increased postnatal weight loss, and the risk of dehydration remains unclear. Given this uncertainty and the clinical importance of individualised care, we suggest either lower or higher parenteral fluid volumes may be used, guided by the infant's condition, humidity settings, local protocols and biochemical results.

Subgroup considerations

No subgroup analysis was available by gestational age, birthweight or ethnicity. Individualised care based on gestation, clinical status, and fluid balance monitoring is particularly crucial for extremely preterm and extremely low birthweight infants, who may be more vulnerable to both fluid overload and dehydration.

Implementation considerations

Given the lack of strong evidence favouring one approach over another, standardised yet flexible fluid protocols are recommended. These should include a clear framework for adjusting fluid volumes based on gestational age, postnatal age, clinical condition and weight trends while monitoring consistent fluid balance.

Monitoring and evaluation

Routine data collection on daily fluid intake/output, weight change, biochemistry, and clinical outcomes (e.g. NEC, PDA, BPD) should be part of standard care. If services make trial adjustments to fluid volumes (e.g. more restrictive approaches), then a local audit is essential to assess safety, tolerance, and short-term outcomes. Data should be disaggregated by ethnicity to ensure that equity is monitored and prioritised.

Research priorities

- Studies comparing lower versus higher parenteral fluid volumes in contemporary neonatal care settings, including the use of surfactant, antenatal steroids and early feeding strategies.
- Subgroup analyses based on gestational age, birthweight and ethnicity, particularly for Māori and Pacific populations.

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5 Should routine iodine vs. no additional iodine supplementation be used for preterm infants?

RECOMMENDATION

CONDITIONAL

EtD 5

AA 17

Routine additional iodine supplementation is not recommended. Iodine supplementation may be considered for infants who are at risk of iodine deficiency and reliant on parenteral or low-iodine enteral nutrition.

Justification

Current RCT evidence does not show statistically significant benefits or harms on critical clinical outcomes (e.g. neurodevelopment, mortality, NEC); however, these studies were not conducted in Aotearoa New Zealand where the soil is iodine-deficient.

Subgroup considerations

No subgroup analyses were available by gestational age, birthweight, or ethnicity. In settings where parenteral nutrition or breastmilk is iodine-deficient, supplementation is likely more critical. Further research should stratify outcomes by gestation and type of nutrition provided.

Implementation considerations

Iodine intakes from parenteral and enteral nutrition sources should align with ESPGHAN 2018 and ESPGHAN 2022 recommendations (1–10 µg/kg/day parenterally, 11–55 µg/kg/day enterally). Ensure parenteral intake from standard solutions is on the higher side of the range (≥ 5 µg/kg/day) due to the high risk of iodine deficiency in the Aotearoa New Zealand context.

Monitoring and evaluation

Audit of iodine intake via parenteral/enteral nutrition. Consider monitoring of thyroid function in high-risk infants or those on prolonged parenteral nutrition and monitor urinary iodine.

Research priorities

- RCTs comparing different iodine doses and routes of administration (enteral vs. parenteral) conducted in Aotearoa New Zealand.
- Long-term neurodevelopmental outcomes by iodine exposure level in the Aotearoa New Zealand population.
- Exploration of iodine status in Aotearoa New Zealand's preterm population, especially for pēpi Māori, Pacific families and underrepresented groups.

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6 In preterm infants what is the minimum glucose load (mg/kg/min) administered via IV infusion needed for maintenance of metabolic homeostasis or prevention of hypoglycaemia?

RECOMMENDATION

ADOPTED

CONDITIONAL

AA 6

The minimum glucose load (mg/kg/min) via IV infusion to maintain metabolic homeostasis or prevent hypoglycaemia is at least 4 to 8 mg/kg/minute.

Subgroup considerations

Extremely preterm infants may require lower initial rates and more gradual escalation due to immature glucose metabolism.

Implementation considerations

Protocols for standardised initiation and titration of glucose infusions should be in place; ensure glucose monitoring systems are available.

Monitoring and evaluation

Monitor glucose concentrations at least 4–6 hourly during the first 24–48 hours and audit incidence of hypoglycaemia.

Research priorities

- Trials comparing different glucose initiation strategies in the first 48 hours after birth.

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7 Should insulin vs. glucose reduction be used for hyperglycaemic preterm infants?

RECOMMENDATION

CONDITIONAL

EtD 7

Either insulin or glucose reduction may be used for managing hyperglycaemia. The choice should be guided by clinical judgement, local protocols and the availability of close monitoring, as the evidence does not favour one approach over the other.

Justification

The evidence comparing insulin therapy with glucose reduction for hyperglycaemic preterm infants is of very low certainty and based on small, dated trials with limited reporting on critical outcomes. Insulin treatment may lead to improved weight gain and faster progression to full enteral feeds and was associated with fewer sepsis episodes in one small trial. However, there was no evidence of benefit for mortality, length, head circumference or bronchopulmonary dysplasia and both interventions had similar hypoglycaemia risks. Long-term neurodevelopmental outcomes were not reported. The limited evidence means no strong recommendation can be made. Insulin may benefit nutritional intake but requires careful monitoring due to its potential risks. Glucose reduction is simpler and safer in many settings but could compromise energy intake and growth in some infants. At least 4 to 8 mg/kg/minute is needed to meet the minimum glucose needs to sustain the brain's metabolic needs.

Subgroup considerations

All included studies involved extremely low birthweight infants; however, these are the infants at the highest risk of hyperglycaemia.

Implementation considerations

Insulin use requires protocols for titration, blood glucose monitoring and training to ensure safe administration. Glucose reduction requires careful nutritional monitoring to avoid energy and protein deficits. If glucose load is reduced, ensure the glucose infusion rate is at least 4 to 8 mg/kg/minute to meet the minimum glucose needs to sustain the brain's metabolic needs. If insulin is used, ensure the glucose infusion rate is in the recommended range of 6 to 11 mg/kg/minute (9 to 16 g/kg/day) NICE 2022.

Monitoring and evaluation

Blood glucose should be monitored closely regardless of the method used.

Research priorities

- Large, high-quality trials comparing insulin and glucose reduction in hyperglycaemic preterm infants, with long-term neurodevelopmental follow-up.
- Studies evaluating the safety and efficacy of insulin in different birthweight and gestational age groups.
- Ethnicity-stratified analyses to identify differential impacts and support equitable treatment choices, especially whānau Māori, Pacific families and underrepresented groups experiences.

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8 Are there any indications (e.g. high triglycerides, sepsis) to wean, reduce or restrict parenteral lipid administration?

RECOMMENDATION

ADAPTED

CONDITIONAL

AA 8

When an infant is at risk of hypertriglyceridaemia, for example has a lipaemic blood sample, serum triglyceride concentrations should be monitored. The reduction of lipid emulsion during episodes of sepsis is not recommended.

Subgroup considerations

Caution is needed in extremely preterm infants and those with pre-existing metabolic instability.

Implementation considerations

No implementation required.

Monitoring and evaluation

If serum triglyceride concentrations are monitored, this should be no more than once a day.

Research priorities

- Whether routine monitoring of serum triglyceride concentrations and reduction of the lipid emulsion dose are beneficial and if so at what serum triglycerides concentration should the lipid emulsion dose be reduced.

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9 Should fish oil only based lipids (Omegaven) vs. multi-component lipids (SMOFLipid) be used for prevention or rescue therapy for preterm infants with (any cause) liver disease?

RECOMMENDATION

CONDITIONAL

EtD 9

Fish oil-only-based lipid should not be used for preventing liver disease but may be useful as rescue therapy in infants with established or evolving intestinal failure-associated liver disease.

Justification

Low certainty evidence suggests a large beneficial effect of fish oil only lipids on the resolution of intestinal failure-associated liver disease, with an odds ratio of 6.1 (95% CI 2.3 to 16.6) and a substantial absolute increase in recovery (403 more per 1,000 infants treated). While the data are derived from non-randomised and retrospective studies, they consistently report improved biochemical liver function indices. No increase in adverse effects such as sepsis or mortality has been demonstrated; however, again, the evidence is weak. Fish oil only lipid emulsion is considerably more expensive (~\$110/day vs. ~\$35/day for SMOFLipid in 2025). However, when used selectively as rescue therapy, this cost may be justified given the potential to reduce complications and long-term liver damage.

Subgroup considerations

Infants with established intestinal failure-associated liver disease are most likely to benefit from fish oil-based lipid. There is no direct evidence specific to pēpi Māori but given higher rates of preterm birth and comorbidities, equitable access to rescue therapy is a key consideration.

Implementation considerations

Fish oil-only-based lipid is already used on a case-by-case basis. Local protocols should ensure clear criteria for initiation (e.g. rising conjugated bilirubin, failure to respond to standard management) and should include guidance on volumes of Omegaven required (as this is twice the usual volume of SMOF), amount of fat-soluble and water-soluble vitamins added and to beware of potentially harmful side effects e.g. vitamin E toxicity. Fish oil only based lipid lacks essential fatty acids such as omega 6, which may not meet the complete nutritional needs of growing preterm infants if used long-term or as a sole lipid source. Fish oil-only-based lipids should be used in conjunction with a multidisciplinary approach that includes a referral to the National Intestinal Failure and Rehabilitation Service.

Monitoring and evaluation

Monitor liver function tests (bilirubin, ALT, GGT) and serum fat-soluble vitamins regularly, paying particular attention to vitamin E. Document duration and outcomes of fish oil only based lipid use to inform future evaluations.

Research priorities

- High-quality studies comparing fish oil only with multi-component lipids in infants with intestinal failure-associated liver disease.
- Long-term neurodevelopment and growth outcomes following fish oil only lipid emulsion exposure.
- Optimal dosing and duration of fish oil only lipid emulsion in rescue therapy.
- Ethnic equity analyses to determine access for pēpi Māori, Pacific families and underrepresented groups.

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10 Is there evidence for addition of specific fatty acids in lipid emulsions?

RECOMMENDATION

ADAPTED

CONDITIONAL

AA 10

- To prevent essential fatty acids deficiency a lipid emulsion dose providing a minimum linoleic acid intake of 0.25 g/kg/day should be given (~1.5 g/kg/day SMOFLipid).
- Parenteral LC-PUFA supplementation is recommended where LC-PUFA containing lipid emulsion products are available and cost-effective, e.g. SMOFLipid.
- Routine enteral long chain polyunsaturated fatty acid supplementation is not recommended.

Subgroup considerations

Extremely preterm infants at risk of retinopathy of prematurity may benefit more from LC-PUFAs.

Implementation considerations

~1.5 g/kg/day SMOFLipid ensures an adequate intake of linolenic acid. Most NICUs already use SMOFLipid. Standardisation of parenteral lipid emulsions across units would be beneficial.

Monitoring and evaluation

Track clinical use and any adverse effects related to LC-PUFA products.

Research priorities

- What is the optimal dose of parenteral and enteral LC-PUFA supplementation and do the benefits outweigh the risks.

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11 What is the recommended hang time for aqueous IV nutrition and lipid solutions for preterm infants?

RECOMMENDATION

CONDITIONAL

EtD 11

Aqueous phase: A hang time of at least 48 hours and up to 96 hours is recommended. Lipid emulsion: A hang time of up to 48 hours is recommended.

Justification

The recommendation is based on expert consensus and current practice because the available evidence is of very low certainty and is largely indirect, with limited data specifically addressing very preterm infants. A before-and-after study reported a reduction in catheter-related sepsis and central line-associated bloodstream infections with longer aqueous solution hang times. However, small RCTs reported no significant effect on bloodstream infections when changing lipid sets less frequently. One observational study showed a halving of central line infections (0.4 vs. 0.8 per 1,000 line-days, $p < 0.01$) with longer aqueous hang times. Cost analyses indicated substantial annual savings when switching from 24- to 48-hour hang times and reduced workload for nurses. Nonetheless, concerns about infection risk and nutrient loss persist due to the very low certainty of evidence and lack of data in extremely preterm populations.

Subgroup considerations

Standardised longer hang time protocols may improve the consistency and equity of parenteral nutrition practices nationally. Pēpi Māori are at increased risk of sepsis and suboptimal outcomes; standardised, efficient parenteral nutrition care may reduce these inequities.

Implementation considerations

Hospital policies may need revision to support hang time alignment across centres.

Monitoring and evaluation

Implement audit systems to monitor:

- Rates of CLABSI and other bloodstream infections — specifically include data on Māori and Pacific infants to monitor the impact on equity.
- Cost tracking, nurse workload and satisfaction.

Research priorities

- RCTs in very preterm infants comparing infection rates and mortality across hang time protocols.
- Nutrient and stability and safety data for extended hang times in Aotearoa New Zealand hospital settings.
- Health economic modelling based on local cost data, including costs associated with decreased infection rates.

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12 What is the enteral nutrition criterion (volume) to stop parenteral nutrition? What is the criterion for stopping lipids?

RECOMMENDATION

CONDITIONAL

EtD 12

Parenteral nutrition should continue until enteral feeds reach at least 120 mL/kg/day and can continue until full enteral feeds are established. Ceasing parenteral nutrition at a lower volume of enteral feed (e.g. 60–100 mL/kg/day) is not recommended.

Justification

High- and moderate-certainty evidence shows uncertain effects on mortality, infection, growth and major morbidities, indicating no consistent advantage of ceasing parenteral nutrition at lower fluid volumes. Limited very low-certainty evidence suggests potential growth benefits at or above 120 mL/kg/day, but this requires further confirmation.

Subgroup considerations

There is currently no birthweight, GA or ethnicity-specific data available. Pēpi Māori may be at increased risk of delayed enteral feeding due to systemic barriers. Clear guidance to delay stopping IVN until ≥ 120 mL/kg/day may help standardise care and improve equity.

Implementation considerations

Develop unit protocols that define a minimum enteral volume threshold (e.g. ≥ 120 mL/kg/day) for stopping parenteral nutrition. This is the minimum enteral volume and parenteral nutrition can continue until full enteral feeds are reached. Provide staff training on risks associated with early parenteral nutrition cessation. Ensure adequate lactation and feeding support to promote enteral feed advancement.

Monitoring and evaluation

Track adherence to defined parenteral nutrition cessation thresholds by unit and patient characteristics. Monitor rates of late-onset sepsis and postnatal faltering growth across gestational age groups, birthweights and ethnicities. Evaluate changes in practice and outcomes following the implementation of new guideline.

Research priorities

- Studies comparing different cessation thresholds for stopping parenteral nutrition, including outcomes beyond discharge.
- Research on the impact of parenteral nutrition cessation volume on Māori, Pacific and under-represented groups.
- Cost-effectiveness analyses considering sepsis-related costs and long-term growth/neurodevelopment.

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13 What is the recommended parenteral energy and macronutrient intake by postnatal age?

RECOMMENDATION

ADAPTED

CONDITIONAL

AA 13

Initiate parenteral nutrition on day 1 and adjust for tolerance and clinical condition.

Energy

- Give a starting range of 40 to 60 kcal/kg/day.
- Gradually increase to a maintenance range of 75 to 120 kcal/kg/day. If starting parenteral nutrition more than 4 days after birth give 75 to 120 kcal/kg/day.

Carbohydrate

- Give a starting range of 6 to 9 g/kg/day (equivalent to ~4 to 6 mg/kg/min) glucose.
- Gradually increase to a maintenance range of 9 to 16 g/kg/day (6 to 11 mg/kg/min). If starting parenteral nutrition more than 4 days after birth give 9 to 16 g/kg/day (6–11 mg/kg/min).

Protein

- Give a starting range of 1.5 to 2 g/kg/day amino acid.
- Increase to a maintenance range of 3 to 4 g/kg/day. If starting parenteral nutrition more than 4 days after birth give 3 to 4 g/kg/day.

Protein:Energy ratio

- Ensure protein:energy ratio is 23 to 34 kcal of total energy per g amino acid

Lipid

- Give a starting range of 1 to 2 g/kg/day and increase to 3 to 4 g/kg/day.
- If starting parenteral nutrition more than 4 days after birth give a range of 3 to 4 g/kg/day.

Subgroup considerations

Protocols for energy targets should be standardised.

Implementation considerations

Ensure standard parenteral nutrition solutions that meet these recommendations are available.

Monitoring and evaluation

Audit energy and macronutrient delivery vs. recommendations.

Research priorities

- Early vs. delayed energy escalation.
- Determine optimal energy and macronutrient intake for survival, growth and long-term development.

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14 Should higher parenteral protein (>4 g/kg/day) vs. lower parenteral protein be used for preterm infants and what is the recommended protein intake by postnatal age?

RECOMMENDATION

CONDITIONAL

EtD 14

AA 13

If starting parenteral nutrition in the first 4 days after birth, give a starting range of 1.5 to 2 g/kg/ day amino acid and gradually increase to a maintenance range of 3 to 4 g/kg/day. If starting parenteral nutrition more than 4 days after birth give a range of 3 to 4 g/kg/day.

(As per NICE 2020 recommendations – see Adolopment section)

Justification

Neurodevelopmental outcomes: Evidence is very low to moderate certainty and mostly shows no clear benefit or harm, with some isolated signals of adverse effects (e.g. lower Bayley III Language scores). Evidence at 2 years of potential for harm with higher parenteral protein intakes, but preliminary evidence at 6 years suggests no effect. For growth, moderate-certainty evidence suggests that higher parenteral protein reduces the risk of postnatal faltering growth and modestly improves head circumference growth to discharge. Higher protein intake may increase the risk of refeeding syndrome. No consistent signal for NEC, sepsis or bronchopulmonary dysplasia. Standardising parenteral protein intake and ensuring all infants receive adequate protein supports equity, especially for whānau Māori and Pacific families who experience higher rates of preterm birth and complications.

Subgroup considerations

Most evidence applies to extremely preterm or very low birthweight infants (<32 weeks or <1500 g) as this is the group where the intervention is most applicable.

Implementation considerations

Standardise protocols nationally to start parenteral protein at ≥ 2 g/kg/day on the day of birth, increasing to a maximum of 3.5–4.0 g/kg/day to align with NICE guidance. Monitor clinical parameters of refeeding syndrome, particularly during the first 5-7 days, especially in infants with birthweight <1,000 g or <10th centile. Provide guidance on refeeding syndrome testing and phosphate supplementation. Ensure concurrent non-protein energy supply (at least 65–80 kcal/kg/day) to support protein anabolism and reduce the risk of protein catabolism or acidosis.

Monitoring and evaluation

Track actual protein intakes, not just prescribed. Regularly audit growth and feeding information, e.g. days of parenteral nutrition and Protein:Energy ratio.

Research priorities

- Long-term neurodevelopmental outcomes of different parenteral protein regimens and different amino acids formulations with outcomes by ethnicity.

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15 What is the recommended parenteral vitamin intake by postnatal age? Fat-soluble vitamins (vitamin A, E, D, K), Water soluble vitamins (B vitamins, vitamin C, choline)?

RECOMMENDATION

CONDITIONAL

EtD 15

AA 16

Routine supplementation of additional parenteral vitamins is not supported by the evidence.

Justification

There is evidence of better outcomes with Vitamin A (intramuscular) and D supplementation without harm at low overall cost. However, intramuscular vitamin A injections may not be feasible or acceptable in the Aotearoa New Zealand setting. There is moderate to very low certainty of evidence overall. A few outcomes such as reduction in retinopathy of prematurity (Vitamin A) and bronchopulmonary dysplasia (Vitamin C and D) suggest potential benefits with higher vitamin intake. However, most outcomes show no statistically significant difference between higher and lower doses, and the precision is low across many estimates, with wide confidence intervals and small sample sizes. Despite the limited evidence, the anticipated desirable effects on important outcomes and the very low risk of harm (with no significant increase in adverse outcomes) support a cautious, conditional recommendation in favour of higher vitamin intake. Cost is trivial, and feasibility and acceptability are high, particularly given this practice is already part of standard care in Aotearoa New Zealand.

Subgroup considerations

Supplementation may offer increased benefit to populations at high risk of Vitamin D deficiency.

Implementation considerations

Close monitoring of individual vitamin intakes is warranted due to wide recommended ranges and the potential risk of providing excessive supplementation e.g. vitamin E, which is provided in very high doses in SMOFLipid emulsion. Where available, aiming for ESPGHAN dosing may assist standardisation. Family education and culturally safe communication should be prioritised, especially when engaging with whānau Māori, Pacific families and underrepresented groups.

Monitoring and evaluation

Monitor for signs of both deficiency and toxicity, with appropriate lab tests where indicated. Consider including vitamin supplementation data in national neonatal audits to inform future quality improvement and research.

Research priorities

- High-quality RCTs of individual and combined vitamins in preterm infants (stratified by gestational age), with appropriate pēpi Māori, Pacific families and underrepresented groups representation.
- Pharmacokinetic studies to determine vitamin stability and optimal dosing in diverse preterm populations.
- Research to clarify the role of maternal vitamin status, particularly vitamin D, on neonatal outcomes and maternal supplementation as an option to increase vitamin intakes from breastmilk if feasible.
- Economic evaluations of vitamin supplementation strategies. Evaluation of long-term outcomes, including school-age development.

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16 What is the recommended parenteral intake of: sodium, potassium, chloride, acetate, calcium, phosphorus, magnesium, iron, zinc, selenium, chromium, copper, manganese, molybdenum, fluoride, iodine and vitamins

RECOMMENDATION

ADAPTED

CONDITIONAL

AA 16

Provide parenteral electrolytes, minerals, trace elements and vitamins in accordance with ESPGHAN 2018 recommendations for preterm infants. As Aotearoa New Zealand soil is deficient in iodine, selenium and zinc, use upper half of recommended intake:

Nutrient	Recommended intake/kg/day	Vitamin	Recommended intake/kg/day
Sodium	2 to 7 mmol (<1500 g) 2–5 mmol (>1500 g)	Vitamin A	227 to 455 µg (700-1500 IU)
Potassium	2 to 3 mmol	Vitamin D	2 to 10 µg (80-400 IU)
Chloride	2 to 5 mmol	Vitamin E	2.8 to 3.5 mg
Calcium	1.6 to 3.5 mmol	Vitamin K	10 µg
Phosphorus	1.6 to 3.5 mmol	Vitamin C	15 to 25 mg
Magnesium	0.2 to 0.3 mmol	Thiamin	350 to 500 µg
Iron	200 to 500 µg	Riboflavin	150 to 200 µg
Zinc	400 to 500 µg	Pyridoxine	150 to 200 µg
Copper	40 µg	Vitamin B12	0.3 µg
Iodine	1 to 10 µg	Niacin	4 to 6.8 mg
Selenium	7 µg	Folic acid	56 µg
Manganese	≤1 µg	Pantothenic acid	2500 µg
Molybdenum	1 µg		

Subgroup considerations

Adjustments may be needed in cases of cholestasis or renal impairment.

Implementation considerations

Routine standard solutions and monitoring protocols can facilitate standardisation.

Provide guidance on refeeding syndrome testing and phosphate supplementation.

Monitoring and evaluation

Routine monitoring of biochemical markers and growth parameters is necessary.

Monitor clinical parameters of refeeding syndrome, particularly during the first 5-7 days, especially in infants with birthweight <1,500 g or <10th centile.

Research priorities

- RCTs to determine optimal dosing for micronutrients in extremely preterm and growth-restricted infants.

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02

TOPIC 2

Enteral Nutrition

Initiating and advancing milk feeds, mother's own milk, donor milk, fortification, feed type and feeding practices.

“I think in the early days and everything, you don't quite realise that you're pretty much going to be eat, feed, sleep, pump, repeat, kind of a newborn cycle of eat, change, feed, repeat, kind of thing.”

“I understand that breastmilk is liquid gold, but there is only liquid gold, that much available in me”

“Now, in consultation with the doctors, all that they require is to get my EBM and fortify it and have enough milk supply because now we can focus on growth. For a mum, that's kind of like a challenge as well because yes, my kid needs to grow a certain height and weight because the next test is when the body develops and grows enough, the lungs grow, the lungs will have capacity to get off CPAP.

“It just took that extra bit of help. I don't like asking for help, I don't like bothering anyone ... but she came in and she saw me kind of struggling getting baby to latch and she showed me an easier way, and it just worked for us.”

“It's like everyone here is your family support. And all the other mums know what you're going through. I think that is the best thing ... And you can all help out each other.”

17 When to start enteral feeding after birth, recommended type (breastmilk, formula etc.), route, method, starting feed volume and frequency of enteral feeding?

RECOMMENDATION

ADAPTED

CONDITIONAL

AA 17

Initiate enteral feeding within 24 hours of birth. Use mother's own milk where possible, followed by donor breastmilk and then preterm formula if no breastmilk is available. Use the gastric route and intermittent bolus feeding. Start with 10–20 mL/kg/day and increase by 24 to 30 mL/kg/day depending on tolerance.

Subgroup considerations

Extremely preterm infants may require lower initial rates and more gradual escalation due to an immature gastrointestinal tract.

Implementation considerations

Protocols for standardised initiation and feed advancement are needed.

Monitoring and evaluation

Monitor compliance with feeding protocols and time to full enteral feeds.

Research priorities

- High-quality trials comparing different feeding initiation strategies in the first 48 hours after birth in preterm infants.

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18 Should we give infant formula/donor milk vs. wait for mother's own milk be used for moderate-to-late preterm infants whose mothers' breastmilk is not available at birth?

RECOMMENDATION

CONDITIONAL

EtD 18

- In moderate-to-late preterm infants whose mothers' breastmilk is not available at birth, for how long should we wait for mother's own breastmilk? In moderate-to-late preterm infants wait as long as is clinically feasible for mother's own milk. This may be at least 3 days from birth. Give 10% IV glucose while waiting for mother's own milk. Infant formula or donor milk is not recommended unless there is a specific clinical indication.

Justification

Evidence for the use of infant formula or donor milk is low to very low certainty, based on a single study with no clear benefit for critical outcomes (e.g. mortality, NEC, breastfeeding at discharge). There was no clear gain in growth or earlier discharge and potential delay in establishing breastfeeds. Risks of early formula feeding were not fully captured in the evidence review: May interfere with breastfeeding establishment and lactogenesis, possible impacts on gut microbiota and immune programming, may undermine maternal confidence and motivation to express milk. A recommendation to wait for mother's milk helps protect equity and breastfeeding.

Subgroup considerations

Whānau Māori experience inequities in early milk provision and breastfeeding outcomes.

Implementation considerations

Clear policy is needed: Units should define when and for whom supplemental milk would be justified and clinically appropriate. For parents, communicate risks/benefits clearly and promote informed choice. Prioritise lactation support and timely milk expression to reduce the need for supplementation with formula or donor milk.

Monitoring and evaluation

Track the following by ethnicity and gestational age: Use of donor milk and formula, time to initiation of mother's milk and breastfeeding rates at discharge, lactation support provision.

Research priorities

- Strategies to optimise lactation and reduce early formula use.
- Research needed on whether donor milk is appropriate in this group.

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20 Should donor breastmilk vs. infant formula be used for preterm infants for whom there is insufficient mother's own breastmilk?

RECOMMENDATION

STRONG

Etd 20

Donor breastmilk is preferred over infant formula for all preterm infants with insufficient mother's own expressed breastmilk. Very low birthweight and extremely preterm infants benefit most.

Justification

Strong recommendation for donor milk is based on the critical outcome of reducing NEC, given the negative impact of NEC on the infant, whānau and hospital resources. Recommendation is based on moderate certainty of evidence of large and consistent NEC reduction (33 fewer per 1,000) across studies.

Subgroup considerations

Very preterm / very low birthweight infants benefit most from donor milk as NEC reduction is most relevant in this group. Infant formula may be considered for preterm infants born after 32 weeks' gestation who are at low clinical risk of NEC, provided sufficient time and support has been given for the mother to establish her lactation. There is no evidence relating specifically to pēpi Māori and their whānau; however, Māori are a priority group because studies suggest they are less likely to receive breastmilk and more likely to receive infant formula.

Implementation considerations

All neonatal units should have equitable access to donor milk. The donor breastmilk must either be pasteurised or screened (both the donor and the breastmilk are screened). Consider equitable access to donor milk, especially for rural hospitals and Māori and Pacific whānau. This may involve establishing a national guideline on peer-to-peer donation to support safer, more consistent practices. Consider fortification and supplementation of donor milk to optimise nutritional intake and growth, especially if pasteurised. Support Māori and Pacific-led breastfeeding promotion and milk donation initiatives.

Monitoring and evaluation

Audit NEC, growth and breastfeeding outcomes across units nationally. Monitor access to donor milk by ethnicity, region and gestational age. Evaluate all of the safety and outcomes above based on peer-to-peer vs. unpasteurised screened donor milk use.

Research priorities

- Effects of donor breastmilk on health outcomes to identify potential benefits (e.g. nutrition/NEC) and risks (e.g. pathogens) for the infant.
- The nutritional composition of donor breastmilk compared with preterm mother's own breastmilk is unknown in Aotearoa New Zealand.
- Outcomes in moderate-to-late preterm infants.
- Cost-effectiveness of donor milk vs. formula in the Aotearoa New Zealand context and by gestational age group.
- Safety and effectiveness of double-screened peer-to-peer unpasteurised milk.
- Access to donor breastmilk cultural acceptability and preferences of Māori and Pacific families around donor breastmilk.

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21 Should slower feed advancement vs. faster feed advancement be used for preterm infants who require enteral feeding?

RECOMMENDATION

CONDITIONAL

EtD 21

Enteral feed advancement rates of at least 24 mL/kg/day are recommended.

Justification

The evidence shows little or no difference between slower and faster feed advancement for key outcomes such as NEC, mortality and survival free from neurodisability. Faster feed advancement shortens the time to full enteral feeds and time to regain birthweight but does not appear to affect growth at discharge. Slower advancement may reduce the risk of cerebral palsy, though this is based on low-certainty evidence and hard to interpret given that no other measures of neurodevelopment were different. This conditional recommendation reflects the balance of benefits and risks across outcomes and the low to moderate certainty of evidence.

Subgroup considerations

There is no strong evidence of differential effects for extremely preterm or very low birthweight infants and few data are available for moderate-to-late preterm infants. No evidence is available specifically for pēpi Māori or Pacific infants.

Implementation considerations

Standardised feeding protocols should include feed advancement rates to ensure consistency in clinical decision-making, particularly across neonatal units, which is important to reduce variation. Supporting maternal milk supply is essential, especially when feed volumes increase quickly, and it may be necessary to hold feed volumes and wait for sufficient breastmilk supply. Clear explanations in a culturally appropriate manner can support parent confidence and engagement.

Monitoring and evaluation

Monitor time to full enteral feeds, incidence of NEC, growth at discharge and length of hospital stay. Ethnicity-specific monitoring will help identify and address any inequities in care or outcomes.

Research priorities

- Further enteral feeding rate trials are needed in moderate and late preterm infants.
- Longer-term outcomes such as growth quality and neurodevelopment need investigation.
- Culturally grounded research exploring whānau Māori and Pacific families' experiences with feeding decisions and breastfeeding rates at discharge.

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22 Should routine gastric aspiration before feeds vs. no routine gastric aspiration before feeds be used for preterm infants who require enteral feeding?

RECOMMENDATION

CONDITIONAL

EtD 22

Routine measurement of gastric aspiration volumes before enteral feeds for the monitoring of feed tolerance is not recommended.

Justification

This is a conditional recommendation due to very low to moderate certainty evidence; that suggests routine aspiration may delay full enteral feeding and increase days to regain birthweight without improving clinical outcomes. There is no evidence of benefit from routine gastric aspiration volume monitoring in reducing mortality, NEC or length of hospital stay. Some data suggest it may delay the time to full feeds (MD ~4 days longer) and prolong the time to regain birthweight.

Subgroup considerations

Most evidence is from infants <1500 g, but data on moderate-late preterm or low birthweight infants is limited.

Implementation considerations

Develop and disseminate clear unit protocols recommending: No routine aspiration of gastric residual volumes. Ongoing clinical monitoring of feed tolerance (e.g. abdominal signs, vomiting, distension).

Monitoring and evaluation

Monitor time to full enteral feeds, NEC rates and length of stay. Monitor staff adherence and confidence in revised unit protocols.

Research priorities

- Further RCTs across birthweight and gestational age groups with long-term outcomes such as growth and neurodevelopment.

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23 Should continuous feeds or bolus feeds be used in preterm infants who require enteral feeding?

RECOMMENDATION

CONDITIONAL

EtD 23

Continuous feeds should not be used routinely.

Justification

The evidence is mixed and generally of low to moderate certainty, with most studies underpowered to detect meaningful differences in critical outcomes like NEC or mortality. There is insufficient evidence to make a recommendation on the use of intermittent bolus feeding via a pump.

Subgroup considerations

Continuous or intermittent pump feeds may be preferable in very immature or haemodynamically unstable infants who are at risk of intolerance or delayed gastric emptying. Bolus feeding may be more appropriate once the infant is clinically stable to support usual feeding rhythms.

Implementation considerations

Units should be supported in making decisions based on clinical context rather than enforcing one method. The goal should be to transition the infant to bolus feeds as the standard of care, establish "normal" feeding rhythms and decrease costs associated with extra tubing and plastic waste.

Monitoring and evaluation

Monitor feeding intolerance, NEC, time to full feeds and weight gain across feeding methods.

Research priorities

- Adequately powered trials comparing continuous vs. bolus feeding vs. intermittent bolus via pump stratified by gestational age and birthweight.
- Evaluation of nutrient losses in continuous and intermittent feeds, particularly fat and energy.
- Pēpi Māori, Pacific peoples and underrepresented groups – specific outcome data to address equity and inform culturally responsive care.

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24 In preterm infants does fortified EBM vs. unfortified EBM lead to improved growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?

RECOMMENDATION

CONDITIONAL

EtD 24

Expressed breastmilk should be fortified for preterm infants who are born at <32 weeks or birthweight <2000 g.

Justification

Fortification improves early growth outcomes (weight gain, length, head circumference) and supports bone health. These benefits are more pronounced in very preterm or VLBW infants, who are at the highest nutritional risk. No significant increase in NEC or milk curd obstruction was observed, though the certainty of evidence is low to very low. No significant difference in neurodevelopmental outcomes was shown at 18 months. Fortification may support health equity by addressing higher micronutrient deficiency risk in Māori, Pacific and infants from underrepresented groups due to social determinants of health.

Subgroup considerations

Very preterm or VLBW infants: Most evidence applies to this group.

MLPT infants: Fewer data

Māori: Higher baseline risk of deficiency and adverse outcomes suggests they may benefit more from consistent use of fortifiers.

Implementation considerations

Use standardised feeding guidelines for when to initiate and cease adding commercial breastmilk fortifier. Consider standardised protocols on mixing and preparation to reduce infection risk, ensure consistency and decrease osmolality. Provide information to parents on fortifier (e.g. use of videos or apps) to increase acceptability and knowledge.

Monitoring and evaluation

Audit use of fortifier by gestational age and ethnicity. Monitor serum alkaline phosphatase and markers of growth (weekly z-scores). Collect data on NEC, feeding intolerance and milk curd obstruction.

Research priorities

- RCTs on different formulations of fortifier, including both short- and long-term outcomes beyond 18 months (growth, neurodevelopment, metabolic and bone health) in an Aotearoa New Zealand context to allow for ethnicity data, particularly in those populations at higher risk of deficiencies.
- Alternatives to bovine-based fortifiers (e.g. human milk-derived fortifier).
- Strategies for culturally appropriate communication with families.

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25 In preterm infants does commencing less than full strength fortified EBM compared with full fortified enteral feeds lead to shorter time to full enteral feeds improve growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?

RECOMMENDATION

CONDITIONAL

EtD 25

Breastmilk fortifier should be commenced at full strength.

Justification

There is no direct evidence comparing less than full-strength vs. full-strength breastmilk fortifier in preterm infants. However, theoretical benefits of full-strength fortification include higher nutrient intake, especially protein (and phosphate, potentially reducing the risk of refeeding syndrome) and promoting better growth. In contrast, starting at less than full strength may lead to faltering growth, inaccurate dosing and microbiological risk, with no proven benefit in reducing NEC or improving feed tolerance. Given the lack of evidence and the practical risks associated with altering fortifier doses, commencing breastmilk fortifier at less than full strength is not recommended.

Subgroup considerations

Pēpi Māori are disproportionately affected by preterm birth and may be more vulnerable to inconsistent care practices. Lack of standardisation and culturally safe communication could exacerbate existing health inequities if half-strength fortifier is used without explanation or shared decision-making. Infants at higher risk of NEC (e.g. <28 weeks or growth-restricted) may still require individualised feeding decisions but should be based on clinical indications and evidence-based practice rather than routine half-strength protocols.

Implementation considerations

Full-strength fortifier is easier to administer accurately and safely (1 sachet per 25 mL). Starting at half strength requires dose modification, powder division or a larger volume of breastmilk which increases the risk of contamination or error. Clear protocols and staff education should support consistent fortifier use.

Monitoring and evaluation

Monitor fortifier use, growth, NEC and refeeding outcomes in infants receiving different fortifier strategies.

Research priorities

None.

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26 In preterm infants does individualised fortification of EBM compared with standard fortified enteral feeds using commercially available fortifiers lead to shorter time to full enteral feeds improve growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?

RECOMMENDATION

CONDITIONAL

EtD 26

Routine individualised fortification of expressed breastmilk should not be used over standardised fortification for preterm infants.

Justification

While individualised fortification shows some potential benefits in intermediate growth outcomes, these gains are small, based on low to moderate certainty evidence and not consistently sustained at discharge. It is not clear whether increased fat mass is positive or negative. Importantly, there is no clear evidence of benefit for critical clinical outcomes such as mortality, NEC, sepsis or neurodevelopment, and the undesirable effects (e.g. increased complexity, resource demands) are notable. Individualised fortification requires significant investment in equipment, training, infrastructure and specialist staff. The resources required are substantial, and feasibility across all neonatal units, particularly those caring for pēpi Māori and Pacific infants may be limited. Without national-level investment, there is a significant risk of widening existing health inequities. Given these considerations, standardised fortification remains the more feasible, equitable and pragmatic option.

Subgroup considerations

Most evidence comes from studies involving very preterm and very low birthweight infants; effects for moderate-late preterm infants remain unclear. No data specific to pēpi Māori or Pacific infants were identified, limiting generalisability to priority populations in Aotearoa New Zealand. Infants with specific growth or biochemical concerns may still benefit from targeted, dietitian-led nutritional interventions.

Implementation considerations

If individualised fortification is used in specific clinical scenarios, it should only occur under the direction of a specialist neonatal dietitian with a clear clinical indication (e.g. documented faltering growth on standard fortification) in the context of local multidisciplinary team consensus with robust protocols and access to essential equipment, with a commitment to equity of access and outcome monitoring.

Monitoring and evaluation

If used in select cases, individualised fortification must be accompanied by robust monitoring. Track short-term outcomes (weight gain, growth velocity, feeding tolerance) and long-term developmental follow-up. Document adverse events (e.g. electrolyte disturbances, feeding intolerance, excessive weight gain). Monitor inequities in access and outcomes, particularly across hospital sites and among pēpi Māori and Pacific families.

Evaluate cost and resource use to ensure sustainability and value.

Research priorities

- High-quality trials comparing individualised vs. standard fortification in the Aotearoa New Zealand setting and including pēpi Māori, Pacific infants and underrepresented groups.
- Studies assessing neurodevelopmental outcomes and long-term body composition.
- Cost-effectiveness analyses in Aotearoa, including pēpi Māori-specific outcomes.
- Implementation research on models of fortification that are equitable and sustainable, especially in smaller or under-resourced units.

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27 Should early fortification vs. later fortification of expressed breastmilk be used for preterm infants?

RECOMMENDATION

CONDITIONAL

EtD 27

Fortification of breastmilk should begin at around 75–100 mL/kg/day of enteral feeds or once a feed volume of at least 5 mL is reached, rather than at lower volumes.

Justification

There is no compelling evidence to demonstrate the benefit of very early fortification. No evidence of benefit or harm, but very small numbers in trials, meaning we do not know if there is an effect or not. The consensus decision was based on this and the lack of feasibility of early fortification.

Subgroup considerations

Most infants were <2,000 g, with some studies including infants <1,500 g. There is no specific data for extremely preterm (<28 weeks) or pēpi Māori, Pacific peoples and underrepresented groups. Fortifier studies included human milk-based and bovine-based.

Implementation considerations

Most NICUs already have fortification protocols that vary by volume thresholds (e.g. at 80 mL/kg/day feed volume or when 5 mL every 2 hours is reached). Fortification at these thresholds is feasible with current feed preparation processes. This also allows time to seek parental consent for fortification.

Monitoring and evaluation

Key metrics to monitor and assess by ethnicity to monitor inequities are:

- Timing of fortification.
- Growth z-scores (especially weight and head circumference).
- Time to reach full enteral feeds.
- Rates of NEC and feeding.

Research priorities

- Trials assessing individualised vs. volume-based timing of fortification.
- Impact on bone health, metabolic markers and neurodevelopment.
- Inclusion of pēpi Māori, Pacific peoples and underrepresented groups.

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28 In preterm babies does human milk-based fortifier vs. bovine-based fortifier lead to shorter time to full enteral feeds, improve growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?

RECOMMENDATION

CONDITIONAL

EtD 28

Human milk-based fortifier is not recommended to fortify expressed breastmilk.

Justification

No significant effect on critical outcomes (NEC, mortality, neurodevelopment, adverse effects). High-cost differential: \$37,000–\$56,000 more per infant per admission. Evidence is imprecise, with wide confidence intervals crossing the line of no effect for most outcomes.

In the context of publicly funded neonatal care in Aotearoa New Zealand, the lack of demonstrated clinical benefit does not justify the cost.

Subgroup considerations

No evidence of differential effect by gestational age, birthweight, or ethnicity. Infants <1000 g or <28 weeks may be considered at higher risk of NEC, but current data do not support a tailored recommendation. Equity must be prioritised, restricting access to expensive interventions to only some populations risks widening disparities. Whānau Māori, Pacific families and underrepresented groups, who have higher rates of preterm birth and NEC, must not be disadvantaged by selective use.

Implementation considerations

No implementation considerations are required, given that bovine fortifier is widely used. A human milk-based fortifier is not currently available in New Zealand and would require regulatory approval, procurement contracts, ethical frameworks for its use and equity considerations. Clinical training and new protocols would also be necessary. The cost is prohibitive and would likely not be justifiable under existing neonatal health budgets. Cultural considerations around the use and commercialisation of human milk must be respected.

Monitoring and evaluation

None.

Research priorities

- Large, contemporary RCTs comparing human- vs. bovine-based fortifiers with adequate power for NEC and long-term outcomes in Aotearoa New Zealand, allowing for the recruitment of pēpi Māori, Pacific infants and underrepresented groups.
- Subgroup analyses by gestational age, birthweight and ethnicity.
- Cost-effectiveness modelling tailored to publicly funded health systems.
- Qualitative research on whānau Māori and Pacific families and underrepresented groups views on the commercialisation and use of human milk.

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29 In preterm infants does a preterm formula compared with a term formula lead to improved growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?

RECOMMENDATION

CONDITIONAL

EtD 29

Preterm formula, rather than term formula, should be used for infants born at <32 weeks or birthweight <2000 g when breastmilk is not available or is insufficient.

Justification

This recommendation is based on low to very low certainty evidence and moderate anticipated benefits, weighed against higher cost and analysis of outdated studies. Preterm formula is associated with modestly higher weight gain and head circumference growth in the short term. However, long-term growth outcomes (weight, length, HC at 18 months and 7.5–8 years) show no significant difference. There is a moderate improvement in psychomotor development at 18 months (MD ~6.5 points) and a possible small benefit for mental development with preterm formula. No clear effect on intelligence scores in later childhood.

Preterm formula does not appear to significantly increase NEC or mortality risk, but confidence intervals are wide. No significant adverse effects were reported; however, metabolic bone disease and cardiometabolic outcomes were not measured. Term formula does not meet the nutrient requirements of preterm infants. Potential benefit for neurodevelopment and growth. No evidence for adverse effects over term formula. The composition of preterm formulas has changed substantially since older trials, therefore, there is no evidence on which to recommend a change of practice to use term formula.

Subgroup considerations

In the absence of evidence to guide this subgroup recommendation, it is pragmatic to align the recommendation for which preterm infants should have preterm formula with the recommendation for breastmilk fortifier, i.e. Infants born at <32 weeks or birthweight <2,000 g.

Implementation considerations

Preterm formula is already in widespread use but consistency and availability is important. Ensure consistent protocols and avoid changing to term formula solely for cost reasons.

Consider clear documentation and rationale when selecting a term formula, especially for stable late preterm infants.

Monitoring and evaluation

Growth velocity and z-scores (weight, length, HC), NEC, sepsis and duration of NICU stay. Neurodevelopmental follow-up, where possible.

Research priorities

- Studies including moderate/late preterm, growth-restricted and Māori/Pacific/Indian infants.
- Composition and benefit/harm of preterm formula requires further research for our population using modern formulations of preterm and term formulas.
- Long-term follow-up of neurodevelopment, bone health, and metabolic outcomes.

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30 In preterm infants for whom there is insufficient mother's own breastmilk, does screened pasteurised donor milk vs. screened unpasteurised donor milk improve outcomes (infection, NEC, neurodevelopment, time to full enteral feeds, time to discharge, breastmilk feeding at discharge, growth)?

RECOMMENDATION

CONDITIONAL

EtD 30

Unpasteurised donor milk from a screened donor or pasteurised donor milk should be used for preterm infants for whom mother's own expressed breastmilk is not available. All neonatal units should have equitable access to donor milk.

Justification

Moderate-to-low-certainty evidence suggests that unpasteurised donor milk may shorten the time to achieve full enteral feeds compared with pasteurised donor milk, although effects on mortality and major morbidities remain uncertain. Given the potential benefits of unpasteurised donor milk and the established safety of pasteurised donor milk, either option may be appropriate when mother's own milk is unavailable, provided robust donor screening and safe handling practices are in place. Unpasteurised donor milk has a lower cost per infant compared to pasteurised milk and is more accessible, improving equity, especially for Māori, Pacific peoples and rural communities where pasteurised donor milk is inaccessible.

Subgroup considerations

Access to donor breastmilk in areas without a breastmilk bank would improve if unpasteurised, screened donor milk was used.

Implementation considerations

For unpasteurised breastmilk to be acceptable for use in neonatal care, the donor must be screened and tested for cytomegalovirus (CMV), human immunodeficiency virus type 1 (HIV-1), human immunodeficiency virus type 2 (HIV-2), hepatitis B virus (HBV), hepatitis C virus (HCV), human T-lymphotropic virus type 1 (HTLV-1), human T-lymphotropic virus type 2 (HTLV-2).

Monitoring and evaluation

Monitoring for infection rates, growth outcomes, breastfeeding rates at discharge and parental satisfaction should be incorporated. Special attention should be given to monitoring equity of access across regions and populations.

Research priorities

- Well-conducted RCTs comparing unpasteurised vs. pasteurised donor milk in diverse preterm populations.
- Research on neurodevelopmental outcomes and long-term safety.
- Studies on culturally appropriate models for donor milk banking and informal donation screening practices.
- Research into pēpi Māori, Pacific peoples and underrepresented groups experiences and preferences regarding donor milk access.

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31 Should higher feed osmolality (>450 mOsm/kg) vs. lower feed osmolality be used in preterm infants to reduce feed intolerance and/or necrotising enterocolitis?

RECOMMENDATION

CONDITIONAL

EtD 31

Enteral feeds should be selected based on factors other than osmolality. However, if the osmolality is very high (>600 mOsm/kg), consider practical steps to lower it, such as divided medication doses.

Justification

No evidence that feed osmolality ≤ 450 mOsm/kg reduces feed intolerance or NEC. The overall certainty of the evidence is very low, with minimal research on which to base a recommendation. While no consistent harms were identified, the biological plausibility of increased risk for NEC and feeding intolerance when osmolality exceeds 600 mOsm/kg warrants caution. No study demonstrated clear benefit from lower osmolality feeds on gastric emptying, feed tolerance, or NEC reduction. A precautionary approach is warranted due to the lack of proven benefit and theoretical risks, supporting a conditional recommendation to avoid routinely exceeding 600 mOsm/kg.

Subgroup considerations

Extremely preterm or low birthweight infants may be more susceptible to the effects of high osmolality feeds, though subgroup-specific evidence is lacking. Māori and Pacific pēpi, who are at greater risk for NEC, may face additional harm of higher osmolality feeds.

Implementation considerations

Consider total feed osmolality when combining fortifiers, supplements and medications. Ensure medications (e.g. multivitamins, iron) are diluted in adequate volumes of breastmilk or given in divided doses or separately from feeds if they are hyperosmolar. Avoid exceeding 600 mOsm/kg.

Monitoring and evaluation

None.

Research priorities

- Studies comparing feed tolerance and NEC rates across defined osmolality ranges (<450 vs. 450–600 vs. >600 mOsm/kg).
- Develop osmolality resources to include common feed mixtures, including additive interactions and preparation timing.
- Define minimum dilution volumes for common hyperosmolar medications to ensure safe administration.

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32 In preterm infants requiring a blood transfusion does withholding enteral feeds compared with not withholding enteral feeds improve outcomes for NEC, and aspiration (for extubation)? In preterm infants requiring extubation or an eye examination, does withholding enteral feeds compared with not withholding enteral feeds improve outcomes for NEC, and aspiration (for extubation)?

RECOMMENDATION**CONDITIONAL**

EtD 32

Withholding feeds for transfusion, extubation or eye screening examinations is not recommended. Continue providing feeds unless there is a clinical indication to do otherwise.

Justification

Studies have suggested potential benefits, but also risks associated with withholding feeds, such as sepsis, feed intolerance and delays in reaching full enteral feeding. No high-quality evidence was found that withholding feeds for transfusion, extubation or eye examinations is beneficial.

Subgroup considerations

None.

Implementation considerations

None.

Monitoring and evaluation

None.

Research priorities

- Large RCTs comparing withholding vs. continuing feeds during transfusion, especially in extremely preterm and very low birthweight infants, including specific reporting of ethnicity and outcomes.
- The WHEAT RCT may provide this evidence.
- Studies are needed to assess outcomes around withholding feeds for extubation and eye examination.

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33 What is the recommended enteral fluid intake?

RECOMMENDATION

CONDITIONAL

EtD 33

Full enteral feeds of 180 mL/kg/day should be used for extremely low birthweight infants. Higher enteral volume may be needed if growth is faltering. For other preterm infants, we recommend the enteral fluid intake that is needed for appropriate growth.

Justification

This recommendation is based on expert opinion. Current evidence shows enhanced short-term weight gain with higher volumes but no demonstrated long-term clinical benefit or harm. However, the sample size is small and the proxy outcome is weight, not growth. The certainty of evidence ranges from high for weight gain to very low for long-term outcomes such as growth <10th centile at 12 months' corrected age. Given this uncertainty, a flexible approach, either higher or lower volumes, is appropriate, allowing clinicians to tailor fluid management to individual infant needs while recognising both strategies are reasonable.

Subgroup considerations

Infants who are not receiving breastmilk fortifier will likely require >180 mL/kg/day to grow well. For infants receiving <180 mL/kg/day with faltering growth, the first step is to increase enteral feed volume.

Implementation considerations

Maintain flexibility in clinical practice to use either approach. Local protocols should define the rationale for selecting higher or lower volumes based on clinical and nutritional needs. Ensure that neonatal staff are trained to monitor growth trends and adjust fluid plans as needed.

Monitoring and evaluation

Track fluid intake practices across units and compare growth outcomes, feeding tolerance, and incidence of complications. Include equity audits to ensure fluid targets are being applied consistently across diverse populations and settings.

Research priorities

- RCTs comparing fluid strategies with longer-term follow-up, particularly neurodevelopment and body composition.
- Investigate optimal fluid targets in specific subgroups (e.g. ELBW, growth-restricted infants), including in pēpi Māori, Pacific peoples and underrepresented groups and rural populations.

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34 What is the recommended enteral nutritional intake by postnatal age of energy, protein, carbohydrates, lipids, sodium, potassium and chloride, calcium, phosphorus and magnesium and trace elements: e.g. iron, selenium, iodine, chromium, copper, manganese, molybdenum, fluoride?

RECOMMENDATION

ADOPTED

AA 34

Provide enteral nutrient intakes for preterm infants according to ESPGHAN 2022 guidance. Use individualised plans considering gestational age, tolerance and clinical status. Monitor growth and biochemical markers routinely. As Aotearoa New Zealand soil is deficient in iodine, selenium and zinc, use the upper half of the recommended intake.

Enteral nutrient	Recommended intake/kg/day	Enteral nutrient	Recommended intake/kg/day
Energy	115 to 140–160 kcal	Chromium	0.03 to 2.25 µg
Protein	3.5 to 4.0–4.5 g	Molybdenum	0.3 to 5.0 µg
Carbohydrates	11 to 15–17 g	Thiamine (B1)	140 to 290 µg
Lipids	4.8 to 8.1 g	Pantothenic acid	0.6 to 2.2 mg
Sodium	3.0 to 5.0–8.0 mmol	Biotin	3.5 to 15 µg
Chloride	3.0 to 5.0–8.0 mmol	Niacin	1100 to 5700 µg
Potassium	2.3 to 4.6 mmol	Vitamin C	17 to 43 mg
Calcium	3.0 to 5.0 mmol	Riboflavin (B2)	200 to 430 µg
Phosphorus	2.2 to 3.7 mmol	Pyridoxine	70 to 290 µg
Magnesium	0.4 to 0.5 mmol	Folic acid	23 to 100 µg
Iron	2.0 to 3.0–6.0 mg	Cobalamin (B12)	0.1 to 0.6 µg
Copper	120 to 230 µg	Vitamin A	400 to 1000 µg (1332 to 3330 IU)
Selenium	7 to 10 µg	Vitamin D	10 to 25 µg (400 to 1000 IU)
Manganese	1 to 15 µg	Vitamin E	2.2 to 11 mg
Iodine	11 to 55 µg	Vitamin K	4.4 to 28 µg
Zinc	2 to 3 mg		

Subgroup considerations

Infants <28 weeks or with comorbidities may need higher nutrition intakes.

Implementation considerations

Availability of specific micronutrients and trained staff to support implementation may vary.

Monitoring and evaluation

Audit nutritional intakes, biochemical and anthropometric outcomes regularly.

Research priorities

- More data needed on long-term outcomes of specific micronutrient intakes and optimal timing, specifically for iodine, selenium and zinc.

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35 In preterm infants receiving enteral feeds does enteral additional protein intake improve growth, clinical outcomes or neurodevelopment, or reduce NEC, gastrointestinal complications or less metabolic bone disease?

RECOMMENDATION

CONDITIONAL

EtD 35

Routine protein supplementation (in addition to breastmilk fortification) should not be used. Aim for the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) enteral protein intake recommendation of 3.5 to 4.0 g/kg/day, which may be increased up to 4.5 g/kg/day with a corresponding increase in energy intake where growth is considered too slow.

Justification

Routine additional protein supplementation over baseline is not justified on the evidence. High-certainty evidence supports improved weight gain with additional protein. Gains in length and head circumference are more modest and less certain but directionally favourable. No high-quality evidence of benefit or harm on neurodevelopment, mortality, or NEC. Requires additional dietetic resources, which may limit its acceptability in some neonatal units.

Subgroup considerations

Enteral protein supplementation may be beneficial when growth is faltering or recommended enteral protein intakes are not met.

Implementation considerations

Use should be guided by growth and intake targets, especially where breastmilk fortifier is unavailable or insufficient. Protein powders used must be appropriate for neonatal use and balanced with overall energy intake. Oversight by a neonatal dietitian is needed to ensure individualisation and nutritional adequacy.

Monitoring and evaluation

Track protein intake (g/kg/day), weekly weight, length and head circumference growth outcomes (z-scores) and any adverse effects.

Research priorities

- RCTs with long-term neurodevelopmental outcomes of different protein doses and timing, including for pēpi Māori, Pacific peoples and underrepresented groups.

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36 Should routine glucose polymer supplementation vs. no supplementation be used in preterm infants receiving enteral feeds?

RECOMMENDATION

CONDITIONAL

EtD 36

Routine supplementation of breastmilk with glucose polymer powder is not recommended.

Justification

One small study shows very low-quality evidence of the effects of carbohydrate supplementation of breastmilk in preterm infants. There was a significant effect on weight gain but not on length or head circumference and no data on the short- and long-term health benefits and harms in this population.

Subgroup considerations

Even for groups at risk of growth faltering, evidence is required for an important outcome before this can be recommended.

Implementation considerations

None.

Monitoring and evaluation

None.

Research priorities

- We do not envisage that further trials of glucose polymers will be conducted, except as a component of multi-nutrient breastmilk fortification.

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37 Should routine fat supplementation vs. no supplementation be used in preterm infants receiving enteral feeds?

RECOMMENDATION

CONDITIONAL

EtD 37

Routine enteral fat supplementation is not recommended. Enteral fat supplementation may be beneficial when there is a high energy requirement and faltering growth but should not be used where there is insufficient feed volume and an inadequate intake of other nutrients, such as protein, vitamins and minerals.

Justification

Very low-quality evidence means that there is uncertainty about the effect of fat supplementation on all outcomes.

Subgroup considerations

There may be a subgroup of infants who might benefit (e.g. infants with congenital heart disease) who have restricted fluid intake and high energy needs.

Implementation considerations

Fat supplementation should only be prescribed on specialist advice in consultation with a neonatal dietitian.

Monitoring and evaluation

Growth monitoring (weight, length, head circumference) post commencement of fat supplementation, feed tolerance and gastrointestinal symptoms, nutritional intake (protein, energy balance) and clinical and breastfeeding at discharge outcomes.

Research priorities

- Well-powered RCTs comparing fat supplementation with standard care in different gestational age and weight groups, focusing on body composition, neurodevelopment and long-term cardiometabolic outcomes.
- Equity-focused implementation studies to ensure appropriate use across ethnic and regional groups.

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38 In preterm babies receiving enteral feeds does routine additional vitamin A, vitamin D or folic acid supplementation compared with no supplementation improve growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?

RECOMMENDATION

CONDITIONAL

EtD 15

Routine supplementation of Vitamin D is recommended. The suggested dose is 2 drops (800 IU) cholecalciferol per day for all preterm infants, reducing to 1 drop (400 IU) cholecalciferol at discharge or 40 weeks gestational age (or term corrected). Routine supplementation of other vitamins is not supported by the evidence.

Justification

There is evidence of better outcomes with Vitamin A and D supplementation without harm at low overall cost. However, intramuscular vitamin A injections may not be feasible or acceptable in the NZ setting. There is moderate to very low certainty of evidence overall. A few outcomes, such as reduction in retinopathy of prematurity (Vitamin A) and bronchopulmonary dysplasia (Vitamin C and D), suggest potential benefits with higher vitamin intake. However, most outcomes show no statistically significant difference between higher and lower doses, and the precision is low across many estimates, with wide confidence intervals and small sample sizes. Despite the limited evidence, the anticipated desirable effects on important outcomes and the very low risk of harm (with no significant increase in adverse outcomes) support a cautious, conditional recommendation in favour of higher vitamin intake. Cost is trivial, and feasibility and acceptability are high, particularly given this practice is already part of standard care in Aotearoa New Zealand.

Subgroup considerations

Supplementation may offer increased benefit to populations at high risk of deficiency.

Implementation considerations

Close monitoring of individual vitamin intakes is warranted due to wide recommended ranges and the potential risk of providing excessive supplementation e.g. vitamin E, which is provided in very high doses in SMOFLipid emulsion. Where available, aiming for ESPGHAN dosing may assist standardisation. Family education and culturally safe communication should be prioritised, especially when engaging with whānau Māori, Pacific peoples and underrepresented groups.

Monitoring and evaluation

Monitor for signs of both deficiency and toxicity, with appropriate lab tests where indicated (will need to give guidance on the timing of testing and what to do with results e.g. increase/decrease supplementation and when to recheck) Consider including vitamin supplementation data in national neonatal audits to inform future quality improvement and research.

Research priorities

- RCTs of individual and combined vitamins in preterm infants (stratified by gestational age), with appropriate pēpi Māori, Pacific peoples and underrepresented groups representation.
- Pharmacokinetic studies to determine vitamin stability and optimal dosing in diverse preterm populations.
- Research to clarify the role of maternal vitamin status, particularly vitamin D, on neonatal outcomes and maternal supplementation as an option to increase vitamin intakes from breastmilk if feasible. Economic evaluations of vitamin supplementation strategies.
- Evaluation of long-term outcomes, including school-age development.

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39 In preterm infants who are enterally fed does routine zinc supplementation and monitoring compared with no routine supplementation and zinc monitoring reduce the incidence of zinc deficiency, faltering growth, reduced immune function and impaired neurodevelopment?

RECOMMENDATION

CONDITIONAL

EtD 39

Routine enteral zinc supplementation (5 to 10 mg/day) should be used for all preterm infants until full oral feeds (no tube feeds), term or discharge from neonatal care.

Justification

Moderate-certainty evidence shows zinc supplementation reduces mortality and improves linear growth and weight gain and is associated with improved neurodevelopmental outcomes. Supplemented infants demonstrated significantly increased serum zinc levels. While effects on head circumference and sepsis were uncertain, supplementation reduced the risk of diarrhoea and showed no harm. Given the known low zinc levels in Aotearoa New Zealand soil and the low cost of supplementation, the balance of effects favours the intervention, even with variable evidence quality across outcomes.

Subgroup considerations

Extremely preterm infants (<28 weeks) and VLBW infants (<1500 g) have higher zinc requirements and greater risk of deficiency. Infants with gastrointestinal losses may require individualised higher doses and monitoring. Infants of vegan or vegetarian mothers or from population groups with low zinc intakes (including some Māori, Pacific and refugee/migrant families), may benefit more from supplementation. No subgroup data are available for pēpi Māori or Pacific infants, but these groups face disproportionate health and nutrition inequities, supporting a universal rather than selective approach to supplementation.

Implementation considerations

Zinc should be routinely supplemented, ideally starting when enteral feeds are established. This zinc supplementation is in addition to that received from fortified breastmilk or preterm formula.

Continue zinc supplementation until full oral feeds (no tube feeds), term or discharge from neonatal care.

Monitoring and evaluation

Growth monitoring (weight, length, head circumference) is the primary indicator of effectiveness.

Monitoring serum zinc concentrations may be considered in infants with faltering growth, especially for infants with a stoma.

Audit zinc prescribing, administration and growth outcomes, disaggregated by ethnicity and gestational age.

Research priorities

- High-quality trials assessing the long-term neurodevelopmental impact of zinc supplementation.
- Dose-response studies to refine optimal dosing strategies across different gestational and birthweight strata.
- Cost-effectiveness analyses in the Aotearoa New Zealand context.
- Evaluation of combined micronutrient strategies including zinc and their synergistic effects on growth and infection outcomes including for pēpi Māori, Pacific families and underrepresented groups.

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40 Is switching from fortified EBM/preterm formula vs. to unfortified EBM/ term formula recommended in preterm infants before discharge or term?

RECOMMENDATION

CONDITIONAL

EtD 40

Breastmilk fortifier or preterm formula should be continued until preparing for discharge or until weight gain is excessive. Stopping breastmilk fortifier or preterm formula at a specific weight or gestational age is not recommended.

Justification

No eligible studies were identified for this specific question. Therefore, the recommendation is based on expert opinion of the theoretical benefits and harms. Continuing fortified EBM or preterm formula until term-equivalent age provides substantially more energy and protein, reducing the risk of faltering growth and nutrient deficiencies. Switching to unfortified EBM or term formula may be appropriate in selected infants who are clinically well, growing appropriately and preparing for exclusive breastfeeding or discharge. An abrupt switch at 36 weeks or 2500 g is physiologically arbitrary and may not meet the ongoing nutrient needs of some preterm infants.

Subgroup considerations

All regional centres have access to breastmilk fortifier and preterm formula, and these should be available at all times.

Implementation considerations

Educate staff on the risks of growth inadequacy and nutrient deficiencies that occur after stopping fortifier or preterm formula too early.

Monitoring and evaluation

Monitor:

- Growth parameters (weight, length, head circumference).
- Micronutrient supplementation needs after discontinuing fortifier (e.g. iron, vitamins).
- Time to discharge and post-discharge feeding and growth.

Research priorities

RCTs or high-quality observational studies comparing:

- Timing of fortifier or preterm formula discontinuation (e.g. at 36 weeks vs. term).
- Outcomes such as growth, neurodevelopment, breastfeeding duration and discharge timing.
- Evaluation of gradual weaning strategies (e.g. reducing feed volumes while maintaining fortification).

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41 Should exposure to the smell or taste (or both) of breastmilk or formula administered with tube feeds vs. no exposure be used for preterm infants who are fed via an orogastric or nasogastric tube?

RECOMMENDATION

CONDITIONAL

EtD 41

Smell and taste of breastmilk or infant formula should be provided before all enteral tube feeds.

Justification

Recommendation is based on very low certainty evidence suggesting potential benefits, including a reduction in neurodevelopmental impairment at 2 years with no evidence of harm. While there is no consistent improvement in feeding progression, growth or enteral tolerance, the intervention is low-cost, non-invasive, and feasible in many NICU settings.

Subgroup considerations

We are unsure if smell and taste of the feed should be used in infants <32 weeks' gestation, as there is minimal research in this group. No significant subgroup analyses have been published, but pēpi Māori were included in the DIAMOND trial (15.8%). No differential effects have been shown by gestational age or birthweight.

Implementation considerations

Given the limited evidence and potential for benefit, implementation should be cautious and prioritise equity and cultural safety. Ensuring equitable implementation requires consistent protocols, staff training and meaningful engagement with families to make this practice part of respectful and inclusive neonatal care. Implementation is feasible in most neonatal units with minor workflow adjustments; requires minimal additional resources (e.g. small volumes of milk, swabs/syringes). Staff education and written protocols are needed to ensure consistent delivery and documentation. Must be culturally appropriate, incorporating whānau involvement and sensitivity to parental consent and communication needs. Consider alignment with other feeding protocols and guidelines to promote acceptance by nursing staff.

Monitoring and evaluation

Track implementation among staff and monitor the following outcomes: Time to full enteral feeds and sucking feeds, duration of hospital stay and parent and staff acceptability. Include ethnicity data. Where possible, align with neurodevelopmental follow-up to assess long-term impact.

Research priorities

Larger multicentre RCTs to assess the impact on:

- Neurodevelopment, especially for extremely and very preterm infants.
- Feeding outcomes, body composition, and clinical complications.
- Health economic evaluations in Aotearoa New Zealand settings.
- Qualitative studies exploring parent and staff perspectives, including whānau Māori, Pacific families and underrepresented groups on acceptability.
- Equity-focused implementation research, especially in under-resourced neonatal units.

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03

TOPIC 3

Breastmilk & Breastfeeding

Supporting lactation, expressing, skin-to-skin, and the transition to breastfeeding for preterm pēpi and their whānau.

“With breastfeeding, they are also giving some tips as well, not only lactation consultants but also nurses, which is good as well, because everyone is different and a bit different tips as well, so I find it very helpful.

Not only doctors but also nurses and liaison officers and all the group people who are working here as a collaborate group, it's very helpful, the information we are getting from them. So yeah, we find it helpful.”

“It's a nice feeling, just having her there and close to you, but also this feeling like it's something you can do to help, because right now you do feel like there's not a huge amount you can do, so for me it's like being able to produce breastmilk, doing the skin to skin, and doing the cares are the main things you can do right now to help her develop and grow.”

“When my baby came at 27 weeks, I got to be in their surroundings only for the first two weeks. After that, there has been a huge distance between me and them. Physical distance, I mean. Proximity plays a huge influence on creating breastmilk, and not only that, creating a connection with your kid, and that is why if there's more that can be done to keep mothers in proximity with their little children, I think those kids do better. They will cost less on your system in the long run.”

“You just need to look after yourself and if you look after yourself you produce good milk for your baby ... take care of yourself because if you're well, then your baby is well.”

42 Does breastmilk expression within six hours of birth increase expressed milk volumes and breastfeeding/breastmilk feeding at discharge? Does the frequent expression of breastmilk (minimum of 8 times in 24 hours) after preterm birth reduce the risk of low lactation for the mother? Does double pumping increase mothers' milk supply compared to single/consecutive breast pumping?

RECOMMENDATION

CONDITIONAL

EtD 42a

EtD 42b

EtD 42c

Mothers should be supported to express early (<6 hours post birth), frequently (≥8 times/day) and by double pumping their breastmilk.

Justification

Early expression (<6 hours post birth) is consistently associated with increased breastmilk volume on day 4 and day 14. Double pumping leads to higher yield, but frequent, early expression appears to have the greatest impact when combined. Frequent expression (≥8 times/day) is associated with significantly greater milk yields than <6 times/day. Encouraging early, frequent expression may help reduce disparities, improve milk supply, and promote long-term breastfeeding.

Subgroup considerations

Moderate-to-late preterm infants have suboptimal breastfeeding outcomes and should be an area of focus. Whānau Māori may benefit most from prioritised support for early and frequent milk expression to improve equity.

Implementation considerations

Education about the importance of early and frequent expression antenatally (wherever feasible) or immediately postpartum. Equitable access to high-quality breastmilk pumps (especially for mothers at home). Culturally safe healthcare experience and emotional support for mothers overwhelmed by NICU stress. Early expression within 6 hours can be difficult post-emergency birth, or if mother and infant are separated and rely on support of the midwife post birth.

Access to skilled lactation support is essential for establishing and maintaining breastfeeding in neonatal settings, particularly for preterm and medically complex infants. Workforce planning, funding, and equitable access to International Board Certified Lactation Consultant-level support are recognised as important implementation considerations.

Education for health professionals should be provided on establishing milk supply, expression management, transition to breastfeeding and protection of lactation during periods of mother-infant separation.

Greater recognition of the practical barriers that some whānau face when establishing and maintaining lactation is needed, including:

- geographical distance from neonatal services;
- separation of māmā and pēpi;
- financial pressures associated with travel and accommodation;
- access to breast pumps and expressing equipment;
- availability of lactation support following discharge.

Addressing these barriers through service planning, workforce development and infrastructure investment will be important to achieving equitable outcomes. Consideration should be given to neonatal environments and models of care that enable māmā and pēpi to remain together wherever possible, recognising the importance of parental presence, skin-to-skin care and breastfeeding support for both infant and maternal outcomes.

Monitoring and evaluation

Track and report by ethnicity and gestational age:

- Timing of first breastmilk expression.
- Frequency per 24 hours over first 7–14 days.
- The proportion of preterm infants receiving mother's own milk only at days 3, 7 and 14, and exclusive breastfeeding rates at discharge.

Research priorities

- Randomised trials comparing bundled interventions (timing + frequency + method).
- Data on whānau Māori experience and effectiveness of culturally adapted lactation support.
- Impact on clinical outcomes like NEC, sepsis and time to full enteral feeds.
- Evaluation of maternal wellbeing and acceptability of different expression regimens.
- Whānau Māori experiences of the enablers for early, frequent double pumping to be supported.

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43 Should the first feed for preterm infants be mother's expressed breastmilk vs. other milk to reduce the risk of mothers discontinuing optimal expressing or breastfeeding?

RECOMMENDATION

CONDITIONAL

EtD 43

Infants should receive only mother's own milk for the infant's first feed whenever possible, to support the continuation of expressing and breastfeeding.

Justification

While the evidence is of very low certainty and largely observational, consistent findings across multiple studies suggest that providing mother's own milk as the first feed is associated with higher rates of breastmilk feeding at discharge. Delaying the introduction of alternative milk (formula or donor milk) also appears to improve breastfeeding outcomes. The intervention is aligned with maternal values if they intend to breastfeed, culturally important for whānau Māori, and has the potential to promote equity.

Subgroup considerations

Pēpi Māori and infants from underrepresented ethnic groups are less likely to receive mother's milk as the first feed. They are also significantly less likely to be exclusively breastfed at discharge. Ensuring mother's own milk is used for the first feed could improve equity outcomes for these populations.

Implementation considerations

Implement policies that prioritise timely lactation support and access to expressing equipment immediately after birth. Ensure all staff are trained to support mothers with early expression and understand the importance of the first feed. Include clear documentation protocols to record the type of first feed given. Ensure culturally safe communication with whānau Māori and Pacific families about feeding options and implications.

Monitoring and evaluation

Audit rates of first feed type (mother's EBM vs. donor/formula) by ethnicity, gestational age, and birthweight. Monitor exclusive breastmilk feeding at discharge across all subgroups.

Incorporate feedback from families, particularly Māori and Pacific whānau, on their experiences of lactation support and feeding decisions.

Research priorities

- High-quality prospective studies examining the impact of first feed type on long-term breastfeeding outcomes.
- Implementation studies evaluating structured first-feed protocols on equity and breastfeeding continuation.
- Qualitative research on maternal experiences and decision-making related to early feeding, with an equity lens.

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44 Should mothers of preterm infants have access to lactation consultant services vs. no access to lactation consultant services?

RECOMMENDATION

CONDITIONAL

EtD 44

Specialist neonatal lactation consultants should be embedded within the multidisciplinary neonatal care team.

Justification

While the overall certainty of evidence is very low, the direction of effect favours the intervention, with likely benefits across a range of important outcomes such as earlier provision of breastmilk, increased any breastmilk use during hospital stay and reduced time to full enteral feeds. There is no evidence of harm, and the equity implications may be significant for whānau Māori, Pacific families and underserved groups. Lactation consultants offer critical, targeted support for parents navigating the complex challenges of establishing and maintaining lactation while their infant is in neonatal care. The intervention is likely acceptable to parents and clinicians. While there are cost implications, these could be offset by reduced NICU stay and improved long-term health outcomes. Increasing breastmilk supply and the ability for mothers to breastfeed is an important outcome and the evidence indicates lactation consultants do this.

Subgroup considerations

No specific subgroup analyses were available for extremely preterm or low birthweight infants, but these groups may stand to benefit the most from targeted lactation support. Target and prioritised lactation support is also likely to benefit whānau Māori, Pacific families and underrepresented groups who experience structural barriers to breastfeeding and are more likely to be affected by preterm birth.

Implementation considerations

Lactation consultants should be prioritised for units with the highest rates of preterm births and inequities in breastfeeding outcomes and be available 7 days a week. Services need to be culturally appropriate and delivered in ways that are responsive to the needs of Māori, Pacific and other priority populations. Consider shared care models (e.g. trained lactation nurses, peer supporters) where specialist lactation consultant FTE is limited. Training, protocols and collaboration with midwifery and neonatal teams will be important in the implementation. Workforce planning and ongoing resourcing (e.g. breast pumps, education tools) are essential to sustainability.

Monitoring and evaluation

Track lactation consultant services and breastfeeding outcomes by neonatal unit. Audit time to first breastmilk expression, duration of expression support, and engagement with lactation services. Evaluate impact on time to full enteral feeds, NICU stay and parent-reported experience measures. Collect data by ethnicity and gestational age to evaluate equity impacts

Research priorities

- Research into the cost-effectiveness of lactation consultant services in reducing length of stay and improving breastfeeding rates.
- Explore different models of lactation support delivery (e.g. videos, apps, pamphlets).
- Investigate barriers to access, uptake and impact on long-term breastfeeding continuation and infant outcomes.
- Investigate all of the above by ethnicity.

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45 Should skin-to-skin care vs. no skin-to-skin care be used for mothers of preterm infants to improve breastfeeding and clinical and growth outcomes?

RECOMMENDATION

STRONG

EtD 45

Ongoing, skin-to-skin care should be initiated as early and as often as possible, prioritising mother–infant contact to support lactation, while actively encouraging fathers or partners to provide skin-to-skin care when the mother is unavailable or in addition to maternal contact.

Justification

Skin-to-skin care should be used routinely as it is beneficial and free with known benefits for infants and whānau. Moderate to high certainty evidence shows skin-to-skin care increases the likelihood of exclusive breastfeeding at discharge by 50% and improves breastmilk supply. High-certainty evidence shows skin-to-skin care reduces mortality by 30%, particularly when initiated early. Moderate to low certainty evidence shows large reductions in both hypothermia and hypoglycaemia. Moderate certainty evidence indicates reduced nosocomial infection risk. Low-certainty evidence supports improved weight gain, length, and head circumference. Skin-to-skin care is associated with reduced length of hospital stay and lower healthcare costs. Overall, strong evidence of benefit, no convincing evidence of harm and potential cost savings.

Subgroup considerations

While the evidence includes a range of gestational ages and birthweights, most studies involved low- and very-low birthweight infants. There is less data specific to extremely preterm infants (<28 weeks); however, early initiation of skin-to-skin care is likely to be safe and beneficial with clinical oversight.

Implementation considerations

Barriers may include a lack of private spaces (this has been reported in our interviews), staffing to support parents, or clinician hesitation in unstable infants or with umbilical catheters. Facilitators are education, whānau-centred NICU design, peer support and clear policies promoting skin-to-skin early and often. Ensure that whānau Māori have culturally safe support to participate in skin-to-skin care. Early initiation is critical: within 24 hours where feasible. Pēpi

Māori and Pacific families: Implementation should be prioritised due to the potential to increase equity in breastfeeding and health outcomes. Skin-to-skin care may help redress these inequities by promoting bonding, milk supply, and cultural connection. We suggest exploring whānau perspectives and tikanga expert opinion on how it might be framed as traditional practice.

Monitoring and evaluation

Collect and report data on (by ethnicity): rates of skin-to-skin care initiation (add as a Key Performance Indicator for Australian and New Zealand Neonatal Network), duration per day, timing (early vs. late) and breastfeeding outcomes at discharge, whānau experience and satisfaction.

Research priorities

- Acceptability and cultural preferences of skin-to-skin care for whānau Māori, Pacific families and underrepresented groups.
- Implementation strategies in resource-limited or high-acuity settings.
- Use of skin-to-skin care with extremely preterm or medically fragile infants.

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46 Should additional staff-related interventions vs. standard care be used for improving breastfeeding outcomes in whānau of preterm infants in NICU?

RECOMMENDATION

CONDITIONAL

EtD 46

Provide timely, proactive, specialised staff-led lactation and breastfeeding support, additional targeted staff training and involvement of all NICU staff in lactation and breastfeeding support as an addition to standard care to improve breastfeeding outcomes.

Justification

Although most of the evidence is of low certainty, the direction consistently favours improved breastfeeding outcomes, particularly early expression, milk supply, and exclusive breastfeeding at discharge. Qualitative evidence strongly reinforces that dedicated staff support is essential, valued by whānau, and likely to improve breastfeeding success. Undesirable effects are uncertain and probably small.

Subgroup considerations

Whānau Māori and those with lower access to lactation/breastfeeding support may experience the greatest benefit, given known inequities in breastfeeding outcomes. Effects may differ by gestational age, with parents of extremely preterm or long-stay infants requiring more sustained support. Tailoring to cultural needs and communication preferences is important.

Implementation considerations

Implementation depends on staffing capacity, training, and the design of services. Additional staff time, lactation expertise, or structured programmes may be required. Services will need to ensure culturally safe, skilled, consistent, whānau-centred approaches and consider partnering with Māori to co-design support. Costs and workforce pressures may be barriers.

Monitoring and evaluation

If implemented, services should monitor breastfeeding outcomes (e.g. early expression, exclusive breastfeeding at discharge, breastfeeding after discharge), whānau experience measures, cultural safety, and any unintended impacts on workload or service flow. Equity impacts, particularly for Māori whānau, should be routinely reviewed.

Research priorities

- Further high-quality research is needed to evaluate specific staff-related support models in NICU, including culturally grounded approaches.
- Priority areas include effectiveness on breastfeeding outcomes, long-term infant health, cost-effectiveness, and the impact on equity for Māori and other underserved groups.

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47 Should mana-enhancing tikanga practices be incorporated to support whānau Māori breastfeeding?

RECOMMENDATION

CONDITIONAL

EtD 47

Mana-enhancing tikanga practices that support whānau Māori breastfeeding and Te Ao Māori values (e.g. whanaungatanga, manaakitanga) should be incorporated as part of good clinical care to support breastfeeding. Māmā Māori would like to have a whānau approach (e.g. include Kuia, sisters, partner) to support breastfeeding.

Justification

Evidence (mainly qualitative and from broader Māori populations) suggests tikanga-aligned practices support breastfeeding, strengthen whānau involvement and improve cultural safety. No major harms were identified, but the effectiveness in preterm infants is uncertain. Despite low certainty within the preterm population, the likely benefits and alignment with Te Tiriti support a conditional recommendation. Enacting this will contribute to increasing health equity for Māori.

Subgroup considerations

Interventions may be easier to implement for moderate-late preterm infants than for extremely preterm or medically complex pēpi. First-time mothers and whānau with fewer supports may need tailored approaches. Regional resourcing, urban/rural differences and deprivation may influence feasibility and effectiveness.

Implementation considerations

Implementation should be Māori-led and co-designed, with staff training in tikanga, support for whānau involvement, and strengthened lactation support both in NICU and post-discharge. Ensure policies enable skin-to-skin, minimise separation where safe and provide adequate resources for equipment and specialist support.

Monitoring and evaluation

Track breastmilk feeding during admission and breastfeeding rates at discharge and post-discharge, monitor equity gaps between Māori and non-Māori, gather whānau feedback, and review staff training uptake.

Research priorities

- Further research into which aspect is the most effective in supporting wāhine Māori to achieve exclusive breastfeeding.
- Prioritise NICU-specific, Māori-led implementation studies, trials evaluating breastfeeding outcomes in preterm infants, equity-focused research, and work assessing which components of tikanga-aligned breastfeeding support are most effective.

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04

TOPIC 4

Monitoring Nutrition & Growth

Assessing growth, biochemical monitoring and how to respond when growth falters.

“When I see my baby growing and when they weigh him, I always look forward to that. To me, it made me have a bit more peace, knowing that as he grows older, as he gains more weight, he will be able to handle those situations. Not as fragile, not as tiny, not as weak, and he’s more independent, I mean, he’s breathing on his own. When he reaches those milestones, it gives me such comfort and peace and hope”

“It’s still sort of fresh (first time meeting baby after birth), but just every day looking at her, how much she’s grown, put on clothes already. We can see the light at the end of the tunnel at least now, that yes, we will be taking her home soon”

- 48 Monitoring parameters and equipment/tools: What equipment and monitoring tools i.e. growth charts, are recommended for accurately measuring and monitoring the growth of neonates? What specific growth parameters (e.g. weight, length, head circumference, BMI) should be included in growth monitoring, and how frequently should they be monitored?**
- 49**

RECOMMENDATION**ADAPTED****STRONG****AA 48**

Measure weight, length and head circumference at least weekly. Use calibrated digital scales (to nearest 5 g) for weight, a neonatometer for length (to nearest mm) and non-stretch tape for head circumference. Apply Fenton 2025 growth charts from birth to 50 weeks post-menstrual age, then switch to WHO standards. Correct for gestational age up to 2 years.

Subgroup considerations

Particularly important in very preterm or growth-restricted infants where early deviations have long-term consequences.

Implementation considerations

Units should ensure access to standard equipment and train staff in correct technique and use of growth charts.

Monitoring and evaluation

Audit compliance with measurement protocols and consistency in growth chart use.

Research priorities

- Further research needed on the accuracy of growth tools in extreme prematurity and long-term outcomes based on early monitoring trends.

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50 What are acceptable growth goals for appropriate for gestational age (AGA) and small for gestational age (SGA) infants?

RECOMMENDATION

ADOPTED

STRONG

AA 50

Nutritional management and growth assessment for infants born with fetal growth restriction and/or SGA should be the same as those born AGA, although initial weight loss is often less (up to 7% of birthweight is acceptable).

Subgroup considerations

Extremely preterm and SGA infants may require nuanced plans based on clinical complexity.

Implementation considerations

Requires multidisciplinary input and education to avoid overtreatment. To calculate z-score, use the NeoGrowth Fenton 2025 (iOS) or AnthroCalc (Android) mobile phone application.

Monitoring and evaluation

Track longitudinal growth and ensure proportionality of weight and length gain.

Research priorities

- More evidence needed on long-term outcomes of different SGA growth trajectories and the best nutrition practices.

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51 What is the definition of faltering growth that requires attention or nutritional intervention for preterm infants?

RECOMMENDATION

CONDITIONAL

EtD 51

Assess after 2–3 weeks of age, and once birthweight is regained. Use these recommendations to screen for and intervene to resolve faltering growth:

Weight z-score change from birth

To calculate z-score, use the NeoGrowth Fenton 2025 (iOS) or AnthroCalc (Android) mobile phone application.

- Infants with mild malnutrition (loss of >0.8 z-score) may require a higher feed volume/nutrient intake.
- Infants with moderate malnutrition (loss of >1.2 z-score) should be referred to a neonatal dietitian for individual assessment of their growth and intervention if needed.

Justification

Until there is a clearer definition of when nutritional intervention is required with faltering growth in preterm infants, it is reasonable to use international recommendations suggested by (Goldberg et al., 2018) to screen for and characterise faltering growth.

Subgroup considerations

ELBW infants may follow different growth trajectories and require earlier and more frequent monitoring. No specific evidence was found for Māori or Pacific infants, but systemic factors affecting growth (e.g. access to lactation support, early nutrition and hospital resource variation) must be considered when applying thresholds across populations.

Implementation considerations

Use serial growth monitoring using weight, length and head circumference z-scores with validated preterm growth charts (e.g. Fenton 2025). Train neonatal teams in interpreting growth trajectories and z-score changes.

Monitoring and evaluation

Monitor implementation through routine audit of adherence to the recommended screening criteria, documentation of growth assessment methods and appropriateness and timeliness of dietitian referral. Findings should be reviewed regularly to support quality improvement and consistent application across services.

Research priorities

- What faltering growth criteria are associated with adverse outcomes in preterm infants?
- Does screening for growth faltering in preterm infants reduce morbidity or adverse outcomes?

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52 Biochemical monitoring to monitor parenteral nutritional adequacy and tolerance. If, why and when should these be measured/monitored and for how long? What are the reference ranges for the neonatal population?

- Sodium
- Calcium
- Phosphate
- Magnesium
- Potassium
- Blood gases
- Blood glucose
- Triglycerides
- Ammonia
- Blood urea nitrogen
- Bicarbonate
- Creatinine
- Haemoglobin
- Ferritin
- Alkaline phosphatase
- Parathyroid hormone
- Liver function tests
- Trace elements
- Blood pH
- Full blood count (including reticulocytes)
- Fat-soluble vitamins
- Albumin and protein
- Urinary sodium and phosphate
- Urinary glucose

RECOMMENDATION

ADAPTED

CONDITIONAL

AA 52

Biochemical monitoring for babies on parenteral nutrition should follow the schedule below. N.B. There is insufficient evidence to specify who should be monitored (gestational age, birthweight, steroids, short gut syndrome).

Recommended monitoring for refeeding syndrome

For babies with a birthweight <1,500 g or <10th centile, monitor serum phosphate and calcium on days 3, 5 and 7 and then alternate days until commenced on fortified breastmilk or preterm formula.

Urea

Limiting amino acid intake based on serum urea alone is not warranted. Urea levels up to 14 mmol/L may be considered acceptable in infants on parenteral nutrition provided there are no other parameters to suggest protein intolerance (e.g. hyperammonaemia >122 µmol/L).

Triglycerides

The routine monitoring of plasma triglyceride concentrations is not recommended.

Also linked to Parenteral Nutrition Question 8 “Are there any indications (e.g. high triglycerides, sepsis) to wean, reduce or restrict parenteral lipid administration?” (AA8)

Biochemical monitoring for babies on parenteral nutrition

Investigation	Neonatal reference range	Before clinical and metabolic stabilisation		Once clinically and metabolically stable		
		Every 1–2 days	As required*	Every 1–2 weeks	After one month on PN, then monthly	As required*
Glucose	2.6–6.5 mmol/L	X		X		
Blood gases (capillary)	pH 7.35–7.45, PCO ₂ 4.7–6.0 kPa, HCO ₃ 22–26 mmol/L	X		X		
Sodium	134–148 mmol/L	X		X		
Potassium	4.5–6.0 mmol/L	X		X		
Chloride	90–114 mmol/L	X				X
Calcium	Total 1.8–2.1 mmol/L, Ionised 1.15–1.45 mmol/L	X			X	
Phosphorus	1.4–2.5 mmol/L (see footnote for frequency)	X			X	
Magnesium	0.7–1.0 mmol/L		X			X
Zinc	9–17 µmol/L		X			X
Total protein	45–75 g/L		X			X
Albumin	25–40 g/L		X			X
Urea	1.0–4.0 mmol/L		X			X
Creatinine	<95 µmol/L		X			X
Triglycerides	<3 mmol/L		X			X
Bilirubin (conjugated)	<20 µmol/L		X		X	
AST	<80 U/L		X		X	
ALT	<45 U/L		X		X	
GGT	<150 U/L		X		X	
ALP	80–600 U/L (up to 1000 U/L in growth phase)		X		X	
PTH	1.7–7.3 pmol/L		X		X	
Vitamin A	0.7–1.5 µmol/L (200–430 µg/L)		X		X	
Vitamin B12	170–800 pmol/L		X		X	
Vitamin D	50–150 nmol/L		X		X	
Vitamin E	11–46 µmol/L Auckland; 5–50 µmol/L Waikato; 23–70 µmol/L Christchurch		X		X	
INR	Lab-dependent norm		X		X	
Trace elements: Se, Zn, Cu	Lab-dependent norms					X
C-reactive protein	0–5 mg/L		X			X
Iron	10–31 µmol/L		X			X
Ferritin	15–400 µg/L		X			X
Urine electrolytes	Urinary Na >30 mmol/L adequate for growth					X

AST aspartate aminotransferase, ALT alanine aminotransferase, GGT gamma-glutamyl transferase, ALP alkaline phosphatase, INR International normalised ratio (an elevated INR may indicate vitamin K deficiency), PTH parathyroid hormone, PN parenteral nutrition

*no routine monitoring is recommended. Individualised monitoring may be needed based on the clinical situation.

Subgroup considerations

Extremely preterm or metabolically unstable infants require more intensive and frequent testing; stable infants may require reduced frequency.

Implementation considerations

Protocols should specify monitoring intervals and available tests. Regional centres may need referral pathways or courier services for specialist assays.

Monitoring and evaluation

Audit testing compliance, turnaround time, complication rates and frequency of critical abnormal results to guide practice improvement.

Research priorities

- Define optimal monitoring frequency; validate predictive biochemical markers of nutrient adequacy and toxicity; evaluate less invasive testing strategies.

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53 Recommendations for biochemical monitoring of enteral nutritional adequacy for vitamin D, zinc, full blood count, ferritin, sodium, potassium, phosphate, blood glucose, blood urea nitrogen, prealbumin and albumin, conjugated bilirubin, bone mineral status (alkaline phosphatase, calcium, phosphate, vitamin D, parathyroid hormone). Who should be monitored and when (gestational age, birthweight, steroids, short gut syndrome)?

RECOMMENDATION

ADAPTED

CONDITIONAL

AA 53

Biochemical monitoring of enteral nutrition:

- **Zinc:** Consider measuring serum zinc in infants with faltering growth and low serum alkaline phosphatase, especially if they have excessive gastrointestinal fluid losses.
- **Urinary sodium:** Consider measuring urinary sodium in infants with faltering growth and normal serum sodium.
- **Urea:** Plasma urea concentration can be used to indicate whether standard breastmilk fortification is sufficient to support appropriate growth. More protein may be needed if serum urea is <2.0 mmol/L.
- **Bone mineral status:** Phosphorus, calcium, ALP and parathyroid hormone status should be monitored regularly.
- **Vitamin D:** Serum Vitamin D (25-hydroxyvitamin D) should be measured at one month of age in infants born before 32 weeks' gestation or birthweight <1500 g. If low, adjust dose and monitor every 10 – 14 days until well into the reference range.

Subgroup considerations

Extremely preterm or severely unwell infants may require case specific changes to the testing they receive, such as reduced frequency of testing.

Implementation considerations

Protocols should define recommended monitoring intervals and the available investigations, with established referral or courier pathways to ensure regional access to specialised assays.

Monitoring and evaluation

Review compliance with testing protocols, turnaround times, complication rates, and the incidence of critical abnormal results to support quality improvement initiatives.

Research priorities

- Establish evidence-based monitoring frequency, identify and validate biochemical markers of nutrient sufficiency and toxicity, and explore less invasive testing methodologies.

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54 Does access to a specialist neonatal dietitian vs. no access improve preterm infant outcomes?

RECOMMENDATION

CONDITIONAL

EtD 54

Neonatal dietitians who meet the Australasian Neonatal Dietitians Network (ANDiN) Neonatal Dietitian Skill Requirements for the level of neonatal care should be embedded within the multidisciplinary neonatal care team.

Justification

Despite the very low certainty of evidence from non-randomised implementation studies, access to a specialist neonatal dietitian is associated with improved growth outcomes and more consistent nutrition practice. Justification is based on common sense around knowledge of the often-complex nutritional needs of preterm infants. Access to a neonatal dietitian is likely to improve equity as expert dietetic input is more likely to lead to a consistent approach for all infants around the country. International guidelines recommend the inclusion of dietitians in neonatal teams, reinforcing this as best practice.

Subgroup considerations

While standardisation of neonatal nutrition care is a clear goal, neonatal dietitians have a critical role in individualising care, where dietitian-led clinical judgement overrides standard protocols particularly for:

- Fortification strategies.
- Micronutrient supplementation.
- Faltering growth.
- Complex or high-risk infants.
- Consideration of social factors and whānau preferences.

Access to a neonatal dietitian is particularly important for units serving large populations of Māori, Pacific and under-resourced communities, who may otherwise receive inconsistent nutrition support.

Implementation considerations

Use British Dietetic Association (BDA)/British Association of Perinatal Medicine (BAPM)/ Australasian Neonatal Dietitians Network (ANDiN) staffing guidelines to inform workforce planning (e.g. 0.1 FTE per Level 3 cot). Recommended neonatal dietetic staffing levels can be calculated using ANDiN-endorsed BDA recommendations. Support smaller units with remote/telehealth access to neonatal dietitians. Prioritise investment in neonatal nutrition roles in under-resourced hospitals that have neonatal intensive care units. Incorporate dietitians into nutrition policy development, growth monitoring, research and education.

Monitoring and evaluation

Audit the availability of dietetic services across neonatal units by cot level and region.

Research priorities

- Evaluate long-term outcomes (neurodevelopment, rehospitalisation, growth) associated with access to neonatal dietitians.
- Conduct cost-effectiveness analyses of neonatal dietitian-led models of care.
- Investigate parent and whānau experiences of dietitian involvement in neonatal feeding journeys.

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05

TOPIC 5

Whānau Education and Involvement

How whānau are supported, informed and involved in the nutritional care of their pēpi — education, communication and culturally safe partnership.

"I don't mind if they did put it on a flyer, like a small book to give it to me to read sometimes, but the advice is good. The only thing for me, because different people start different shift, so every person has different advice sometimes, so your kind of confused because if you're doing the one that they tell you and then here comes the next shift and that nurse will tell you something different, like no, no, that's not how you do it, do it like this. So I'm confused as to which one I to listen to. [...] it's always the small things that I wish there was a small book about."

"I'm not your burden just because my kid is stable. Just because he doesn't have an interesting condition that requires an x-ray every two days. Sometimes I feel like they're doing a nurse and doctor drama, interested in the very serious kids. There's heaps for them to do [...] He's just as interesting as the kid who has a heart condition."

"When at Level 3, as they increased weight, I think the third day, because I was just getting colostrum and my milk supply was coming but it wasn't a lot, and the charge nurse who did the rounds with the doctors was very pushy on the donor milk. I got very emotional because she's like, well, you know you have to do this, it has to be done or else your baby's not going to grow. That's the thing that we were getting. It was a very abrupt conversation, basically, in relation to that. I guess I would like them, when they're speaking to parents, I know it's their job and they do this day in, day out, but also have a little bit of empathy towards the parents because this is hard, especially seeing your baby in a cubicle, incubator, enclosed like that."

"The difference between having somebody who comes in and is just like bang bang bang ... then somebody who's just like "all right we're gonna get to know each other"."

"When I was in maternity a lady would come and teach us how to hand express, and then she gave us little pamphlets. And an app, 'mama aroha', I downloaded that as well, that helped me, I would go back, 'cause you know how they had little videos, it was useful, especially the videos. I just downloaded that and good from there."

55 How do Māori whānau prefer to engage in discussions and receive information when making shared decisions about the care of their preterm pēpi?

RECOMMENDATION

STRONG
EtD 55

Whānau Māori should be included and are essential members of the team caring for their pēpi. Healthcare professionals need to communicate in a culturally safe way, as determined by whānau Māori. Incorporating Māori values (e.g. whanaungatanga (connectedness) and manaakitanga (kindness and hospitality)) when providing healthcare will help contribute to increasing health equity for whānau Māori.

Justification

There is clear qualitative evidence supporting the inclusion of whānau as essential team members. Communication by healthcare professionals has also been highlighted as champions for whānau. The foundations of Te Ao Māori values provide the fundamental pou (pillar) for care.

Subgroup considerations

Subgroup considerations include diversity in iwi and hapū affiliations, levels of connection to te ao Māori, whānau structures and decision-making roles, geographic distance from rohe, language preferences, socioeconomic barriers, and prior experiences of healthcare and racism. Culturally safe care requires responsiveness to these differences as defined by whānau Māori themselves.

Implementation considerations

Implementation will require staff training in cultural safety and relationship-centred communication, support from Māori health teams, and processes that enable whakawhanaungatanga. Services should also ensure the environment supports extended whānau involvement and consistent, clear information-sharing. Recruiting more Māori staff would benefit the overall cultural care of the whānau Māori. Implementation should include a designated cultural support role, such as a Māori health worker, kaiāwhina or Whānau Ora navigator, to support culturally safe communication and care planning as determined by whānau Māori, rather than relying on individual staff availability or discretion.

Monitoring and evaluation

Monitoring should focus on whānau experience measures, cultural safety audits, and regular equity-focused quality-improvement reviews. Feedback from whānau Māori should guide iterative improvements, using structured methods such as PDSA cycles.

Research priorities

- Future research should evaluate specific communication models, test scalable culturally informed interventions, and measure outcomes identified as important by whānau Māori.
- Studies examining system changes that sustainably support culturally safe neonatal care are also needed.

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56 How do Pacific peoples and their families prefer to engage in discussions and receive information when making shared decisions about the care of their preterm pēpi?

RECOMMENDATION

CONDITIONAL

EtD 56

Pacific families *should be regarded and therefore included as essential members of the team* in nutrition care discussions for their pēpi. Healthcare professionals should communicate as determined by Pacific Families and include relationship-centred, culturally safe communication that nurtures and recognises this value, Teu Le Vā, respects and supports expressions of faith and spirituality, and actively includes extended family members who are central to decision-making.

Justification

The limited available evidence shows that Pacific families place the highest value on relationship-centred care, where trust, time, respect and spirituality are honoured, and where extended family are included in decision-making. Without culturally grounded engagement that aligns with these values, communication is less effective and can conflict with traditional practices, reducing the acceptability and uptake of nutrition care advice.

Subgroup considerations

Pacific communities are diverse; communication preferences differ across Polynesia, Melanesia and Micronesian countries. The extended family, including grandparents and aunties, often play central roles and may require information in Pacific languages. Considerations also differ for extremely preterm, VLBW, and moderate-to-late preterm infants due to different care journeys and stressors.

Implementation considerations

Implementation will require Pacific peoples' expertise, cultural leadership, and workforce development, using the principles of Yavu, culturally safe spaces for prayer and family presence, and translated or visual health information. Services will need support to shift from transactional information-giving to relationship-centred, family-inclusive communication.

Monitoring and evaluation

Evaluation should prioritise families' experience, culturally safe structured methods and include safety feedback, and the effectiveness of communication processes for Pacific families. Monitoring should assess focus on Pacific families' experiences and frequent equity-focused quality-improvement audits (whether the extended family feel informed, involved, and culturally supported) and whether changes reduce disparities in neonatal outcomes and experience.

Research priorities

- There is an urgent need for research directly involving Pacific families of preterm infants, using Pacific research methodologies.
- Priorities include identifying preferred communication models in NICU/SCBU, evaluating culturally grounded interventions, supporting common values between Pacific Peoples whilst understanding subgroup differences across Pacific Peoples nations, and assessing impacts on feeding, engagement, and clinical outcomes.

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57 Should whānau-led tikanga around food be integrated into supporting whānau Māori in the nutritional care of pēpi Māori?

RECOMMENDATION

CONDITIONAL

EtD 57

Whānau-led tikanga around food should be integrated into supporting whānau Māori in the nutritional care of pēpi Māori. Kai is an important aspect of tikanga Māori. It is important that manaakitanga is extended to both pēpi and whānau Māori; therefore, ensure whānau have access to an area to prepare and share kai. When possible, if there is more than one whānau member in NICU, offer more than one meal to the whānau.

Justification

There are no direct intervention studies assessing the effects of integrating tikanga-based kai practices in NICU. The existing qualitative evidence consistently indicates that kai is integral to whānau wellbeing, connection, manaakitanga and breastfeeding success, and that hunger and lack of culturally appropriate food negatively impact whānau Māori. However, the absence of measurable neonatal or maternal clinical outcomes means certainty of effect remains very low.

Subgroup considerations

Extremely preterm, VLBW and MLPT pēpi Māori may experience different lengths of stay, levels of parental stress, and reliance on whānau support; therefore, the importance of tikanga-based kai practices may be even greater in families spending long periods in NICU. Rural whānau and those cared for far from home may particularly benefit due to food insecurity and reduced access to extended whānau support. It is important that whānau Māori are offered the option to have traditional tikanga like karakia involved in the process. Some whānau Māori will not take up the option, and some may be offended by health practitioners assuming they know what's best in this regard for whānau Māori.

Implementation considerations

Implementing tikanga-based kai practices requires careful co-design with whānau Māori, consideration of space for communal food preparation and eating, culturally appropriate kai options and reviewing visiting policies to support extended whānau involvement. It is critical more health providers have staff with bicultural skills.

Monitoring and evaluation

If implemented, services should monitor whānau satisfaction, cultural safety indicators, breastfeeding outcomes and whānau stress. Measuring uptake and acceptability among staff and whānau Māori will be essential to guide refinement.

Research priorities

- High-quality kaupapa Māori research is needed to evaluate the clinical and whānau outcomes of tikanga-based kai practices in NICU, including impacts on breastfeeding and other outcomes.
- Research should also explore cost implications, equity gains and be co-led by Māori.

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58 Should early breastfeeding education vs. standard care be used for mothers of preterm infants?

RECOMMENDATION

CONDITIONAL

EtD 58

Early education on breastfeeding should be part of routine postnatal care, given the benefits of breastfeeding for infants and mothers. Breastfeeding information, discussion and advice should also be included in routine antenatal care.

Justification

Small positive effect, but no harm. While the overall certainty of evidence is very low, the potential benefits of early education are in important outcomes, such as increased breastfeeding rates, improved maternal engagement, lactation and provision of breastmilk. The effects are uncertain due to imprecision and high heterogeneity, but the direction of effect generally favours education, and harms are minimal or not demonstrated. Given the low cost, likely acceptability and existing practice in some units, early education can be considered a low-risk, potentially high-benefit intervention. The equity implications are substantial, particularly for pēpi Māori, Pacific peoples and underrepresented groups who face systemic barriers to breastfeeding.

Subgroup considerations

No specific data were available for pēpi Māori, but disparities in outcomes support prioritising education for Māori. Some studies included moderate-to-late preterm and low birthweight infants, which may limit generalisability to extremely preterm infants. The effect of education may differ depending on gestational age, timing and content of education and availability of breast pumps and lactation support.

Implementation considerations

Education should be timely, structured and culturally responsive, ideally beginning antenatally or shortly after birth. Implementation could be variable depending on staffing, parental presence, and resources (e.g. breast pumps, space, interpreters). Content should include the importance of early and frequent expression, use of nutritional supplements, and fortification. Services should prioritise Māori and ensure whānau-centred care and include equity-focus. Te Ao Māori input into the education would be needed to ensure it had the most benefit. May require staff education or protocols to standardise messaging and support.

Monitoring and evaluation

Track exclusive breastfeeding at discharge. Monitor early expression practices, milk volume and maternal confidence/knowledge (e.g. use of Breastfeeding Self-Efficacy Scale). Collect feedback from parents on experience, barriers and support received. Consider auditing equity of access and outcomes by ethnicity and gestation.

Research priorities

- High-quality RCTs that examine early education packages stratified by gestational age and with the inclusion of whānau Māori and Pacific peoples.
- Studies on delivery methods (in-person, digital, peer-led) and culturally specific approaches.
- Cost-effectiveness evaluation.
- Whānau Māori perspectives on what is helpful is essential.

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59 Should additional education around the nutrition and/or care of their preterm infants throughout their NICU stay be delivered through different methods (face-to-face, written, online) vs. standard care be used for families of preterm infants?

RECOMMENDATION

CONDITIONAL

EtD 59

Alongside standard care, additional education for whānau of preterm infants should be through a mix of delivery methods (face-to-face, written, online) and tailored to cultural and contextual needs.

Justification

The evidence from qualitative and observational studies demonstrates consistent benefits for whānau when additional education is provided. These include improved satisfaction, greater confidence in caregiving, reduced stress and depression, and enhanced decision-making.

While effects on clinical outcomes (e.g. breastfeeding at discharge, infant growth) are uncertain or low certainty, the intervention aligns with principles of whānau-centred care and is likely acceptable. Importantly, additional education methods must be culturally appropriate, accessible, and delivered in ways that support relational, inclusive, and meaningful communication. Given the variability in resource availability and delivery methods and the moderate-to-low certainty of some outcome data, a conditional recommendation is appropriate.

Subgroup considerations

Whānau Māori benefit when education is provided in ways that honour tikanga Māori, promote kanohi ki te kanohi (face to face) interaction, and support whānau empowerment and tino rangatiratanga. Pacific families value collective, visual, and oral methods of learning. Involving the wider family in education and tailoring content to their cultural needs increases its impact. Families from rural, migrant, or low-resource backgrounds may need flexible delivery modes (e.g. online, interpreters, translated materials) to ensure equitable access.

Implementation considerations

Education should combine written, face-to-face, and digital tools. Staff time and training may be needed to deliver content appropriately and culturally safely. Co-design with whānau Māori and Pacific providers is essential to ensure relevance and acceptability.

Monitoring and evaluation

Collect whānau feedback on education methods and satisfaction with communication. Monitor indicators of parental wellbeing, confidence, and readiness for discharge and type of feeding at discharge. Audit the consistency of education delivery across units and assess access by ethnicity, language, and socioeconomic status. Monitor feeding and clinical outcomes.

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60 How does encouraging parents to be involved in tube feeding (feeding, changing tubes and using feeding pumps) and preparing supplements (fortification and similar supplements) of their infants affect breastmilk expression and establishment of breastfeeding and their confidence, participation and overall care experience, as well as the health and development of their infants?

RECOMMENDATION

CONDITIONAL

EtD 60

Support and encourage parents to be involved in tube feeding (feeding, changing tubes and using feeding pumps if needed) and preparing supplements (fortification and similar supplements) for their infants, as this may enhance parental confidence, engagement and satisfaction with care.

Justification

The available evidence is of low to very low certainty. While no clear clinical benefits were observed in outcomes such as mortality, NEC, breastfeeding at discharge, or growth, one RCT reported reduced feeding intolerance and improved parental wellbeing and confidence.

These effects, though modest, align with broader goals of family-integrated care. Importantly, encouraging parental participation may contribute to improved equity, cultural safety, and bonding, especially when implemented with appropriate support.

Subgroup considerations

For whānau Māori, engagement in feeding-related tasks may promote tino rangatiratanga, support breastfeeding intentions, and restore traditional caregiving roles. However, historical mistrust and systemic barriers must be addressed through culturally safe, inclusive practices. Pacific families may face barriers such as time, language and health literacy. Tailored, respectful education and support is essential to enable meaningful participation. Families from rural, migrant or low-resource settings may require flexible visiting policies, interpreters and additional support to ensure inclusion.

Implementation considerations

Requires staff training to coach and support parents safely and confidently, especially for technical tasks like tube feeds or fortifier measurement. Needs clear protocols to manage risk and standardise parental involvement, alongside documentation of consent and competency.

Time and workload implications should be balanced against potential gains in parental confidence, infant wellbeing and care satisfaction.

Monitoring and evaluation

Monitor uptake and consistency of parent involvement in feeding-related tasks across units. Collect qualitative feedback from parents and staff about barriers, facilitators and acceptability.

Research priorities

Studies assessing the impact of parent involvement in tube feeding and supplement preparation on:

- Breastfeeding initiation and continuation, parental stress, confidence, and bonding.
- Māori-and Pacific-led qualitative research on parental experiences and culturally safe implementation strategies.
- Cost-benefit and feasibility studies, particularly in resource-limited settings.

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A

A P P E N D I C E S

Appendices

Contributors, methods, glossary and abbreviations, conflicts of interest, key outcomes, systematic reviews, the full Evidence-to-Decision tables, adoption tables, research gaps and consultation.

A – K

appendix sections

H.1 – H.5

evidence to decision

Glossary

terms & abbreviations

Appendix A. Contributors to the Guideline

STEERING GROUP MEMBERS

	Name	Role	Department	Organisation	Location
1	Barbara Cormack (Chair)	Principal Investigator Researcher Neonatal Dietitian	Liggins Institute Starship Child Health	University of Auckland Te Whatu Ora	Auckland
2	Catherine Belfield-Haines	Project Manager	Liggins Institute	University of Auckland	Auckland
3	Frank Bloomfield	Professor of Neonatology	Deputy Vice Chancellor (Research)	University of Auckland	Auckland
4	Haunui Royal (Parehauraki, Ngāti Raukaha and Ngāpuhi)	Kaiārahi	Liggins Institute	University of Auckland	Auckland
5	Kim Ward	Researcher	Faculty of Medical and Health Sciences	University of Auckland	Auckland
6	Lilia Delgado Páramo	Researcher PhD student	Liggins Institute	University of Auckland	Auckland
7	Lisa Kremer (Ngāi Tahu / Kāi Tahu; Kāti Māmoe; Waitaha)	Pharmacist Researcher	School of Pharmacy	University of Otago	Dunedin
8	Liza Edmonds (Ngāpuhi; Ngāti Whātua)	Neonatologist Researcher	Neonatal Service	Victoria University and Te Whatu Ora Wairarapa	Dunedin Wairarapa
9	Sarah Rusholme	Lived Experience Representative	Chief Executive Officer, The Little Miracles Trust		Wellington
10	Tamara Nickerson (Te Whakatōhea/ Ngā Puhi)	Neonatal Nurse Clinical Nurse Specialist Kaiārahi Nāhi	Māori Health, Te Toka Tumai	Auckland City Hospital	Auckland
11	Taniith Alexander	Neonatal dietitian Researcher	Newborn Services Middlemore Hospital	University of Auckland Te Whatu Ora	Auckland

GUIDELINE DEVELOPMENT GROUP MEMBERS

Name	Role	Department	Organisation	Location
Adrienne Lynn	Neonatologist	Newborn Services	Christchurch Women's Hospital, Te Whatu Ora	Christchurch
Annette Murphy (from April 2025)	Nurse Practitioner - Neonatal	Special Care Baby Unit	North Shore Hospital Te Whatu Ora	Auckland
Angelica Allermo Fletcher (left April 2025)	Neonatologist	Newborn Services	Wellington Hospital Te Whatu Ora	Wellington
April Reece	Lived Experience Representative	Parent	Consumer	Palmerston North
Barbara Cormack	Principal Investigator Researcher Neonatal dietitian	Liggins Institute Starship Child Health Auckland City Hospital	University of Auckland Te Whatu Ora	Auckland
Catherine Belfield-Haines	Project Manager	Liggins Institute	University of Auckland	Auckland
Carol Bartle (from April 2025)	Policy Analyst Lactation Consultant	Policy Analyst	NZ College of Midwives	Christchurch
Chloe Bell (from Dec 2024)	Lived Experience Representative (ex-preterm baby) Medical Intern	Liggins Institute	University of Auckland	Auckland
Eleanor Hoare	Nurse Specialist - Lactation	Newborn Services Starship Child Health	Auckland City Hospital Te Whatu Ora	Auckland
Frank Bloomfield	Deputy Vice Chancellor (Research) Professor of Neonatology	Liggins Institute	University of Auckland	Auckland
Haunui Royal (Parehauraki, Ngāti Raukaha and Ngāpuhi) (joined May 2023)	Kaiārahi	Liggins Institute	University of Auckland	Auckland
Jutta van den Boom	Neonatologist Head of Department	Neonatal Intensive Care	Waikato Hospital Te Whatu Ora	Hamilton
Kim Ward	Researcher - Qualitative Research Specialist	Faculty of Medical and Health Sciences	University of Auckland	Auckland
Lela Yap (Niue, Ngāti Pikiao) (from March 2024)	Neonatologist	Newborn Services	Dunedin Hospital Wellington Hospital Te Whatu Ora	Dunedin Wellington
Lilia Delgado Páramo	Researcher PhD student	Liggins Institute	University of Auckland	Auckland
Lindsay Joseph	Neonatologist	Newborn Services	Middlemore Hospital Wellington Hospital Te Whatu Ora	Auckland Wellington

Name	Role	Department	Organisation	Location
Lisa Kremer (Ngāi Tahu / Kāi Tahu; Kāti Māmoe; Waitaha)	Pharmacist Health Researcher	School of Pharmacy	University of Otago	Dunedin
Liza Edmonds (Ngāpuhi; Ngāti Whātua)	Neonatologist Associate Professor Research	Neonatal Service National Centre for Women's Health Research	Te Whatu Ora Wairarapa Victoria University	Wairarapa Wellington
Luling Lin	Researcher-Systematic Review specialist	Liggins Institute	University of Auckland	Auckland
Mariam Buksh	Neonatologist Clinical Director	Newborn Services Starship Child Health	Auckland City Hospital Te Whatu Ora	Auckland
Rachel Friend (left in Aug 2024)	Lived Experience Representative Chief Executive Officer	The Little Miracles Trust	Consumer organisation	Auckland
Sarah Rusholme (from Aug 2024)	Lived Experience Representative Chief Executive Officer	The Little Miracles Trust	Consumer organisation	Wellington
Tamara Nickerson (Te Whakatōhea/ Ngā Puhi)	Neonatal Nurse Clinical Nurse Specialist, Kaiārahi Nāhi	Starship Child Health	Auckland City Hospital Te Whatu Ora	Auckland
Tanith Alexander	Researcher Neonatal Dietitian	Liggins Institute Newborn Services	Middlemore Hospital Te Whatu Ora	Auckland
Terin Port (left March 2025)	Nurse Specialist - Lactation	Newborn Services Starship Child Health	Auckland City Hospital Te Whatu Ora	Auckland
Violet Clapham (from July 2023)	Midwife	Midwifery Advisor - Professional Projects	NZ College of Midwives	Wellington

The GDG was chaired by Professor Frank Bloomfield. All GDG members had equal roles and responsibilities, contributing collaboratively to the scope, questions, evidence appraisal, drafting, review and finalisation of recommendations. The project methodologist, Associate Professor Vanessa Jordan attended meetings to provide methodological advice and guidance throughout the project.

Appendix B. Translations

MĀORI WORDS USED IN THE GUIDELINE

Aroha — *compassion and empathy*

Hapū — *kinship group, clan, tribe, subtribe - section of a large kinship group and the primary political unit in traditional Māori society*

Hauora — *health*

He Tamariki Kokoti Tau — *Babies born preterm*

He Whakaputanga o te Rangatiratanga o Nū Tirenī — *The Declaration of Independence of New Zealand, 1835*

Iwi — *extended kinship group, tribe, nation, people, nationality, race - often refers to a large group of people descended from a common ancestor and associated with a distinct territory*

Kai — *food*

Kaiārahi — *guide, escort, counsellor, conductor, leader, mentor, pilot, usher.*

Kaiāwhina — *helper, assistant, contributor, counsel, advocate.*

Kaimahi — *worker*

Kanohi ki te kanohi — *face to face*

Karakia — *to recite chants, a spell, say grace or a prayer*

Karakia tīpuna — *ancestors chants or prayers*

Kaupapa Māori — *Māori approach, Māori topic, Māori customary practice, Māori institution, Māori agenda, Māori principles, Māori ideology - a philosophical doctrine, incorporating the knowledge, skills, attitudes and values of Māori society.*

Kōrero — *to tell, say, speak, read, talk, address.*

Kuia — *elderly woman, grandmother, female elder.*

Mana — *prestige authority, influence and spiritual power*

Mana Māori — *Māori autonomy or Māori authority or Māori rights*

Mana Motuhake — *self-determination*

Mana tangata — *equity across life course*

Mana whakahaere — *Governance, authority, jurisdiction*

Manaakitanga — *showing respect, generosity and care*

Manatū Hauora — *Ministry of Health*

Mātauranga — *knowledge*

Mātauranga Māori — *Māori knowledge*

Mauri — *life forces or life principle, vital essence*

Ngā kupu — *words*

Noa — *free from tapu, ordinary and everyday*

Pēpi — *baby, infant*

Pou — *pillar*

Pūrākau — *story*

Rangatiratanga — *Chieftainship or chiefly autonomy or the rule of chiefs*

Rohe — *territory or area*

Rongoā — *remedy or medication*

Tamariki — *to be young.*

Tapu — *be sacred, prohibited, restricted, set apart, forbidden*

Te Ao Māori — *refers to "the Māori world", encompassing the knowledge, understandings, and practices that arise from the distinct cultural context of Aotearoa New Zealand. It includes aspects such as te reo Māori (the Māori language) and tikanga Māori (customs and protocols), reflecting a holistic worldview that emphasizes the interconnections between people and nature*

Te Hā o Whānau — *A culturally responsive framework of maternal care*

Te Whatu Ora — *Health New Zealand*

Te taiao — *the environment and natural world*

Te Tiriti o Waitangi — *The Treaty of Waitangi, 1840*

Tikanga — *cultural protocols and processes*

Tino rangatiratanga — *self-determination*

Tūpuna — *ancestors*

Wahakura — *woven harakeke bassinet for infants*

Wahine — *female gender*

Wairua — *importance of spiritual wellbeing*

Wawe — *to be early, quickly, too soon, prematurely, immediately*

Whakamā — *embarrassed*

Whakamana — *empowerment*

Whakawhanaunga — *building relationships*

Whakawhanaungatanga — *process of establishing relationships*

Whanaungatanga — *connectedness*

Whānau Māori — *extended family, family group, a familiar term of address to a number of people - the primary economic unit of traditional Māori society. In the modern context the term is sometimes used to include friends who may not have any kinship ties to other members*

Whenua ki te whenua — *returning placenta to the earth*

PACIFIC WORDS USED IN THE GUIDELINE

Milimili — *gentle rubbing of the abdomen*

Mokomoko — *coconut milk*

Pia — *arrowroot starch*

Sua alaisa — *a special Samoan soup*

Talanoa — *talk or discussion*

Teu Le Vā — *the building and nurturing of relationships*

Yavu — *foundation*

Appendix C. Glossary of Clinical and Technical Terms used in the Guideline

Amino acids — Small components of protein that are essential for growth, tissue repair, and normal body function in newborn babies.

Appropriate for gestational age (AGA) — A baby whose birthweight is within the expected range (10th to 90th percentile) for their gestational age (how many weeks of pregnancy at birth).

Aqueous intravenous (IV) nutrition — Delivery of fluids and nutrients such as glucose, amino acids, and electrolytes directly into a baby's bloodstream through an intravenous line.

Biochemical monitoring — Blood tests used to assess a baby's metabolic and nutritional status and to guide clinical care.

Bronchopulmonary dysplasia (BPD) — A chronic lung condition that affects some preterm infants who require prolonged breathing support or oxygen therapy.

Cholestasis — A condition where bile flow from the liver is reduced or blocked, which can occur in babies receiving prolonged intravenous nutrition.

Continuous positive airway pressure (CPAP) — A non-invasive form of breathing support that delivers continuous air pressure to keep the lungs open and improve oxygen levels.

Enteral feed advancement — The gradual increase in milk feed volumes to support safe progression to full feeding while allowing the gut to adapt.

Extubation — Removal of a breathing tube once a baby is able to breathe adequately without mechanical ventilation.

Eye screening examination — A specialised eye assessment performed in preterm infants to detect conditions such as retinopathy of prematurity.

Faltering growth — Growth that is slower than expected, based on weight, length, or head circumference measurements over time.

Fatty acids — Components of fats that provide energy and are important for brain and overall development.

Feeding intolerance — Difficulty tolerating milk feeds, often indicated by vomiting, abdominal distension, or delayed progression to full feeds.

Fenton growth charts — Growth charts specifically designed to monitor the growth of preterm infants up to around 50 weeks' post-menstrual age.

Fortification — The addition of nutrients (such as protein, energy, vitamins and minerals) to breastmilk to meet the increased nutritional needs of preterm infants.

Gastric aspiration — Removal of stomach contents via a feeding tube to assess feeding tolerance or confirm tube placement.

Hyperammonaemia — Elevated levels of ammonia in the blood, which may indicate a metabolic problem and can affect brain function.

Hyperglycaemia — Higher-than-normal blood glucose levels, which are common in preterm infants, particularly those receiving intravenous nutrition.

Hypertriglyceridaemia — Elevated levels of triglycerides (a type of fat) in the blood, often associated with intravenous lipid administration.

Hyperosmolar — A state in which blood or fluids have a high concentration of dissolved substances, which can affect fluid balance.

Hypothermia — A body temperature below 36.5°C, which is particularly concerning in preterm infants due to their increased risk of heat loss.

Intermittent bolus feeding — Administration of set volumes of milk at regular intervals (e.g. every 2–3 hours), rather than continuous feeding.

Intraventricular haemorrhage (IVH) – Bleeding into the brain's ventricular system, most commonly occurring in very preterm infants.

Fetal growth restriction (FGR) – A condition where a baby does not grow as expected during pregnancy.

Lipaemic – Describes blood that contains a high level of fat, giving it a milky appearance.

Lipid emulsion – A fat-containing intravenous solution used to provide energy and essential fatty acids in parenteral nutrition.

Ketosis – A metabolic state in which the body uses fat rather than glucose as its main energy source.

Metabolic bone disease – Reduced bone mineralisation in preterm infants, increasing the risk of weak bones or fractures.

Metabolic homeostasis – The body's ability to maintain stable internal conditions necessary for normal function and growth.

Nasogastric tube – A tube passed through the nose into the stomach to provide milk feeds in babies unable to feed orally.

Necrotising enterocolitis (NEC) – A serious inflammatory condition of the bowel that primarily affects preterm infants.

Neonatal intensive care unit (NICU) – A specialised hospital unit providing intensive medical care for preterm or critically ill newborn infants.

Neurodevelopmental impairment – Difficulties with brain development that may affect movement, learning, behaviour, or communication.

Oedema – Swelling caused by excess fluid in the body's tissues.

Orogastric tube – A feeding tube inserted through the mouth into the stomach.

Osmolality – A measure of how concentrated a fluid is, which can influence feeding tolerance and safety.

Patent ductus arteriosus (PDA) – A condition where a normal fetal blood vessel remains open after birth, affecting blood flow between the heart and lungs.

Plasma triglyceride concentrations – Blood levels of triglycerides, used to monitor tolerance to intravenous lipid therapy.

Refeeding syndrome – A metabolic disturbance that can occur when nutrition is started or increased, leading to significant shifts in electrolytes such as phosphate.

Renal impairment – Reduced kidney function, affecting fluid and electrolyte balance.

Sepsis – A serious bloodstream infection that can rapidly become life-threatening, particularly in preterm infants.

Special Care Baby Unit (SCBU) – A hospital unit providing care for babies who require additional support but not full intensive care.

Small for gestational age (SGA) – A baby whose birthweight is below the expected range for their gestational age.

Transfusion – Administration of blood or blood products to treat anaemia or blood loss.

Tube feeding (enteral feeding) – Delivery of nutrition directly into the stomach or intestine via a tube when oral feeding is not possible.

Vascular access – Placement of a line into a vein or artery to provide fluids, medications or nutrition and to take blood samples.

Very low birthweight (VLBW) – A birthweight of less than 1500 grams, associated with increased medical and nutritional needs.

Appendix D. Abbreviations and Acronyms

Abbreviation	Meaning
AdjMD	Adjusted mean difference
AGREE II	Appraisal of Guidelines for Research and Evaluation II
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
ANDiN	Australasian Neonatal Dietitians Network
aOR	Adjusted odds ratio
AST	Aspartate aminotransferase
BAPM	British Association of Perinatal Medicine
BDA	British Dietetic Association
BPD	Bronchopulmonary dysplasia
CASP	Critical appraisal skills programme checklist
CENTRAL	Cochrane Central Register of Controlled Trials
CGA	Corrected gestational age
CI	Confidence interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CLABSI	Central line-associated bloodstream infection
CMV	Cytomegalovirus
CSPEN	Chinese Society of Parenteral and Enteral Nutrition
DIAMOND trial	Different Approaches to MOderate & late preterm Nutrition
EBM	Expressed breastmilk
ELBW	Extremely low birthweight

Abbreviation	Meaning
Embase	Excerpta Medica Database
EN	Enteral nutrition
ESPGHAN	European Society for Paediatric Gastroenterology Hepatology and Nutrition
ESPR	European Society of Paediatric Research
EtD	Evidence to Decision document
FOLE	Fish oil only lipid emulsion
FTE	Full time equivalent
g	Gram
GDG	Guideline development group
GGT	Gamma-glutamyl transferase
GPP	Good Practice Point
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HBV	Hepatitis B virus
HC	Head circumference
HCV	Hepatitis C virus
HIPG	High intensity pumping group
HIV-1	Human immunodeficiency virus type 1
HIV-2	Human immunodeficiency virus type 2
hsPDA	Haemodynamically significant patent ductus arteriosus
HTLV-1	Human T-lymphotropic virus type 1
HTLV-2	Human T-lymphotropic virus type 2
I2	Heterogeneity index
IBFAT	Infant Breastfeeding Assessment Tool

Abbreviation	Meaning
ICTRP	The WHO International Clinical Trials Registry Platform
INR	International normalised ratio
IU	International unit
IV	Intravenous
kcal	Kilocalorie
kg	Kilogram
L	Litre
LIPG	Low intensity pumping group
LOE	Level of Evidence
MD	Mean difference
MEDLINE	Medical Literature Analysis and Retrieval System Online
mg	Milligram
mIU/L	Milli-International units per litre
mL/kg/day	Millilitres per kilogram per day
mmol	Millimole
mOsm	Milliosmole
N/A	Not appropriate
NEC	Necrotising enterocolitis
NICE	National Institute for Health and Care Excellence
NICU	Newborn intensive care
nmol	nanomole
NZD	New Zealand dollars
OR	Odds ratio

Abbreviation	Meaning
GoR	Grade of Recommendation
PDA	Patent ductus arteriosus
PI	Principal investigator
PICO	Patient/Population, Intervention, Comparison, and Outcome
PN	Parenteral nutrition
ProVIDe trial	Protein IntraVenous nutrition for extremely low birthweight babies: Impact on Development
PTH	Parathyroid hormone
QALYs	Quality-adjusted life-years
RCT	Randomised controlled trial
RR	Risk ratio
SCBU	Special care baby unit
SD	Standard deviation
Steering Group	Steering group
SIFT trial	Speed of Increasing milk Feeds Trial
SMD	Standardised mean difference
SoF	Summary of Findings
US\$	United States dollars
USA	United States of America
VLBW	Very low birthweight
WHEAT trial	WithHolding Enteral feeds Around packed red cell Transfusion to prevent necrotising enterocolitis in preterm neonates
WHO	World Health Organisation
µg	Microgram

Appendix E. Conflicts of Interest

CONFLICT OF INTEREST POLICY

Purpose

The purpose of this Conflict-of-Interest policy is to establish guidelines and procedures for identifying, disclosing, and managing conflicts of interest that may arise among Steering Group and Guideline Development Group Members for the Aotearoa Nutrition Guideline for Preterm Babies Project.

Definitions

Chair is the nominated chairperson of the committee

Conflict of interest exists where the responsibilities of a member of the Steering Group and Guideline Development Group members are, or could be, or could be perceived to be, affected by some other personal, financial or academic interest or duty that the member may have in relation to a particular matter or person. The term includes actual, potential or perceived conflicts of interest.

Member(s) includes all of the Aotearoa Nutrition Guideline for Preterm Babies Project Steering Group and Guideline Development Group Members and employees.

Relationship means a connection that could affect how other people view a member's impartiality.

Principles

The guiding principles for the identification and management of declared interests in any situation are as follows:

1. Steering Group and Guideline Development Group Members for the Aotearoa Nutrition Guideline for Preterm Babies Project must be seen at all times to behave in an impartial and transparent manner within in their role (outlined in the terms of reference) to the project.
2. It is important to understand that the existence of an interest does not necessarily imply wrongdoing on the part of any person. However, any interests which could give rise to a conflict of interest must be disclosed.
3. Members' interests that may give rise to actual, potential or perceived conflicts must be dealt with quickly and transparently; that is, they must be:
 - a. Acknowledged;
 - b. Disclosed;
 - c. Put on record, where appropriate, and
 - d. Effectively managed or avoided.
4. If a member has any doubt as to whether an interest is relevant, they should disclose the matter to the chair of the Aotearoa Nutrition Guideline for Preterm Babies Project who will confirm this with the Project Manager and Senior Research Fellow.
5. Disclosure of interests may involve disclosing personal information. This information must be handled with due regard to the privacy of the individual concerned.
6. If a person has declared an interest relating to a matter being considered, this does not necessarily mean that the member cannot participate in the discussion; rather, it indicates that the interest must be managed in the most appropriate manner. Once an interest is declared, the member's ability to participate in the discussion will be determined by the members of the committee, with the final decision resting with the Chair.

Identification and effective management of conflicts of interest

- Members and Staff must identify and disclose any interest that may be actual, potential or perceived to give rise to a conflict that may affect, or may be seen to affect, their impartiality when acting on behalf of the Aotearoa Nutrition Guideline for Preterm Babies Project.
- Each conflict-of-interest situation must be dealt with as soon as reasonably practicable after it is identified.
- The situation must then be reviewed, managed and recorded by the Project Manager or chair in a manner that is appropriate to the circumstances.
- The project team (chair and Project Manager) must help to build awareness of conflict-of-interest situations, and support those who report to them to comply with their obligations under this policy.

REGISTER OF INTERESTS

All conflicts of interest and relevant manager responses are to be submitted for inclusion in the relevant conflicts of interest register maintained for the project by the Project Manager.

REVIEW AND AMENDMENTS

This policy shall be reviewed periodically and may be amended as necessary to ensure its effectiveness and compliance with applicable laws and regulations.

GUIDELINE DEVELOPMENT GROUP CONFLICTS OF INTEREST REGISTER

Name	Conflict of interest	Assessment
Adrienne (Adie) Lynn	Neonatal Paediatrician for Te Whatu Ora – Waitaha Canterbury Member of the Perinatal Society of New Zealand Perinatal Society of Australia and New Zealand Involvement in nutrition research including some evidence considered by the Guideline Development Group	The majority of declared interests were considered not to represent a conflict. When the panel considered evidence that this researcher was involved in they did not participate in the discussion unless asked for clarification of the facts by the GDG.
Angelica Allermo Fletcher	Neonatologist, Newborn Services, Wellington Hospital, Te Whatu Ora (at the time of GDG membership)	This disclosure was considered not to represent a conflict and did not require further management
April Mihaere (Reece)	Consumer representative for the Perinatal Society Growth Assessment Protocol (GAP) Advisory Group Admin of the NZ NICU, SCBU parent support group. Administrative officer for a tube support group and a child respiratory support group.	This disclosure was considered not to represent a conflict and did not require further management
Barbara Cormack	Australasian Neonatal Dietitians Network Steering Group member Member of the Clinical Expert advisory group for Badgernet Neonatal Nutrition Compounding Reference Group for NZ Health Partnerships member Membership of Perinatal Society of New Zealand, Membership of Perinatal Society of Australia and New Zealand Scientific Advisory Group member for Nestle Nutrition Institute (past member) Former Paediatric Scientific Advisory Group member for Nutricia (past member) Principal Investigator of the AVlatioN study ProVIDe trial investigator	Some of these declared interests were considered not to represent a conflict. When the panel considered evidence that this researcher was involved in they did not participate in the discussion unless asked for clarification of the facts by the GDG. For questions relating to formula Barbara was not involved in writing the EtD, or chairing these sessions in order to avoid perceived conflict from her work with Nestle and Nutricia. No further management was required.
Carol Bartle	Policy Analyst NZ College of Midwives La Leche League NZ – Professional Advisory Group member World Breastfeeding Trends Initiative - Core Committee member Committee member – meeting fee is paid. Quarterly meetings Ministry of Health / Public Health Association – International Code Compliance Panel	This disclosure was considered not to represent a conflict and did not require further management

Name	Conflict of interest	Assessment
Catherine Belfield-Haines	Project Manager	This disclosure was considered not to represent a conflict and did not require further management
Chloe Bell	Clinical Research Intern, Liggins Institute, University of Auckland funded by the Aotearoa Foundation. Conducted research on neonatal nutrition including some of the evidence synthesis considered by the Guideline Development Group.	The majority of declared interests were considered not to represent a conflict. When the panel considered evidence that this researcher was involved in they did not participate in the discussion unless asked for clarification of the facts by the GDG.
Eleanor (Ellie) Hoare	Nurse Specialist – Lactation, Newborn Services, Starship Child Health, Auckland City Hospital, Te Whatu Ora	This disclosure was considered not to represent a conflict and did not require further management
Frank Bloomfield	PI of the ProVIDe trial PI of the DIAMOND trial Member of ESPGHAN Deputy Vice-Chancellor (Research and Innovation) and Professor of Neonatology, University of Auckland. Chair of the Board of Auckland UniServices Limited. Membership of Perinatal Society of New Zealand, Perinatal Society of Australia and New Zealand, European Society of Gastroenterology, Hepatology and Nutrition, the Australian Clinical Trials Alliance and the Perinatal Research Society of the US, recipient of grants for research relating to nutrition, perinatology, clinical trials and preterm birth from the Health Research Council of New Zealand, Cure Kids, Lotteries Grants Board, A+ Trust, Gravida: National Centre for Growth and the Nurture Foundation. Disclosed receipt of travel support to deliver lectures from Hot Topics in Neonatology, NeoPaeds Australia, Hospital for Sick Children Toronto, Japanese Society for the Developmental Origins of Health and Disease and Nestlé Nutrition Institute. Disclosed having conducted research and published on neonatal nutrition including some of the evidence synthesis considered by the Guideline Development Group.	The majority of declared interests were considered not to represent a conflict. When the panel considered evidence that this researcher was involved in they did not participate in the discussion unless asked for clarification of the facts by the GDG.
Haunui Royal (Parehauraki, Ngāti Raukaha and Ngāpuhi)	Kaiārahi, Liggins Institute, University of Auckland	This disclosure was considered not to represent a conflict and did not require further management
Jutta van den Boom	Neonatal consultant/specialist Member of Aotearoa Milk Bank steering group President of Perinatal Society of NZ Member of PSANZ - PERT – subcommittee Board member – Waikato Sick Babies Trust Board Member – Perinatal Society of Australia and New Zealand (PSANZ) Chair of the Neonatal Medication Aotearoa New Zealand (NMANZ) Working Group	This disclosure was considered not to represent a conflict and did not require further management
Kim Ward	Governance group member and panel member. Employment as registered nurse and senior lecturer with the School of Nursing, Waipapa Taumata Rau. Conducted research and published on participant experience related to neonatal research, including some of the primary evidence considered by the Guideline panel. Recipient of grants for research relating to nutrition and preterm birth from the Health Research Council of New Zealand.	The majority of declared interests were considered not to represent a conflict. When the panel considered evidence that this researcher was involved in they did not participate in the discussion unless asked for clarification of the facts by the GDG.

Name	Conflict of interest	Assessment
Lela Yap (Niue, Ngāti Pikiao)	Neonatologist and General Paediatrician for Te Whatu Ora - Southern and Capital, Coast and Hutt Valley Membership of Perinatal Society of New Zealand, Perinatal Society of Australia and New Zealand Board member of Australia and New Zealand Neonatal Network Panel member of National Limits of viability Honorary Senior Lecturer, Paediatrics, Child and Youth Health, New Zealand at the University of Auckland Membership of Te Kāhui Mātai Arotamariki o Aotearoa/ The Paediatric Society of New Zealand	This disclosure was considered not to represent a conflict and did not require further management
Lilia Delgado Páramo	PhD student, Liggins Institute	This disclosure was considered not to represent a conflict and did not require further management
Lindsay Joseph	Neonatologist at Wellington Hospital and membership of the Perinatal Society of New Zealand and the Perinatal society of Australia. Honorary Senior Lecturer, Paediatrics, Child and Youth Health, New Zealand at the University of Auckland	This disclosure was considered not to represent a conflict and did not require further management
Lisa Kremer (Ngāi Tahu / Kāi Tahu; Kāti Māmoe; Waitaha)	Member of the ON TRACK clinical trials network Associate Dean Māori for He Rau Kawakawa (School of Pharmacy), Ōtākou Whakaihū Waka (University of Otago) Membership of Perinatal Society of New Zealand, Perinatal Society of Australia and New Zealand member Member of Ngā Kaitiaki o Te Puna Rongoā o Aotearoa (Māori Pharmacists' Association) Member of the ON TRACK clinical trials network	This disclosure was considered not to represent a conflict and did not require further management
Liza Edmonds (Ngāpuhi; Ngāti Whātua)	Current Te Whatu Ora Wairarapa senior medical officer Te Tātai Hauoro o Hine, Victoria University Wellington University of Otago Honorary Associate Professor Te Whatu Ora Southern senior medical officer He Mutunga Kore - National Mortality Review Committee Chair University of Waikato advisory board member Paediatric Society of New Zealand member ANZNN CPI committee member ASMS member PI and co-PI on research involving whānau Māori funding from HRC and Cure kids. Sub-editor Journal of Paediatrics and Child Health Past Kōhatu Centre for Hauora Māori University of Otago Ronald McDonald House Charity Board member Health Research South Board member Carosika Collaborative Steering group member Te Aka Whai Ora clinical adviser Perinatal Society of Australia and New Zealand member	This disclosure was considered not to represent a conflict and did not require further management
Luling Lin	Employment as Research Fellow, Liggins Institute, University of Auckland. Having conducted research and published on neonatal nutrition including much of the evidence synthesis considered by the Guideline.	The majority of declared interests were considered not to represent a conflict. When the panel considered evidence that this researcher was involved in they did not participate in the discussion unless asked for clarification of the facts by the GDG.
Mariam Buksh	Neonatologist and current service clinical director for Newborn Services, at Starship Child Health, Te Toka Tumai Honorary senior lecturer in department of Paediatrics and Child Health, University of Auckland. Member of ANZNN Advisory Council. Member of Newborn Clinical Network Member of the Clinical Expert advisory group for Badgernet Neonatal Research interest in body composition in 2-year-olds and transitional care (Thesis topics)	This disclosure was considered not to represent a conflict and did not require further management

Name	Conflict of interest	Assessment
Rachel Friend	Board member Little Miracles Trust Carosika Collaborative	This disclosure was considered not to represent a conflict and did not require further management
Sarah Rusholme	CEO of Little Miracles Trust Board member of The New Zealand Dyspraxia Support Group Board member of the Okiwi-Eastbourne Bays Community Trust	This disclosure was considered not to represent a conflict and did not require further management
Tamara Nickerson (Te Whakatōhea/ Ngā Puhī)	Neonatal Nurse, Clinical Nurse Specialist Kaiārahi Nāhi, Māori Health, Te Toka Tumai, Auckland	This disclosure was considered not to represent a conflict and did not require further management
Tanith Alexander	PI of the DIAMOND trial President of the Perinatal Society of NZ Member of the ON TRACK clinical trials network Australasian Neonatal Dietitians Network Steering Group member (Chair) Connection with Hāpai Te Hauora (husband is CEO) Disclosed employment as Neonatal Dietitian at Counties Manukau Health, Te Whatu Ora. Disclosed honorary appointment as Senior Research Fellow at the Liggins Institute, University of Auckland. Disclosed executive committee member of the Perinatal Society of New Zealand and the Australasian Neonatal Dietitians' Network (ANDiN). Disclosed membership of the Perinatal Society of New Zealand, Perinatal Society of Australia and New Zealand, and the Paediatric Society of New Zealand. Disclosed recipient of research funding from the Health Research Council of New Zealand, the Nurture Foundation, and Counties Manukau Health for studies relating to preterm infant nutrition. Disclosed involvement in the DIAMOND trial and other research on nutritional strategies for moderate and late preterm infants, and qualitative research, including evidence synthesis considered by the Guideline Development Group.	The majority of declared interests were considered not to represent a conflict. When the panel considered evidence that this researcher was involved in they did not participate in the discussion unless asked for clarification of the facts by the GDG.
Terin Port	Nurse Specialist – Lactation, Newborn Services, Starship Child Health, Auckland City Hospital, Te Whatu Ora	This disclosure was considered not to represent a conflict and did not require further management
Violet Clapham	Midwifery Advisor - Professional Projects, NZ College of Midwives, Wellington	This disclosure was considered not to represent a conflict and did not require further management

Appendix F. Key Outcomes and Thresholds for Decision-Making

Outcome	Trivial	Small	Moderate	Large
<i>Judgement of effect size (absolute risk difference per 1,000 babies)</i>				
Critical outcomes				
Mortality	<1	1-9	10-20	>20
Neurodevelopmental impairment	<10	10-19	20-50	>50
Adverse effects (Depending on outcome, this one is for feed intolerance, more minor effects thresholds would be higher)				
Fully breastmilk feeding at hospital discharge	<20	20-49	50-100	>100
Important but not critical				
Fully breastfeeding at hospital discharge	<20	20-49	50-100	>100
Time to full enteral feeds (days)	<0.5	0.5-0.9	1-2	>2
Duration of initial hospital stay (days)	<0.5	0.5-0.9	1-2	>2
Bronchopulmonary dysplasia	<10	10-19	20-50	>50
Necrotizing enterocolitis	<1	1-9	10-20	>20
Sepsis: proven or suspected	<10	10-19	20-50	>50
Retinopathy of prematurity	<10	10-19	20-50	>50
Anaemia of prematurity	<10	10-19	20-50	>50
		Negligible	Moderate	Large
Cost: cost of intervention, cost of neonatal care and life-long cost (NZD per baby)		<\$5,000	\$5,000-10,000	>\$10,000
Growth outcomes				
Faltering growth/body composition (z-score change)	<0.5	0.5-0.9	1-2	>2

Appendix G. Publications

Systematic Reviews

1. Bronnert, A., P. M. Bloomfield, L. D. Paramo, L. Lin, F. H. Bloomfield, and B. E. Cormack. "The Effect of Vitamin Supplementation on Neurodevelopmental and Clinical Outcomes in Very Low Birth Weight and Very Preterm Infants: A Systematic Review and Meta-Analysis." *PLoS One* 20, no. 7 (2025): e0327628.
<https://doi.org/10.1371/journal.pone.0327628> <https://www.ncbi.nlm.nih.gov/pubmed/40632831>
2. Das, S., T. McClintock, B. E. Cormack, F. H. Bloomfield, J. E. Harding, and L. Lin. "High Protein Intake on Later Outcomes in Preterm Children: A Systematic Review and Meta-Analysis." *Pediatr Res* 97, no. 1 (Jan 2025): 67-80.
<https://www.ncbi.nlm.nih.gov/pubmed/38858504>
3. Delgado Paramo, L., A. Bronnert, L. Lin, F. H. Bloomfield, M. Muelbert, and J. E. Harding. "Exposure to the Smell and Taste of Milk to Accelerate Feeding in Preterm Infants." *Cochrane Database Syst Rev* 5, no. 5 (May 9 2024): CD013038.
<https://doi.org/10.1002/14651858.CD013038.pub3> <https://www.ncbi.nlm.nih.gov/pubmed/38721883>.
4. Meiliana, M., T. Alexander, F. H. Bloomfield, B. E. Cormack, J. E. Harding, O. Walsh, and L. Lin. "Nutrition Guidelines for Preterm Infants: A Systematic Review." *JPEN J Parenter Enteral Nutr* 48, no. 1 (Jan 2024): 11-26.
<https://doi.org/10.1002/jpen.2568> <https://www.ncbi.nlm.nih.gov/pubmed/37855274>
5. Bell CM, Cormack BE, Buksh M, Bloomfield FH, Lin L. Standardised versus individualised fortification of expressed breastmilk for preterm outcomes: a systematic review and meta-analysis. *Neonatology*. Accepted 2026 (in press).

Appendix H. Evidence to Decision Tables

Please note: When reviewing the evidence for each EtD, consideration was given to the evidence (or lack thereof) for Māori and non-Māori babies and their whānau. Consideration was also given to the evidence (or lack thereof) for extremely preterm or extremely low birthweight (Birthweight; <1,000 g), and moderate to late preterm, very low birthweight (<1,500 g) and low birthweight (<2,500 g) subgroups

Appendix H.1 – Evidence to Decision: Parenteral Nutrition

EtD 1. In moderate-to-late preterm infants whose mothers' breastmilk is not available at birth, while we wait for mothers' breastmilk what method of nutrition (parenteral nutrition vs. 10% glucose vs. infant formula vs. donor milk), is best for breastfeeding at discharge, neurodevelopment, weight loss/growth in first week, mode of feeding at discharge?

POPULATION:	Moderate-to-late preterm infants whose mother's breastmilk is not available at birth, while we wait for mother's breastmilk
INTERVENTION:	Parenteral nutrition
COMPARISON:	10% glucose
MAIN OUTCOMES:	Critical outcomes Mortality Neurodevelopmental impairment Fully breastfed or breastmilk feeding at hospital discharge Important but not critical Adverse effects Time to full enteral feeds Duration of initial hospital stay Sepsis: proven or suspected Bronchopulmonary dysplasia Necrotising enterocolitis Retinopathy of prematurity Anaemia of prematurity Faltering growth/body composition Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation: population perspective
BACKGROUND:	The choice of nutrition support for moderate-to-late preterm infants when mothers' breastmilk is not yet available may have a significant impact on short- and long-term outcomes. Parenteral nutrition (PN) ensures the direct provision of essential nutrients into the bloodstream. While PN supports early growth and prevents malnutrition, it is invasive and poses risks such as catheter-related infections, biochemical imbalances and liver dysfunction. Parenteral 10% glucose is often used temporarily to prevent dehydration and hypoglycaemia in the absence of enteral nutrition, but it does not provide the protein, fat, and micronutrients necessary for growth and development. Use for more than a few days leads to nutrient deficits. Infant formula is nutritionally complete and supports growth when human breastmilk is unavailable. However, it lacks the bioactive components of breastmilk, increasing the risk of feeding intolerance and necrotising enterocolitis (NEC). Donor breastmilk, when available, is preferred to infant formula because it provides bioactive factors that promote immunity, gut maturation, and neurodevelopment while lowering the risk of NEC. However, the protein and energy content may be lower than infant formula, necessitating additional fortification. Selecting the optimal feeding method involves balancing the immediate

CONFLICT OF INTERESTS:	fluid and nutritional needs of the infant with the long-term benefits of waiting for mother's own breastmilk to promote breastfeeding, optimal neurodevelopment and long-term health.
	The following DIAMOND study investigators and co-authors (references 1, 3 and 4) are on the Guideline Development Group: Tanith Alexander and Frank Bloomfield

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence is based on two randomised trials (RCT)[1,2] and a cohort analysis [3]. Mortality: RCT: Little or no effect on mortality between parenteral nutrition and 10% glucose (1/269 for parenteral nutrition and 0/263 for 10% glucose). [Critical] Fully breastfed or breastmilk feeding at hospital discharge: RCT: No significant effect on increased breastfeeding at discharge for infants receiving parenteral nutrition (2 more per 1,000; 83 fewer to 76 more). [Critical] Fully breastfed or breastmilk feeding at hospital discharge: Cohort: Receiving exclusively breastmilk at discharge was more likely for infants who successfully transitioned from IV fluids onto mother's own milk only [OR (95% confidence intervals) 4.9 (2.3–10.6)] and who received only mother's own milk in the first week after birth [4.8 (2.2–10.4)], both $p < 0.0001$. Pēpi Māori transitioned off IV fluids more quickly than other ethnicities but were less likely to achieve a successful transition to mother's own milk only (43%) than Pacific (74%, $p = 0.02$) and Caucasian (70%, $p = 0.03$) infants. Pēpi Māori received alternative nutrition earlier than infants of other ethnicities ($p = 0.007$); by day 3, 55% of Māori, 22% of Pacific, 20% of Caucasian, and 28% of Asian infants were receiving alternative nutrition that was not mother's own milk. Pēpi Māori were significantly less likely to receive exclusively breastmilk at discharge compared with Caucasian infants [OR= 0.2 (0.1–0.6), $p < 0.01$]. Full enteral feeds: RCT: Large effect for faster time to full enteral feeds for parenteral nutrition (Adj HR 1.05 days higher; 0.88 higher to 1.25 higher). [Important] Duration of initial hospital stay: RCT: No significant effect on duration of hospital stay between parenteral nutrition and 10% glucose (Adj MD 0.32 days lower; 1.91 lower to 1.28 higher). [Important] Sepsis: RCT: Little or no effect between parenteral nutrition and 10% glucose for incidence of sepsis (3/269 for parenteral nutrition and 1/263 for 10% glucose). [Important] Necrotising enterocolitis (NEC): RCT: Little or no effect between parenteral nutrition and 10% glucose for incidence of NEC (1/269 for parenteral nutrition and 0/263 for 10% glucose). [Important]	Population information for included evidence [1,2] New Zealand. RCT + cohort analysis Moderate- to late-preterm infants. [3] Australia. RCT. Infants of 30-33 weeks' gestation. [4] New Zealand: Conference proceedings: Neurosensory impairment was similar at 2 years in amino acid and glucose group (no data provided in abstract).

No faltering growth/body composition: RCT: Small effect for increases in growth outcomes for parenteral nutrition for day 7 weight z score (Adj MD 0.11 points higher; 0.07 higher to 0.15 higher); day 14 weight z score (Adj MD 0.09 points higher; 0.04 higher to 0.14 higher); day 21 weight z score (Adj MD 0.1 points higher; 0.03 higher to 0.18 higher). No significant effect on day 28 weight z score (Adj MD 0.11 points higher; 0.01 lower to 0.22 higher). Small increase in discharge weight z score (Adj MD 0.07 points higher; 0.01 higher to 0.14 higher). No significant effect on 4 months corrected age weight z score (Adj MD 0.08 points higher; 0.1 lower to 0.26 higher); day 7 length z score (Adj MD 0.04 points higher; 0.06 lower to 0.14 higher); day 14 length z score (Adj MD 0.1 points higher; 0.01 lower to 0.21 higher); day 21 length z score (Adj MD 0.08 points higher; 0.06 lower to 0.21 higher); day 28 length z score (Adj MD 0.17 points higher; 0.02 lower to 0.37 higher); discharge length z score (Adj MD 0.06 points higher; 0.06 lower to 0.18 higher); 4 months corrected age length z score (Adj MD 0.15 points higher; 0.05 lower to 0.35 higher); day 7 head circumference z score (Adj MD 0.08 points higher; 0.02 lower to 0.18 higher); day 14 head circumference z score (Adj MD 0.06 points higher; 0.04 lower to 0.17 higher); day 21 head circumference z score (Adj MD 0.07 points higher; 0.06 lower to 0.19 higher); day 28 head circumference z score (Adj MD 0.11 points higher; 0.07 lower to 0.3 higher); discharge head circumference z score (Adj MD 0.04 points higher; 0.06 lower to 0.14 higher); 4 months corrected age circumference z score (Adj MD 0.01 points lower; 0.2 lower to 0.17 higher). Increase in discharge fat mass z score (Adj HR 1.06 points higher; 0.81 higher to 1.37 higher). [Important]

Desirable effects for Māori - see table below

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with 10% glucose	Risk difference with parenteral nutrition
Mortality	532 (1 RCT)	⊕○○○ Very low ^{a,b}	-	1/269 for parenteral nutrition and 0/263 for 10% glucose	
Neurodevelopmental impairment - not measured	-	-	-	-	-
Fully breastfed or breastmilk feeding at hospital discharge: RCT	528 (1 RCT)	⊕⊕⊕○ Moderate ^a	OR 1.01 (0.69 to 1.49)	Study population	
				704 per 1,000	2 more per 1,000 (83 fewer to 76 more)
Fully breastfed or breastmilk feeding at hospital discharge: RCT assessed with: Breastmilk (any) on discharge home	84 (1 RCT)	⊕⊕○○ Low ^{c,d}	Adj OR 0.8 (0.2 to 3.3)	Study population	
				891 per 1,000	178 fewer per 1,000 (713 fewer to 2,050 more)

Fully breastfed or breastmilk feeding at hospital discharge: Cohort	151 (1 non-randomised study)	⊕○○○ Very low ^a	-	n=151 late and moderate preterm infants. Of these, 65 (43%) received IV glucose and 86 (53%) received parenteral nutrition, with 70% of the latter receiving IV lipid emulsion in addition to an amino acid solution. A total of 93 (63%) infants	
				successfully transitioned from IV fluids onto mother's own milk. Late preterm infants transitioned off IV fluids onto only enteral feeds more quickly than moderate preterm infants and late preterm took the least time to transition. Receiving exclusively breastmilk at discharge was more likely for infants who successfully transitioned from IV fluids onto mother's own milk only [OR (95% confidence intervals) 4.9 (2.3–10.6)] and who received only mother's own milk in the first week after birth [4.8 (2.2–10.4)], both $p < 0.0001$. Multiples were less likely to achieve a successful transition to mother's own milk only than singletons (46 vs. 67%, $p = 0.02$), and this was particularly the case for late preterm infants (33 vs. 68%, $p = 0.007$). Pēpi Māori transitioned off IV fluids more quickly than other ethnicities but were less likely to achieve a successful transition to mother's own milk only (43%) than Pacific (74%, $p = 0.02$) and Caucasian (70%, $p = 0.03$) infants. Pēpi Māori received alternative nutrition earlier than infants of other ethnicities ($p = 0.007$); by day 3, 55% of Māori, 22% of Pacific, 20% of Caucasian, and 28% of Asian infants were receiving alternative nutrition that was not mother's own milk. Pēpi Māori were significantly less likely to receive exclusively breastmilk at discharge compared with Caucasian infants [OR= 0.2 (0.1–0.6), $p < 0.01$].	
Adverse effects: RCT assessed with: Hypoglycaemia requiring treatment	92 (1 RCT)	⊕○○○ Very low ^{a,c,e}	Adj OR 0.5 (0.1 to 2.0)	Study population	
				160 per 1,000	80 fewer per 1,000 (144 fewer to 160 more)
Time to full enteral feeds: RCT assessed with: Days	526 (1 RCT)	⊕⊕⊕○ Moderate ^a	-	The mean time to full enteral feeds: RCT was 5.8 days	Adj HR 1.05 higher (0.88 higher to 1.25 higher)
Time to full enteral feeds: RCT assessed with: Days (120 mLs/kg/d)	92 (1 RCT)	⊕⊕⊕○ Moderate ^c	-	The mean time to full enteral feeds: RCT was 6.2 days	Adj ratio of means 1.1 higher (0.9 higher to 1.2 higher)
Duration of initial hospital stay: RCT assessed with: Days	532 (1 RCT)	⊕⊕○○ Low ^{a,e}	-	The mean duration of initial hospital stay: RCT was 25 days	Adj MD 0.32 lower (1.91 lower to 1.28 higher)
Duration of initial hospital stay: RCT assessed with: Days	92 (1 RCT)	⊕⊕⊕○ Moderate ^c	-	The mean duration of initial hospital stay: RCT was 35.6 days	Adj ratio of means 1 higher (0.9 higher to 1.1 higher)
Sepsis: proven or suspected: RCT assessed with: confirmed sepsis	92 (1 RCT)	⊕○○○ Very low ^{c,b}	Adj OR 2.1 (0.2 to 19.0)	Study population	
				20 per 1,000	22 more per 1,000 (16 fewer to 360 more)
Sepsis: proven or suspected: RCT assessed with: Culture-proven late-onset sepsis	532 (1 RCT)	⊕○○○ Very low ^{a,b}	-	3/269 for parenteral nutrition and 1/263 for 10% glucose	
Sepsis: proven or suspected: RCT assessed with: Probable late-onset sepsis	532 (1 RCT)	⊕○○○ Very low ^{a,b}	-	3/269 for parenteral nutrition and 1/263 for 10% glucose	
Bronchopulmonary dysplasia - not measured	-	-	-	-	-

Necrotising enterocolitis	532 (1 RCT)	⊕○○○ Very low ^{a,b}	-	1/269 for parenteral nutrition and 0/263 for 10% glucose	
Retinopathy of prematurity - not measured	-	-	-	-	-
Faltering growth/body composition: RCT assessed with: Time to regain birthweight (days)	90 (1 RCT)	⊕○○○ Very low ^{a,c,b}	-	The mean faltering growth/body composition: RCT was 12.3 days	Adj ratio of means 0.8 higher (0.7 higher to 0.9 higher)

Anaemia of prematurity - not measured	-	-	-	-	-
Faltering growth/body composition: RCT assessed with: Day 7: Weight z score	493 (1 RCT)	⊕⊕○○ Low ^{a,e}	-	The mean faltering growth/body composition: RCT was -0.92 points	Adj MD 0.11 higher (0.07 higher to 0.15 higher)
Faltering growth/body composition: RCT assessed with: Day 14: Weight z score	428 (1 RCT)	⊕⊕○○ Low ^{a,e}	-	The mean faltering growth/body composition: RCT was -0.97 points	Adj MD 0.09 higher (0.04 higher to 0.14 higher)
Faltering growth/body composition: RCT assessed with: Day 21: Weight z score	309 (1 RCT)	⊕⊕○○ Low ^{a,e}	-	The mean faltering growth/body composition: RCT was -0.93 points	Adj MD 0.1 higher (0.03 higher to 0.18 higher)
Faltering growth/body composition: RCT assessed with: Weight gain from birth to day 21, g/d	92 (1 RCT)	⊕⊕○○ Low ^{c,e}	-	The mean faltering growth/body composition: RCT was 14.8 g/day	Adj MD 4.4 higher (1.9 higher to 7 higher)
Faltering growth/body composition: RCT assessed with: Day 28: Weight z score	182 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -0.77 points	Adj MD 0.11 higher (0.01 lower to 0.22 higher)
Faltering growth/body composition: RCT assessed with: Discharge: Weight z score	524 (1 RCT)	⊕⊕⊕○ Moderate ^a	-	The mean faltering growth/body composition: RCT was -0.80 points	Adj MD 0.07 higher (0.01 higher to 0.14 higher)
Faltering growth/body composition: RCT assessed with: 4 months corrected age: Weight z score	401 (1 RCT)	⊕○○○ Very low ^{a,d,e}	-	The mean faltering growth/body composition: RCT was -0.07 points	Adj MD 0.08 higher (0.1 lower to 0.26 higher)
Faltering growth/body composition: RCT assessed with: Day 7: Length z score	469 (1 RCT)	⊕○○○ Very low ^{a,d,e}	-	The mean faltering growth/body composition: RCT was -0.20 points	Adj MD 0.04 higher (0.06 lower to 0.14 higher)
Faltering growth/body composition: RCT assessed with: Day 14: Length z score	415 (1 RCT)	⊕○○○ Very low ^{a,d,e}	-	The mean faltering growth/body composition: RCT was -0.32 points	Adj MD 0.1 higher (0.01 lower to 0.21 higher)
Faltering growth/body composition: RCT assessed with: Day 21: Length z score	299 (1 RCT)	⊕○○○ Very low ^{a,d,e}	-	The mean faltering growth/body composition: RCT was -0.35 points	Adj MD 0.08 higher (0.06 lower to 0.21 higher)
Faltering growth/body composition: RCT assessed with: Day 28: Length z score	178 (1 RCT)	⊕○○○ Very low ^{a,d,e}	-	The mean faltering growth/body composition: RCT was -0.49 points	Adj MD 0.17 higher (0.02 lower to 0.37 higher)
Faltering growth/body composition: RCT assessed with: Discharge: Length z score	495 (1 RCT)	⊕⊕⊕○ Moderate ^e	-	The mean faltering growth/body composition: RCT was -0.20 points	Adj MD 0.06 higher (0.06 lower to 0.18 higher)
Faltering growth/body composition: RCT assessed with: Length gain to discharge (mm/d)	87 (1 RCT)	⊕⊕⊕○ Moderate ^c	-	The mean faltering growth/body composition: RCT was 1.0 mm/day	Adj MD 0.3 higher (0 to 0.5 higher)
Faltering growth/body composition: RCT assessed with: 4 months corrected age: Length z score	401 (1 RCT)	⊕○○○ Very low ^{a,d,e}	-	The mean faltering growth/body composition: RCT was 0.48 points	Adj MD 0.15 higher (0.05 lower to 0.35 higher)
Faltering growth/body composition: RCT assessed with: Day 7: Head circumference z score	472 (1 RCT)	⊕○○○ Very low ^{a,d,e}	-	The mean faltering growth/body composition: RCT was -0.27 points	Adj MD 0.08 higher (0.02 lower to 0.18 higher)

Faltering growth/body composition: RCT assessed with: Day 14: Head circumference z score	420 (1 RCT)	⊕○○○ Very low ^{a,d,e}	-	The mean faltering growth/body composition: RCT was -0.24 points	Adj MD 0.06 higher (0.04 lower to 0.17 higher)
Faltering growth/body composition: RCT assessed with: Day 21: Head circumference z score	299 (1 RCT)	⊕○○○ Very low ^{a,d,e}	-	The mean faltering growth/body composition: RCT was -0.16 points	Adj MD 0.07 higher (0.06 lower to 0.19 higher)
Faltering growth/body composition: RCT assessed with: Day 28: Head circumference z score	178 (1 RCT)	⊕○○○ Very low ^{a,d,e}	-	The mean faltering growth/body composition: RCT was -0.01 points	Adj MD 0.11 higher (0.07 lower to 0.3 higher)
Faltering growth/body composition: RCT assessed with: Discharge: Head circumference z score	500 (1 RCT)	⊕⊕⊕○ Moderate ^d	-	The mean faltering growth/body composition: RCT was 0.04 points	Adj MD 0.04 higher (0.06 lower to 0.14 higher)
Faltering growth/body composition: RCT assessed with: Head circumference to discharge (mm/d)	86 (1 RCT)	⊕⊕○○ Low ^{c,d}	-	The mean faltering growth/body composition: RCT was 0.9 mm/day	Adj MD 0.1 higher (0.1 lower to 0.2 higher)
Faltering growth/body composition: RCT assessed with: 4 months corrected age: Head circumference z score	401 (1 RCT)	⊕○○○ Very low ^{a,d,e}	-	The mean faltering growth/body composition: RCT was 0.75 points	Adj MD 0.01 lower (0.2 lower to 0.17 higher)
Faltering growth/body composition: RCT assessed with: Discharge: Fat mass z score	173 (1 RCT)	⊕○○○ Very low ^{a,d,e}	-	The mean faltering growth/body composition: RCT was -0.3 points	Adj MD 0 (0.2 lower to 0.2 higher)
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds: RCT assessed with: Days	519 (1 RCT)	⊕⊕○○ Low ^{a,e}	-	The mean time to full sucking feeds: RCT was 22.5 days	Adj HR 1.06 higher (0.81 higher to 1.37 higher)

- a. Downgraded one level for indirectness as evidence is based on a single study
b. Downgraded two levels for imprecision as result has very low or no events
c. Downgraded one level for concerns for risk of bias
d. Downgraded one level for imprecision with confidence intervals crossing the line of no effect
e. Downgraded one level for imprecision due to wide confidence intervals or low sample numbers

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Undesirable effects for Māori Pēpi Māori transitioned off IV fluids more quickly than other ethnicities but were less likely to achieve a successful transition to mother's own milk only (43%) than Pacific (74%, p= 0.02) and Caucasian (70%, p= 0.03) infants. Pēpi Māori received alternative nutrition earlier than infants of other ethnicities (p= 0.007); by day 3, 55% of Māori, 22% of Pacific, 20% of Caucasian, and 28% of Asian infants were receiving alternative nutrition that was not mother's own milk.	

	Pēpi Māori were significantly less likely to receive exclusively breastmilk at discharge compared with Caucasian infants [OR= 0.2 (0.1–0.6), p < 0.01]. No additional evidence available	
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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Low to very low certainty of evidence overall mainly due to the body of evidence being from a single trial, albeit well conducted. Certainty of evidence for Māori: No additional evidence available	

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment - not measured	CRITICAL	-
Fully breastfed or breastmilk feeding at hospital discharge: RCT	CRITICAL	⊕⊕⊕○ Moderate
Fully breastfed or breastmilk feeding at hospital discharge: Cohort	CRITICAL	⊕○○○ Very low
Adverse effects: RCT assessed with: Hypoglycaemia requiring treatment	IMPORTANT	⊕○○○ Very low
Time to full enteral feeds: RCT assessed with: Days	IMPORTANT	⊕⊕⊕○ Moderate
Duration of initial hospital stay: RCT assessed with: Days	IMPORTANT	⊕⊕○○ Low
Sepsis: proven or suspected: RCT assessed with: Culture-proven late-onset sepsis	IMPORTANT	⊕○○○ Very low
Sepsis: proven or suspected: RCT assessed with: Probable late-onset sepsis	IMPORTANT	⊕○○○ Very low
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Necrotising enterocolitis	IMPORTANT	⊕○○○ Very low
Retinopathy of prematurity - not measured	IMPORTANT	-

Anaemia of prematurity - not measured	IMPORTANT	-
Faltering growth/body composition: RCT assessed with: Day 7: Weight z score	IMPORTANT	⊕⊕○○ Low
Faltering growth/body composition: RCT assessed with: Day 14: Weight z score	IMPORTANT	⊕⊕○○ Low
Faltering growth/body composition: RCT assessed with: Day 21: Weight z score	IMPORTANT	⊕⊕○○ Low
Faltering growth/body composition: RCT assessed with: Day 28: Weight z score	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Discharge: Weight z score	IMPORTANT	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT assessed with: 4 months corrected age: Weight z score	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Day 7: Length z score	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Day 14: Length z score	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Day 21: Length z score	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Day 28: Length z score	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Discharge: Length z score	IMPORTANT	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT assessed with: 4 months corrected age: Length z score	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Day 7: Head circumference z score	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Day 14: Head circumference z score	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Day 21: Head circumference z score	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Day 28: Head circumference z score	IMPORTANT	⊕○○○ Very low

Faltering growth/body composition: RCT assessed with: Discharge: Head circumference z score	IMPORTANT	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT assessed with: 4 months corrected age: Head circumference z score	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Discharge: Fat mass z score	IMPORTANT	⊕○○○ Very low
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds: RCT assessed with: Days	NOT IMPORTANT	⊕⊕○○ Low

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ Important uncertainty or variability ☒ Possibly important uncertainty or variability ☐ Probably no important uncertainty or variability ☐ No important uncertainty or variability	Possibly important uncertainty or variability in how much people value the main outcomes Values for Māori: No additional evidence available	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ Favours the comparison ☐ Probably favours the comparison ☐ Does not favour either the intervention or the	Parenteral nutrition compared with 10% glucose - low certainty evidence Uncertain effect on fully breastfed or breastmilk feeding at hospital discharge Quicker time to full enteral feeds Increase in growth/body composition (day 7, 14, 21 and discharge weight z-score) Parenteral nutrition compared with 10% glucose - very low certainty evidence No difference for mortality	

comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Uncertain effect for duration of initial hospital stay, NEC, sepsis, faltering growth/body composition (4 months corrected age weight z score; day 7, 14, 21, 28, discharge and 4 months corrected age length z score) Increase in growth/body composition (day 28 weight z-score) Balance of effects for Māori: No additional evidence	
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Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Assuming clinician time to prescribe standardised parenteral and enteral nutrition and nursing time to administer and may be similar for both. Costs for parenteral nutrition: Glucose, amino acid and electrolyte standard solution (aqueous phase) Aqueous solution: Company A approx. \$140 (used for 48 hours) Company B \$118 (used for 96 hours) = \$29.50 to \$70 per day SMOFLipid including vitamins per syringe: approx. \$51 to \$71 (used for 48 hours) = \$25.50 to \$35.50 Total \$55 to \$105 per day plus catheter, giving sets and IV pump Costs for 10% glucose: \$7.00 for 500 mL bag of 10% glucose plus catheter, giving sets and IV pump Blood tests for parenteral nutrition monitoring, etc Courier delivery may be required for regional centres Resources required for Māori: No additional evidence available	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ● High ○ No included studies	Costs are known. Certainty of evidence of required sources for Māori: No additional evidence available	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	There are no studies that assess the specific cost-effectiveness of parenteral nutrition versus 10% glucose whilst waiting for mother's own milk, particularly in the context of preterm infants. However, the costs are reasonably certain. Cost effectiveness for Māori: No additional evidence available	
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Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Influenced by the effects of colonisation, pēpi Māori are more likely to be born preterm, admitted to NICU, born at extremely low birthweight and fewer survive. There is also a greater burden for Māori of morbidities associated with nutrition practices such as intraventricular haemorrhage, sepsis, bronchopulmonary dysplasia and neurodisability. Pēpi Māori may also experience different nutritional transitions in early life. In one recent Aotearoa New Zealand study, pēpi Māori transitioned off parenteral fluids more quickly than other ethnicities but were less likely to achieve a successful transition to mother's own milk only, with just 43% reaching this compared to 74% of Pacific and 70% of European infants. By day three, 55% of pēpi Māori had received alternative nutrition that was not mother's own milk, which was substantially higher than Pacific at 22%, European at 20% and Asian at 28%. Furthermore, pēpi Māori were significantly less likely to be exclusively breastmilk fed at discharge compared with European infants. Implementing standardised parenteral nutrition practices in Aotearoa New Zealand will help address these inequities by supporting equitable nutrition and feeding outcomes for preterm pēpi Māori and their whānau. Equity for Pacific families Implementing standardised parenteral nutrition practices in Aotearoa New Zealand will contribute directly to reducing health disparities across all ethnicities and under-represented groups. While Pacific infants were more likely to successfully transition to mother's own milk only by comparison to Māori and European pēpi, 74% versus 43% and 70% respectively, they still had a high rate of receiving alternative nutrition by	If recommended but not implemented in rural settings this would reduce equity.

	day three, with 22% affected. These findings highlight that variation in early nutrition practices affects all groups and addressing these differences through consistent care will promote more equitable outcomes for all preterm pēpi and their families. Equity for underrepresented groups Families from underrepresented backgrounds may struggle to understand complex feeding options during a critical and emotional time. Without timely, accessible explanations, parents may feel excluded from decisions. Equity requires culturally responsive guidance and clear communication to ensure all families are supported while awaiting breastmilk and making early nutritional choices.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☐ Varies ☐ Don't know	Probably acceptable.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☐ Probably yes ☐ Yes ☒ Varies ☐ Don't know	Feasibility would vary depending on the hospital location.	An urgent need for quality initiatives to support and encourage mothers of moderate- and late-preterm infants in their lactation.

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE	Trivial	Small	Moderate	Large		Varies	Don't know

	JUDGEMENT						
EFFECTS							
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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EtD 4. Should lower parenteral fluid vs. Higher parenteral fluid be used for preterm infants receiving parenteral nutrition?

POPULATION:	Preterm infants receiving parenteral nutrition
INTERVENTION:	Lower parenteral fluid
COMPARISON:	Higher parenteral fluid
MAIN OUTCOMES:	Critical outcomes Mortality Necrotising enterocolitis Bronchopulmonary dysplasia Adverse effects – patent ductus arteriosus Faltering growth/body composition Important but not critical Neurodevelopmental impairment Fully breastfed or breastmilk feeding at hospital discharge Time to full enteral feeds Duration of initial hospital stay Sepsis: proven or suspected Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical guideline recommendation. Patient perspective
BACKGROUND:	The fluid and electrolyte requirements of preterm infants are unique due to significant fluid shifts in the first days and weeks after birth. At birth, preterm infants have an excess of extracellular fluid, which naturally decreases during the initial postnatal period. However, their immature organ systems often limit their ability to take in sufficient water and nutrients orally, leaving them unable to regulate water balance effectively. Inadequate water intake can lead to dehydration, while excessive water intake can cause complications such as heart and lung problems or intestinal damage. Intravenous or parenteral fluid therapy is, therefore, a critical aspect of neonatal care. It aims to maintain optimal hydration, electrolyte balance and nutritional support while minimising the risk of complications, such as patent ductus arteriosus (affecting the heart), bronchopulmonary dysplasia (affecting the lungs), or necrotising enterocolitis (causing intestinal damage). Fluid requirements vary with postnatal age and gradually increase during the first week after birth to meet growing metabolic demands. Parenteral fluid volumes are carefully adjusted based on factors such as birthweight, gestational age, clinical condition, blood biochemistry, and urine output. Excessive fluid intake has been linked to a higher risk of patent ductus arteriosus, bronchopulmonary dysplasia, and necrotising enterocolitis, underscoring the importance of precise fluid management. Conversely, insufficient fluid provision can result in dehydration, electrolyte imbalances and inadequate weight gain. Standardised fluid management which is then adjusted for individual requirements is essential to support the health and development of preterm infants. However, due to a lack of evidence, there is great variation in fluid management protocols in

CONFLICT OF INTERESTS:	clinical practice.
	None

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence is based on a Cochrane review [1] and observational studies [2] looking at whether early fluid restriction prevents bronchopulmonary dysplasia. 1 RCT [3] and 11 observational studies were identified [4-14]. The data from these additional studies has not been combined due to the heterogeneity of study design and populations and eras of clinical practice. Restricted versus liberal fluids Mortality: RCT: There was no difference for restricted versus liberal fluids for death (28 fewer per 1,000; 68 fewer to 34 more) [Critical]. Bronchopulmonary dysplasia: RCT: There was no difference for restricted versus liberal fluids for bronchopulmonary dysplasia (38 fewer per 1,000; 94 fewer to 36 more) [Critical]. Bronchopulmonary dysplasia: Observational study: A pre-post cohort study (Diderholm 2022) [6] found no significant difference in bronchopulmonary dysplasia (Restricted 24/63; 38% vs 41/112; 36%). A cohort study reported that significantly more infants in the high-fluid group developed bronchopulmonary dysplasia in week 1 (low fluid 10/51; 20% vs. intermediate fluid 27/102; 26% vs. high fluid 27/51; 53%; $P < 0.001$) [Critical]. Necrotising enterocolitis (NEC): RCT: Restricted fluids was associated with a decreased risk for NEC compared with liberal fluids (52 fewer per 1,000; 72 fewer to 12 fewer) [Critical]. Adverse effects: RCT: Restricted fluids were associated with a significant decrease in patent ductus arteriosus (144 fewer per 1,000; 189 fewer to 81 fewer) [Critical]. Adverse effects: Observational study: A pre-post cohort study (Diderholm 2022) found no significant difference in patent ductus arteriosus ligation (Restricted 20/63; 32% vs. 39/112; 34%). A cohort study (Stephens 2008) [14] reported that significantly more infants in the high-fluid group developed patent ductus arteriosus in week 1 (low fluid 3/51; 6% vs. intermediate fluid 7/102; 7% vs. high fluid 10/51; 20%; $P = 0.024$) [Critical]. No faltering growth/body composition: Observational study: A pre-post cohort study (Diderholm 2022) found no significant difference in % weight change at day 8 of life (Restricted -9 +/- 7% vs. Liberal -10 +/- 6%). A cohort study (Stephens 2008) reported that infants in the low-fluid group had significantly lower average daily weight loss during week 1 than infants in the intermediate or high-fluid group (-8.3 +/- 11.6 vs. -12.8 +/- 10 vs. -14.4 +/- 13 g/kg/day, respectively) [Critical].	The review by Bollaboina [2] included 5 studies of mixed design including a case control study, 3 cohort studies and a post-hoc analysis of a RCT. The methodological quality of the studies is good. The data were not pooled. The Bell systematic review only included 5 RCTs comparing liberal versus restricted water intake provided primarily via parenteral infusion [1]. Liberal water was considered the standard. There was variability between studies on the commencement and duration of water intake. The studies were conducted in the pre-surfactant era. There was inconsistency in the definition of the volume of fluids provided in the restricted and liberal groups Sweden [4]: Retrospective cohort study: Infants born 22-23 weeks' gestational age ($n = 36$). Fluid balance data for infants in high humidification incubators (80 to 85%). USA [5]: Retrospective cohort study: Extremely low birthweight infants ($n = 226$). Identified 151/226 (67%) of infants with moderate to severe bronchopulmonary dysplasia, 75/226 acted as controls.

	Fluid balance Mortality: Observational studies: A retrospective cohort study (Rallis 2024) found no significant difference in mortality between infants with fluid overload $\geq 5\%$ in first 24 hours (2/42; 5%) or those with no fluid overload (6/61; 10%). A retrospective chart review study (Levinson 2018) found no significant difference in mortality between infants receiving no additional/$<15\%$ additional fluids vs. $\geq 15\%$ to 40% additional fluids vs. $\geq 40\%$ additional fluids (1/112; 9% vs. 13/68; 19% vs. 4/20; 20%). A retrospective cohort study (Matsishita 2020) reported that 71/219 (32.4%) of infants died. Fluid overload in the first 72 hours after birth in an extremely preterm infant is associated with higher mortality rate (HR 3.07, 95%CI 1.71 to 5.53). Infants with severe fluid overload had a significantly higher mortality rate (72.2%) compared with groups with negative fluid balance (28.6%), mild (30.4%), and moderate (23.4%) fluid overload $P = 0.002$). Infants with severe fluid overload died significantly earlier during the neonatal intensive care unit stay than those without or less fluid overload ($P < 0.0005$) [Critical]. Bronchopulmonary dysplasia: Observational studies: A retrospective cohort study (Rallis 2024) found no significant difference in bronchopulmonary dysplasia between infants with fluid overload $\geq 5\%$ in first 24 hours (20/42; 48%) or those with no fluid overload (23/61; 38%). A retrospective chart review study (Levinson 2018) found no significant difference in bronchopulmonary dysplasia between infants receiving no additional/$<15\%$ additional fluids vs. $\geq 15\%$ to 40% additional fluids vs. $\geq 40\%$ additional fluids (67/112; 60% vs. 49/68; 72% vs. 15/20; 75%) [Critical]. Necrotising enterocolitis: Observational studies: A retrospective chart review study (Levinson 2018) found no significant difference in bronchopulmonary dysplasia between infants receiving no additional/$<15\%$ additional fluids vs. $\geq 15\%$ to 40% additional fluids vs. $\geq 40\%$ additional fluids (9/112; 8% vs. 1/68; 1% vs. 2/20; 10%) [Critical]. Adverse effects: RCT: A RCT (Reller 1985) did not find a statistical difference in the incidence of haemodynamically stable patent ductus arteriosus between fluid intake and percent of birthweight loss during the first five days of life 17/26 (65.4%) in the restricted group 1 and 15/24 (62.5%) in the more restricted group 2 [Critical]. Adverse effects: Observational studies: A retrospective cohort study (Rallis 2024) found infants with fluid overload $\geq 5\%$ in first 24 hours were more likely to be diagnosed with haemodynamically significant patent ductus arteriosus compared with infants without fluid overload (48% vs. 20% respectively; $P=0.004$). A retrospective chart review study (Levinson 2018) found no significant difference in patent ductus arteriosus between infants receiving no additional/$<15\%$ additional fluids vs. $\geq 15\%$ to 40% additional fluids vs. $\geq 40\%$ additional fluids (38/112; 34% vs. 30/68; 44% vs. 11/20; 55%). A retrospective cohort study (Mirza 2023) found that higher fluid intake in first 2 days of life is associated with prolonged duration of haemodynamically significant patent ductus arteriosus (hsPDA) in extremely preterm infants (Day 1: <1 week hsPDA median 110 (IQR 94 to 127) mL/kg/day vs. ≥ 1 week hsPDA median 130 (IQR 112 to 148) mL/kg/day; $P<0.001$ and Day 2: <1 week hsPDA median 142 (IQR 125 to 154) mL/kg/day vs. ≥ 1 week hsPDA median 158 (IQR 135 to 180) mL/kg/day; $P<0.009$) [Critical]. No faltering growth/body composition: Observational study: A retrospective cohort study (Agren 2022) looked at fluid balance in infants 22-23 weeks' gestation. With a total fluid intake starting at a mean of 127 $\pm$ 23 mL/kg/day on day 1, there was a maximum weight loss of -9$\pm$-	[6] Sweden: Pre-Post cohort study: Infants born 22-26 weeks' gestation. N=63 restrictive regimen (initial total fluid volume of 65 mL/kg/day was recommended with a scheduled daily stepwise increase of 10 mL/kg/day up to 170 mL/kg/day). N=112 liberal regimen (total fluids were started at 95 mL/kg/day (GA 22-24 weeks) and 85 mL/kg/day (GA 25-26 weeks), respectively, daily stepwise increase of 10 mL/kg/day at clinical discretion. Taiwan: Retrospective chart review [7]: Infants (n=75) <32 weeks' gestation and birthweight <1500 g. USA: Retrospective chart review [9]: Very low birthweight infants (N=200). Fluid management day 1 of life. Three groups no additional/$<15\%$ additional fluids (n=112) received mean 100 $\pm$ 13 mL/kg/day vs. $\geq 15\%$ to 40% additional fluids received mean 132 $\pm$ 16 mL/kg/day vs. $\geq 40\%$ additional fluids received mean 157 $\pm$ 20 mL/kg/day. USA: Prospective cohort [10]: Infants with birthweight 500 to 1500 g. Fluid management and bronchopulmonary dysplasia (n=865 of whom 224 (26%) had chronic lung disease). Brazil: Retrospective cohort study [11]: Infants with birthweight <1000 g (n=219) USA: Retrospective cohort [12]: Extremely preterm infants <29 weeks' gestation with haemodynamically significant patent ductus arteriosus
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	5% at a mean postnatal age of 3 days. At 1-week postnatal age, mean weight loss was $-2\pm 7\%$, with 16/36 (44%) of infants having regain birthweight. The total fluid intake on day 7 was a mean of 178 ± 22 mL/kg/day. Sepsis: Observational studies: A retrospective cohort study (Rallis 2024) found no significant difference in sepsis between infants with fluid overload $\geq 5\%$ in first 24 hours (14/42; 33%) or those with no fluid overload (26/61; 43%) [Important]. Duration of hospital stay: Observational studies: A retrospective cohort study (Rallis 2024) found no significant difference in length of stay between infants with fluid overload $\geq 5\%$ in first 24 hours (median 83 days; IQR 64, 99) or those with no fluid overload (median 77; IQR 56,94) [Important]. Fluids and risk/prevention of bronchopulmonary dysplasia Bronchopulmonary dysplasia: Observational studies in systematic review: In a case-control study of 157 infants, a seven-day cumulative fluid overload threshold of 36.2% was the most accurate predictor for developing BPD in preterm neonates. A cohort study reported 159/389 infants with BPD; infants with a lower intake of energy and lipids and a higher intake of fluids in the first week after birth were more susceptible to BPD. In a retrospective cohort study of 191 preterm infants (23-28 weeks' gestational age), higher cumulative fluid balance was linked to increased odds of death (BPD). The absolute odds ratio (AOR) was 1.56 (95%CI 1.11-2.25). In a post-hoc analysis of an RCT including 1,382 ELBW infants, higher fluid intake and a lack of weight loss were significantly associated with a greater risk of death or BPD ($p < 0.001$ and 0.006, respectively). Note that the RCT was conducted during the surfactant era. A prospective cohort study of 69 ventilated infants showed that a fluid volume of more than 131 mL/kg/day on day seven was associated with an increased risk of BPD (RR 2.09, 95% CI 1.14-3.85). Bronchopulmonary dysplasia: Observational study: A prospective cohort study (Marshall 1999) found that each 10 mL increase in fluids on day 2 of life was associated with an increase in BPD (OR 1.06; 95%CI 1.01 to 1.11). On each of the first five days of life, infants receiving greater amounts of fluid and experiencing less weight loss were at greater risk of developing BPD (Day 1 infants with BPD 120 ± 68 mL/kg/day vs. no BPD 100 ± 26 mL/kg/day; $P=0.0001$; Day 5 infants with BPD 153 ± 39 mL/kg/day vs. no BPD 142 ± 28 mL/kg/day; $P=0.0002$). A retrospective chart review (Guo 2015) found severe BPD was associated with higher volume of fluids received on Day 2 to 4 of life compared with infants with non-severe BPD (346.44 ± 42.38 mL/kg vs. 323.91 ± 27.62 mL/kg, $p=0.007$). Infants who received more than 345 mL/kg of total fluids from the 2nd to 4th days after birth were around 6.25 times more likely to develop severe BPD. A retrospective cohort study (Al-Jebawi 2020) found that during the first week after birth, the mean fluid intake was significantly higher in the moderate-severe BPD group than the control group. Higher fluid intake was associated with the risk of moderate to severe BPD (BPD fluid intake 172 ± 41 mL/kg/day vs. control 147 ± 14 mL/kg/day; $P, 0.001$; OR 1.03; 95%CI 1.01 to 1.04 [Critical]. Desirable effects for Māori	for < 1 week ($n=50$) and for ≥ 1 week ($n=75$). From Day 1- 4 of life the actual fluid intake was significantly higher than prescribed fluids in both groups. Greece: Retrospective cohort study [13]: 103 infants ≤ 30 weeks' gestation and ≤ 1500g. Infants started on 80-100 mL/kg/day. Looked at effects of fluid overload $> 5\%$ in first 24 hours of life. USA: RCT [3]: very low birthweight infants 750 to 1500 g, 27 to 33 weeks' gestation. Infants in group 1 received a mean of 80 mL/kg/day of fluid on the first day of life; input was then gradually increased to 140 mL/kg/day by the fourth and fifth days of life. Infants in group 2 received an average of 65-70 mL/kg/day of fluid for the first three days of life, then input was increased to an average of 80 mL/kg/day by Day 5. USA: Retrospective cohort study [14]: 204 extremely low birthweight infants. Grouped into low-intermediate- and high-fluid intake. Day one Low ($n=51$) < 96 mL/kg/day; intermediate ($n=102$) 96-125 mL/kg/day; high ($n=51$) > 125 mL/kg/day. Day 5 Low < 135 mL/kg/day; intermediate 135-170 mL/kg/day and high > 170 mL/kg/day.
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	None reported				
Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects ^a (95% CI)	
				Risk with higher parenteral fluid	Risk difference with lower parenteral fluid
Mortality: RCT	582 (5 RCTs)	⊕⊕○○ Low ^{a,b}	RR 0.81 (0.54 to 1.23)	Study population 148 per 1,000	28 fewer per 1,000 (68 fewer to 34 more)
Necrotising enterocolitis: RCT	526 (4 RCTs)	⊕○○○ Very low ^{a,b,c}	RR 0.43 (0.21 to 0.87)	Study population 91 per 1,000	52 fewer per 1,000 (72 fewer to 12 fewer)
Bronchopulmonary dysplasia: RCT	526 (4 RCTs)	⊕○○○ Very low ^{a,b,d}	RR 0.85 (0.63 to 1.14)	Study population 255 per 1,000	38 fewer per 1,000 (94 fewer to 36 more)
Adverse effects: RCT assessed with: Patent ductus arteriosus	526 (4 RCTs)	⊕○○○ Very low ^{a,b,c}	RR 0.52 (0.37 to 0.73)	Study population 300 per 1,000	144 fewer per 1,000 (189 fewer to 81 fewer)
Faltering growth/body composition: RCT assessed with weight loss (% of birthweight)	326 (3 RCTs)	⊕⊕○○ Low ^{a,b}	-	The mean faltering growth/body composition: RCT was 0	MD 1.94 higher (0.82 higher to 3.07 higher)
Neurodevelopmental impairment - not measured	-	-	-	-	-
Fully breastfed or breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Time to full enteral feeds - not measured	-	-	-	-	-
Duration of initial hospital stay - not measured	-	-	-	-	-
Sepsis: proven or suspected - not measured	-	-	-	-	-
Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds (<0.5 days) - not measured	-	-	-	-	-

a. Downgraded one level due to concerns of risk of bias

b. Downgraded one level due to indirectness due to lack of consistency in the regimens applied for commencing and the duration of restricted or liberal water intake

c. Downgraded one level for inconsistency with I2 >60%

d. Downgraded one level for imprecision with confidence intervals that cross the line of no effect

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Faltering growth or body composition: RCT: Postnatal weight loss was higher with restricted versus liberal fluids (MD 1.94% of birthweight higher, 8.2 higher to 37 higher). Undesirable effects for Māori No additional data	The review by Bollaboina (2023) included 5 studies of mixed design including a case control study, 3 cohort studies and a post-hoc analysis of a RCT. The methodological quality of the studies is good. The data were not pooled. The Bell (2014) systematic review only included 5 RCTs comparing liberal versus restricted water intake provided primarily via intravascular infusion. Liberal water was considered the standard. There was variability between studies on the commencement and duration of water intake. The studies were conducted in the pre-surfactant era.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	All of the observational studies and post-hoc analysis of a RCT in the Bollaboina (2023) review concurred that fluid restriction in the early days will decrease the risk of bronchopulmonary dysplasia. The quality of the evidence is good for observational studies. The Bell (2014) review found that restricted water intake significantly increased postnatal weight loss and significantly reduced the risks of patent ductus arteriosus and NEC. But there were associated non-significant trends for increased risk of dehydration and reduced risks of bronchopulmonary dysplasia, intracranial haemorrhage, and death. Certainty of evidence for Māori No additional data	The reviews do not consider sodium/potassium intake.

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability Values for Māori No additional data	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Lower parenteral fluid reduced postnatal weight but reduced the risk of bronchopulmonary dysplasia, patent ductus arteriosus and NEC. The risk of dehydration needs to be monitored. Balance of effects for Māori No additional data	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Minimal resources needed. Resources required for Māori No additional data	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Very low ○ Low ○ Moderate ● High ○ No included studies	No cost data identified Certainty of evidence of required resources for Māori No data identified	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No cost data identified Cost effectiveness for Māori No data identified	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Influenced by the effects of colonisation, pēpi Māori are more likely to be born preterm, have more sepsis and neurodisability, both of which are associated with parenteral nutrition practices, and fewer survive. Thus, implementing standardised parenteral nutrition practices in Aotearoa New Zealand will contribute to achieving equitable health outcomes for preterm pēpi Māori and their whānau. Equity for Pacific families Implementing standardised parenteral nutrition practices in Aotearoa New Zealand will contribute directly to reducing health disparities for all ethnicities and underrepresented groups. Equity for underrepresented groups Families living rurally or outside tertiary centres may experience variable IV fluid practices due to resource gaps or local protocols. Inconsistent care can impact infant outcomes and prolong hospitalisation. Nationally standardised, equity-informed guidance is essential to ensure all preterm infants receive safe and appropriate IV fluid therapy regardless of setting.	

Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Probably acceptable Acceptability for Māori No additional data	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Probably feasible Feasibility for Māori No evidence available	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know

	JUDGEMENT						
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ●	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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EtD 5. Should routine iodine vs. no additional iodine supplementation be used for preterm infants?

POPULATION:	Preterm infants
INTERVENTION:	Routine Iodine
COMPARISON:	No additional iodine supplementation
MAIN OUTCOMES:	Critical outcomes Mortality Neurodevelopmental impairment Adverse effects (prevention of unnecessary blood tests) Important but not critical Faltering growth/body composition Retinopathy of prematurity Bronchopulmonary dysplasia Fully breastfed or breastmilk feeding at hospital discharge Time to full enteral feeds Duration of initial hospital stay Sepsis: proven or suspected Necrotising enterocolitis Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation: population perspective
BACKGROUND:	Iodine is a critical micronutrient required for thyroid hormone synthesis, which supports growth, neurodevelopment and metabolic regulation. Preterm infants are particularly vulnerable to iodine deficiency due to limited in utero iodine accumulation, reduced postnatal stores and reliance on parenteral nutrition. This vulnerability is compounded by maternal iodine deficiency, which is prevalent in Aotearoa New Zealand due to low environmental iodine content. Congenital hypothyroidism, the most common preventable cause of intellectual disability worldwide, has a significantly higher incidence among preterm infants (1:100–150) compared to term infants (1:2000). While often transient in preterm infants, congenital hypothyroidism can have severe biochemical presentations (thyroid stimulating hormone >50 milli-International units per litre (mIU/L) that if untreated may impact neurodevelopment. Factors such as the immaturity of the hypothalamic-pituitary-thyroid axis, iodine deficiency and illnesses like respiratory distress syndrome are believed to contribute to this condition. Maternal iodine supplementation during pregnancy and breastfeeding is recommended to reduce the risk of iodine deficiency in newborns. However, studies show that up to 30% of women of reproductive age in Aotearoa New Zealand may remain iodine deficient despite supplementation guidelines. For preterm infants, the iodine content of parenteral nutrition is critical. Previous parenteral iodine recommendations (1

CONFLICT OF INTERESTS:	µg/kg/day) were set intentionally low due to the use of iodine-containing antiseptics. However, practices have since changed, and more recent guidelines have increased parenteral iodine intake to 1–10 µg/kg/day, though this remains below the recommended enteral intake of 10–55 µg/kg/day. Research indicates that even 3 µg/kg/day IV iodine may lead to a negative iodine balance in preterm infants, highlighting the need for updated and evidence-based intake recommendations.
	The following 2019 Cochrane systematic review (Walsh <i>et al</i>) co-author wrote this Evidence to Decision document: Julie Brown

Assessment

Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence from one Cochrane review [1] and the ESPGHAN/ESPEN/ESPR/CSPEN guidelines [2]. Parenteral Nutrition guidelines ESPGHAN/ESPEN/ESPR/CSPEN (2018) [2] Iodine should be provided with parenteral nutrition at a daily dose of 1–10 µg/kg/day in preterm infants (strong recommendation, strong consensus). Patients on long-term parenteral nutrition should be regularly monitored for iodine status by measuring at least thyroid hormone concentrations (conditional recommendation, strong consensus). Enteral Nutrition guidelines ESPGHAN (2022) [3] recommends enteral iodine should be provided at 11–55 µg/kg/day Mortality: RCT: No significant effect of additional iodine supplementation compared with no additional iodine supplementation on the incidence of death before hospital discharge (1 more per 1,000; 24 fewer to 37 more). [Critical] Neurodevelopment impairment: RCT: No significant effect of additional iodine supplementation compared with no additional iodine supplementation on Bayley-III Cognitive composite score: 2 years of age corrected for prematurity (MD 0.3 points lower; 2.44 lower to 1.84 higher); Bayley-III Motor composite at 2 years of age corrected for prematurity (MD 0.2 points higher; 2.15 lower to 2.55 higher); Bayley-III Language composite score at 2 years of age corrected for prematurity (MD 0.1 points lower; 2.5 lower to 2.3 higher); auditory impairment (1 more per 1,000; 13 fewer to 30 more). No significant effect for a low score (neurodevelopmental impairment) in any main Bayley domain (<85) or death (25 more per 1,000; 29 fewer to 83 more) and visual impairment (10 fewer per 1,000; 19 fewer to 12 more). [Critical].	Population information for included evidence 2 RCTs in the Cochrane review [1]: One RCT (n=1273) from the United Kingdom iodine given at 30 µg/kg/day either parenterally or enterally until 34 weeks postmenstrual age. One RCT (n= 121) from United Kingdom iodine supplemented "preterm" formula milk (272 µg/L, approx 40 to 49 µg/kg/day) versus unsupplemented with iodine concentration (68 µg/L, approx 10 to 12 µg/kg/day)

	Retinopathy of prematurity: RCT: No significant effect in retinopathy of prematurity for additional iodine supplementation compared with no additional iodine supplementation (2 fewer per 1,000; 23 fewer to 31 more). [Important]				
	Desirable effects for Māori No additional data				
Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with placebo/no supplementation	Risk difference with routine iodine
Mortality: RCT assessed with: Mortality before hospital discharge	1380 (2 RCTs)	⊕⊕○○ Low ^{a,b}	RR 1.01 (0.72 to 1.42)	Study population	
				87 per 1,000	1 more per 1,000 (24 fewer to 37 more)
Neurodevelopmental impairment: RCT assessed with: Bayley-III Cognitive composite score: 2 years of age corrected for prematurity Scale from: 1 to 100	1259 (1 RCT)	⊕○○○ Very low ^{a,c}	-	The mean Neurodevelopmental impairment: RCT was 89.2 points	MD 0.3 lower (2.44 lower to 1.84 higher)
Neurodevelopmental impairment: RCT assessed with: Bayley-III Motor composite at 2 years of age corrected for prematurity Scale from: 1 to 100	1259 (1 RCT)	⊕○○○ Very low ^{a,c}	-	The mean neurodevelopmental impairment: RCT was 88.0 points	MD 0.2 higher (2.15 lower to 2.55 higher)
Neurodevelopmental impairment: RCT assessed with: Bayley-III Language composite score at 2 years of age corrected for prematurity Scale from: 1 to 100	1259 (1 RCT)	⊕○○○ Very low ^{a,c}	-	The mean neurodevelopmental impairment: RCT was 85.2 points	MD 0.1 lower (2.5 lower to 2.3 higher)
Neurodevelopmental impairment: RCT assessed with: Low score in any main Bayley domain (< 85) or death	1259 (1 RCT)	⊕⊕○○ Low ^{a,b}	RR 1.05 (0.94 to 1.17)	Study population	
				490 per 1,000	25 more per 1,000 (29 fewer to 83 more)
Neurodevelopmental impairment: RCT assessed with: Visual impairment	1092 (1 RCT)	⊕⊕○○ Low ^{a,b}	RR 0.63 (0.28 to 1.45)	Study population	
				26 per 1,000	10 fewer per 1,000 (19 fewer to 12 more)
Neurodevelopmental impairment: RCT assessed with: Auditory impairment	1093 (1 RCT)	⊕⊕○○ Low ^{a,b}	RR 1.05 (0.51 to 2.16)	Study population	
				26 per 1,000	1 more per 1,000 (13 fewer to 30 more)
Faltering growth/body composition - not measured	-	-	-	-	-
Adverse effects - not measured	-	-	-	-	-

Retinopathy of prematurity	1257 (1 RCT)	⊕⊕⊕○ Moderate ^a	RR 0.97 (0.64 to 1.49)	Study population	
				64 per 1,000	2 fewer per 1,000 (23 fewer to 31 more)
Bronchopulmonary dysplasia / assessed with: Bronchopulmonary dysplasia in surviving infants (supplemental oxygen requirement at 36 weeks' postmenstrual age)	1377 (1 RCT)	⊕⊕○○ Low ^{a,d}	RR 1.07 (0.94 to 1.22)	Study population	
				377 per 1,000	26 more per 1,000 (23 fewer to 83 more)
Fully breastfed or breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Time to full enteral feeds - not measured	-	-	-	-	-
Duration of initial hospital stay - not measured	-	-	-	-	-
Sepsis: proven or suspected - not measured	-	-	-	-	-
Necrotising enterocolitis: RCT	1259 (1 RCT)	⊕⊕⊕○ Moderate ^a	RR 1.24 (0.98 to 1.56)	Study population	
				164 per 1,000	39 more per 1,000 (3 fewer to 92 more)
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life- long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-
Total plasma thyroxine: RCT assessed with: (nmol/L) at 34–36 weeks' postmenstrual age.	1121 (2 RCTs)	⊕⊕⊕○ Moderate ^c	-	The mean Total plasma thyroxine: RCT was 83.45 nmol/L	MD 0.29 higher (1.51 lower to 2.09 higher)
Thyroid-stimulating hormone: RCT assessed with: (mU/L) at 34–36 weeks' postmenstrual age.	1119 (2 RCTs)	⊕⊕⊕○ Moderate ^c	-	The mean thyroid-stimulating hormone: RCT was 1.8 mU/L	MD 0.05 higher (0.09 lower to 0.18 higher)

- a. Downgraded one level as reports on outcomes of iodine supplementation but does not compare relevant doses
- b. Downgraded one level for imprecision with confidence intervals crossing the line of no effect
- c. Downgraded two levels for imprecision with very wide confidence intervals that cross the line of no effect.
- d. Downgraded one level for inconsistency as I² is between 50 and 80%

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Necrotising enterocolitis: RCT: No significant increase in necrotising enterocolitis for additional iodine supplementation compared with no additional iodine supplementation (39 more per 1,000; 3 fewer to 92 more). Bronchopulmonary dysplasia: RCT: No significant increase in bronchopulmonary dysplasia for additional iodine supplementation compared with no additional iodine supplementation (26 more per 1,000; 23 fewer to 83 more) [Important]. Thyroid function at 34-36 weeks' post-menstrual age: RCT: No significant effect of iodine on thyroid function for additional iodine supplementation compared with no additional iodine supplementation for thyroid-stimulating hormone: MD 0.05 mU/L higher; 0.09 lower to 0.18 higher) or total plasma thyroxine (MD 0.29 nmol/L higher; 1.51 lower to 2.09 higher) [Not important]. Undesirable effects for Māori - No additional data	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High	Moderate to very low certainty evidence overall	Evidence is primarily based on one large, well-designed study. However, there is only one study conducted in the United Kingdom and the critical outcomes have large treatment effects with wide

○ No included studies		confidence intervals crossing the line of no effect.
Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT assessed with: Mortality before hospital discharge	CRITICAL	⊕⊕○○ Low
Neurodevelopmental impairment: RCT assessed with: Bayley-III Cognitive composite score: 2 years of age corrected for prematurity Scale from: 1 to 100	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: Bayley-III Motor composite at 2 years of age corrected for prematurity Scale from: 1 to 100	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: Bayley-III Language composite score at 2 years of age corrected for prematurity Scale from: 1 to 100	IMPORTANT	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: Low score in any main Bayley domain (< 85) or death	CRITICAL	⊕⊕○○ Low
Neurodevelopmental impairment: RCT assessed with: Visual impairment	CRITICAL	⊕⊕○○ Low
Neurodevelopmental impairment: RCT assessed with: Auditory impairment	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition - not measured	CRITICAL	-
Adverse effects - not measured	CRITICAL	-
Retinopathy of prematurity	IMPORTANT	⊕⊕⊕○ Moderate
Bronchopulmonary dysplasia assessed with: Chronic lungdisease in surviving infants (supplemental oxygen requirement at 36 weeks' postmenstrual age)	IMPORTANT	⊕⊕○○ Low
Fully breastfed or breastmilk feeding at hospital discharge - not measured	IMPORTANT	-
Time to full enteral feeds - not measured	IMPORTANT	-
Duration of initial hospital stay - not measured	IMPORTANT	-
Sepsis: proven or suspected - not measured	IMPORTANT	-
Necrotising enterocolitis: RCT	IMPORTANT	-

Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-
Total plasma thyroxine: RCT assessed with: (nmol/L) at 34–36 weeks' postmenstrual age.	NOT IMPORTANT	⊕⊕⊕○ Moderate
Thyroid-stimulating hormone: RCT assessed with: (mU/L) at 34–36 weeks' postmenstrual age.	NOT IMPORTANT	⊕⊕⊕○ Moderate

Certainty of evidence for Māori

No additional data

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ Important uncertainty or variability ☐ Possibly important uncertainty or variability ☒ Probably no important uncertainty or variability ☐ No important uncertainty or variability	Probably no important uncertainty or variability. Values for Māori No additional data	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ Favours the comparison	Iodine versus no iodine - moderate certainty evidence Little or no difference in thyroid function	

○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Uncertain effect on necrotising enterocolitis, retinopathy of prematurity Iodine versus no iodine - low certainty evidence Uncertain effect on mortality, bronchopulmonary dysplasia, neurodevelopmental impairment (auditory and visual impairment; Low score in any main Bayley domain (<85) or death Iodine versus no iodine - very low certainty evidence Uncertain effect on neurodevelopmental impairment (Bayley III cognitive, motor, language) Balance of effects for Māori No additional data	
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Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Dose approx. 50 µg iodine per day. Potassium iodate 253 µg tablet (equivalent to 150 µg iodine) - \$0.07 per tab The cost of iodine supplementation is negligible, \$0.07 per day	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ● High ○ No included	The cost of iodine supplementation is minimal and certain. Certainty of evidence of required resources for Māori No additional data	

studies		
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	There are no studies that assess the specific cost-effectiveness of iodine supplementation compared with no iodine supplementation, particularly in the context of preterm infants. Cost effectiveness for Māori No additional data	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori In 2008/09, 44% of wāhine Māori had moderate iodine deficiency, with urinary iodine concentrations below 50 µg/L, and 80% had levels below 100 µg/L, indicating mild deficiency. While the overall proportion of women with iodine levels below 100 µg/L was similar between Māori and non-Māori, wāhine Māori were significantly more likely to have moderate deficiency, even after adjusting for age (Ministry of Health, 2012). To address the re-emergence of iodine deficiency, mandatory use of iodised salt in bread-making was introduced in late 2009. By 2014/15, urinary iodine levels had nearly doubled across all age, gender, and ethnic groups. Iodine status was considered adequate for Māori, Pacific, and Asian women, while European/other women continued to show mild deficiency (NZ Health Survey, 2014/15). Since	

	2010, a subsidised iodine-only tablet (150 µg) has been available in Aotearoa New Zealand, and the Ministry of Health recommends daily supplementation for all pregnant and breastfeeding women. However, access to this supplement requires awareness of the pregnancy and access to a prescriber or maternity carer, which may present barriers for some. Equity for Pacific families There is likely inequity in iodine status for Pacific Island infants and some other ethnicities, although data specifically focused on ethnic differences in infant iodine levels in Aotearoa New Zealand is limited. Pacific Is women are less likely to receive timely antenatal care, be prescribed iodine supplements and be given clear information about iodine's importance in pregnancy and breastfeeding. This leads to increased risk of iodine deficiency for their infants, especially if exclusively breastfed without maternal supplementation and there is limited consumption of iodine-rich foods (e.g. dairy, seafood, iodised salt). Equity for other underrepresented groups If iodine supplementation is overlooked or inconsistently applied in under-resourced settings, underrepresented infants may face preventable risks to growth and neurodevelopment. Clear national standards and equity-focused monitoring are needed to ensure all preterm infants receive essential micronutrients like iodine regardless of their location or family circumstances. Asian women (especially recent migrants) may also be at risk due to restrictive postnatal dietary practices (e.g. low dairy/iodised salt intake) or lack of health system navigation. Refugee and migrant communities may have low awareness and inconsistent access to supplementation.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Iodine supplementation is easy to administer and is likely to be acceptable to most stakeholders. Acceptability for Māori	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No	Iodine supplementation is feasible in neonatal care.	

○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Feasibility for Māori No additional data available.	
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Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know

	JUDGEMENT						
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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EtD 7. Should Insulin vs. glucose reduction be used for hyperglycaemic preterm infants?

POPULATION:	Hyperglycaemic preterm infants
INTERVENTION:	Insulin
COMPARISON:	Glucose infusion reduction
MAIN OUTCOMES:	Critical for making a decision Mortality Neurodevelopmental impairment Adverse effects Important but not critical Fully breastfeeding at hospital discharge Faltering growth/body composition Duration of initial hospital stay Time to full enteral feeds Bronchopulmonary dysplasia Necrotising enterocolitis (NEC) Sepsis: proven or suspected Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Of limited importance Fully breastmilk feeding at hospital discharge Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation - patient perspective
BACKGROUND:	Hyperglycaemia is a frequent metabolic complication in preterm infants, particularly those born extremely preterm or with very low birthweight. It often arises due to the immaturity of glucose homeostasis, stress-related hyperglycaemia, or the administration of glucose-containing fluids. Hyperglycaemia has been linked to an increased risk of complications, including intraventricular haemorrhage, retinopathy of prematurity, necrotising enterocolitis, sepsis, prolonged hospitalisation, and increased mortality. Managing hyperglycaemia in preterm infants typically involves reducing glucose infusion rates (GIR) or administering insulin. Reducing GIR lowers exogenous glucose delivery but may increase the risk of hypoglycaemia and reduced caloric intake, potentially impairing growth and neurodevelopment. Reducing the glucose infusion rate alone may not be enough to achieve glycaemic control. Prolonged reductions in glucose load can lead to energy deficits, which may negatively affect somatic growth, including weight gain, length and head circumference growth. Conversely, insulin therapy improves glucose utilisation and may maintain energy balance, but it carries risks such as hypoglycaemia, electrolyte imbalances, and the need for close monitoring to avoid adverse outcomes. Evidence on the optimal management strategy for hyperglycaemia in preterm infants remains inconclusive. While some studies suggest that insulin therapy may improve growth outcomes, it also increases the risk of hypoglycaemia, raising concerns about its safety. Reducing glucose load is a more straightforward intervention. Still, it may compromise nutrition especially in infants

CONFLICT OF INTERESTS:	reliant on intravenous nutrition.
	The following systematic review on Guidelines (Meliana M, et al) co-authors are on the Guideline Development Group: Barbara Cormack, Tanith Alexander, Luling Lin and Frank Bloomfield and supervised the first author.

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS			
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence from two randomised trials of ELBW infants from the 1990's [1,2]. Neither of the studies investigated long-term outcomes, and both had very short-term outcomes in hospitals. Mortality: RCT: Little or no evidence of a difference in mortality between insulin and glucose reduction [Critical]. Adverse effects: RCT: Insulin-treated infants tolerated significantly higher glucose infusion rates (20.1 ± 2.5 vs. 13.2 ± 3.2 mg/kg/min; $p<0.01$). No difference between insulin vs. glucose reduction for hypoglycaemia (1% vs. 0%) [Critical]. No faltering growth/body composition: RCT: Weight gain was higher in the insulin-treated group (20.1 ± 12.1 vs. 7.8 ± 5.1 g/kg/day; $p<0.01$). No change in the fractional increase in length (0.05 ± 0.04 vs. 0.05 ± 0.05 [units of measurement not specified]) or head circumference (head circumference (0.17 ± 0.06 vs. 0.19 ± 0.05 [units of measurement not specified]))[Important]. Time to full enteral feeds: RCT: Days to reach 60 kcal/kg/day was significantly lower in the insulin group compared with control ($5.5 \text{ days} \pm 0.6$ vs. $8.6 \text{ days} \pm 1.3$), $p < 0.01$). Bronchopulmonary dysplasia (BPD) / chronic lung disease: RCT: Little or no difference between insulin and control group (77% vs. 66%). [Important] Sepsis: RCT: Incidence of sepsis was lower in the insulin versus glucose reduction group (5 vs. 9 events, $p<0.05$). [Important] Desirable effects for Māori No additional evidence available	USA: RCT [1] ELBW infants. Minimum glucose intake was not defined, and the insulin rate was 0.04 U/hr, adjusted to maintain serum glucose between 5.5–9.9 mmol/L. USA: RCT [2] ELBW infants. Minimum glucose intake of 5 mg/kg/min, and the insulin rate was a minimum dose of 0.01 IU/kg/h to a max of 1.0 U/kg/h to maintain blood sugar levels between 4.4–8.9 mmol/L. Minimal glucose recommendations are usually based on the endogenous glucose production rate and the glucose oxidation capacity. The estimated glucose production and glucose oxidation rates in preterm infants are ~6 mg/kg/min (8.6 g/kg/d) and ~8 mg/kg/min (11.5 g/kg/d), respectively [3-5]. Additional information In a systematic review of international neonatal nutrition guidelines [6] which assessed carbohydrate recommendations. “Seven guidelines recommended a wide range of parenteral carbohydrate intake from 4 to 17 g/kg/day (2.8 to 11.8 mg/kg/min) in the first week and 11–17 g/kg/day (7.6 to 11.8 mg/kg/min) thereafter.			
Outcomes	N of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with glucose reduction	Risk difference with Insulin
Mortality	24	⊕○○○	-	No difference in outcomes between insulin vs. glucose reduction for	

	(1 RCT)	Very low ^{a,b,c}		mortality n=3 vs. n=2.	
Neurodevelopmental impairment - not measured	-	-	-	-	-
Adverse effects: RCT assessed with: Tolerated higher glucose infusion rates	24 (1 RCT)	⊕○○○ Very low ^{a,b,d}	-	Insulin-treated infants tolerated significantly higher glucose infusion rates (20.1 ± 2.5 vs. 13.2 ± 3.2 mg/kg/min; p<0.01).	
Adverse effects: RCT assessed with: Hypoglycaemia	24 (1 RCT)	⊕○○○ Very low ^{a,b,c}	-	No difference in outcomes between insulin vs. glucose reduction for hypoglycaemia (1% vs. 0%).	
Fully breastfeeding at hospital discharge - not measured	-	-	-	-	-
Faltering growth / body composition: RCT assessed with: Weight gain (g/kg/day)	24 (1 RCT)	⊕○○○ Very low ^{a,b,d}	-	Weight gain was significantly higher in the insulin group (20.1 ± 12.1 vs. 7.8 ± 5.1 g/kg/day; p<0.01). Weight was significantly greater in insulin-treated infants from study day 4 through 14 (p <0.05). The insulin-treated infants had a significantly greater fractional increase over baseline weight at the end of the study (0.24 ± 0.14 vs. 0.12 ± 0.10; p <0.05).	
Faltering growth / body composition: RCT assessed with: Length (measurement not specified)	24 (1 RCT)	⊕○○○ Very low ^{a,b,d}	-	No change in the fractional increase in length (0.05 +/- 0.04 vs. 0.05 +/- 0.05).	
Faltering growth / body composition: RCT assessed with: Head circumference (measurement not specified)	24 (1 RCT)	⊕○○○ Very low ^{a,b,d}	-	No change in the fractional increase in head circumference (0.17 +/- 0.06 vs. 0.19 +/- 0.05).	
Duration of initial hospital stay - not measured	-	-	-	-	-
Time to full enteral feeds	24 (1 RCT)	⊕○○○ Very low ^{a,b,d}	-	Days to reach 60 kcal/kg/day was significantly lower in the insulin group compared with control (5.5 +/- 0.6 vs. 8.6 +/- 1.3; p < 0.01).	
Bronchopulmonary dysplasia (BPD) / chronic lung disease	56 (1 RCT)	⊕○○○ Very low ^{a,b,d}	-	No difference in outcomes between insulin vs. glucose reduction for bronchopulmonary dysplasia (77% vs. 66%).	
Necrotising enterocolitis (NEC) - not measured	-	-	-	-	-
Sepsis: proven or suspected: RCT	24 (1 RCT)	⊕○○○ Very low ^{a,b,d}	-	Incidence of sepsis was lower in the insulin vs. glucose reduction group (5 vs. 9, p<0.05).	
Retinopathy of prematurity (ROP) - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Fully breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-

a. Downgraded one level due to concerns of risk of bias
b. Downgraded one level for indirectness as evidence based on a single study
c. Downgraded two levels for imprecision due small sample size and low event rates

a. Downgraded one level for imprecision as sample size very small

a)

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	No other outcomes were reported. Undesirable effects for Māori No additional evidence available	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Very low certainty of evidence overall Certainty of evidence for Māori No additional evidence available	

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment - not measured	CRITICAL	-
Adverse effects: RCT assessed with: Tolerated higher glucose infusion rates	CRITICAL	⊕○○○ Very low
Adverse effects: RCT assessed with: Hypoglycaemia	CRITICAL	⊕○○○ Very low
Fully breastfeeding at hospital discharge - not measured	IMPORTANT	-
Faltering growth / body composition: RCT assessed with: Weight gain (g/kg/day)	IMPORTANT	⊕○○○ Very low
Faltering growth / body composition: RCT	IMPORTANT	⊕○○○

assessed with: Length (measurement not specified)		Very low
Faltering growth / body composition: RCT assessed with: Head circumference (measurement not specified)	IMPORTANT	⊕○○○ Very low
Duration of initial hospital stay - not measured	IMPORTANT	-
Time to full enteral feeds	IMPORTANT	⊕○○○ Very low
Bronchopulmonary dysplasia (BPD) / chronic lung disease	IMPORTANT	⊕○○○ Very low
Necrotising enterocolitis (NEC) - not measured	IMPORTANT	-
Sepsis: proven or suspected: RCT	IMPORTANT	⊕○○○ Very low
Retinopathy of prematurity (ROP) - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Fully breastmilk feeding at hospital discharge - not measured	NOT IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-

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Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	Possibly important uncertainty or variability	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability		

○ Probably no important uncertainty or variability ○ No important uncertainty or variability		
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Insulin versus glucose reduction - very low certainty evidence Uncertain effect on mortality, length, head circumference, bronchopulmonary dysplasia Probable decrease in adverse effects (tolerance, hypoglycaemia), sepsis Probable increase in weight Probable earlier time to reach full enteral feeds Balance of effects for Māori No additional evidence	
Resources required		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings	3 mL vial of Actrapid insulin costs approximately \$8.50. Costs and savings are minimal.	

○ Varies ○ Don't know		
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Costs are moderately certain. Certainty of evidence of required costs for Māori No additional evidence available.	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	There are no studies that assess the specific cost-effectiveness of insulin versus glucose reduction, particularly in the context of preterm infants. Cost effectiveness for Māori No additional evidence available.	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact	Equity for Māori Influenced by the effects of colonisation, pēpi Māori are more likely to be born preterm, have more sepsis and neurodisability, both of which are associated	

○ Probably increased ○ Increased ○ Varies ● Don't know	with parenteral nutrition practices, and fewer survive. Thus, implementing standardised parenteral nutrition practices in Aotearoa New Zealand will contribute to achieving equitable health outcomes for preterm pēpi Māori and their whānau. Equity for Pacific families Implementing standardised parenteral nutrition practices in Aotearoa New Zealand will contribute directly to reducing health disparities for all ethnicities and underrepresented groups. Equity for other underrepresented groups Migrant and low-income families may not receive adequate explanation of hyperglycaemia management or the reasons behind specific treatments like insulin or adjusted glucose loads. This can cause confusion or distress. Equity requires staff to provide understandable, inclusive education so all families feel informed and reassured during clinical decision-making.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Probably acceptable Acceptability for Māori No additional evidence available.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Both interventions are feasible. Feasibility for Māori No additional evidence available.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ●	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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EtD 9. Should fish oil only based lipids (Omegaven) vs. Multi-component lipids (SMOFLipid) be used for prevention or rescue therapy for preterm infants with (any cause) liver disease?

POPULATION:	Preterm infants in neonatal care
INTERVENTION:	Fish oil only based lipids (Omegaven)
COMPARISON:	Multi-component lipids (SMOFLipid)
MAIN OUTCOMES:	Critical outcomes Mortality Adverse effects (prevention of PN associated liver disease) Faltering growth/body composition Retinopathy of prematurity Bronchopulmonary dysplasia Important but not critical Neurodevelopmental impairment Fully breastfed or breastmilk feeding at hospital discharge Time to full enteral feeds Duration of initial hospital stay Sepsis: proven or suspected Necrotizing enterocolitis Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds Resolution of PNALD/cholestasis; Growth rate; Death before discharge; Incidence PNALD/cholestasis; Head growth velocity; Any sepsis;
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation - population perspective
BACKGROUND:	Liver disease in preterm infants, including intestinal failure-associated liver disease is a significant complication of prolonged parenteral nutrition (PN). Lipid emulsions are a key component of PN, providing essential fatty acids and energy, but their composition can influence liver health. Most Aotearoa New Zealand neonatal units use multicomponent lipid emulsions. These containing a mix of soybean, coconut, olive, and fish oils, and aim to balance essential fatty acid provision with reduced pro-inflammatory components, offering a broader spectrum of nutrients. While they may not achieve the same anti-inflammatory effect as fish oil only lipids (FOLE), multicomponent emulsions can provide more comprehensive nutritional support and are less expensive than fish oil only emulsions. Fish oil-based lipid emulsions, rich in omega-3 fatty acids, have been proposed as both a preventive and rescue therapy for liver conditions. These emulsions have anti-inflammatory and immunomodulatory properties, reduce oxidative stress, and may promote bile flow, which can mitigate cholestasis and liver injury. However, fish oil only lipids provide lower amounts of energy and omega-6 fatty acids, potentially

CONFLICT OF INTERESTS:	limiting their capacity to fully support growth and development when used as the sole lipid source.
	None

Assessment

Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	Evidence from a Cochrane review [1] another systematic review [2] and a retrospective review of cases [3]. The Cochrane review [1] included a subgroup analysis of preterm infants with surgical conditions or cholestasis. The review found no evidence from randomised studies to determine with any certainty if fish oil only lipid emulsions offer an advantage in the prevention or resolution of cholestasis or in any other clinical outcome compared with multicomponent lipid emulsions in infants with liver disease. The Park review reported: Adverse effects (Recovery of intestinal failure associated cholestasis): Pooled data - RCT and cohort studies: Use of fish oil was associated with an extremely large and significant increase in recovery from intestinal failure associated cholestasis (403 more per 1,000; 160 more to 606 more). [Critical] Desirable effects for Māori No additional evidence available	Cochrane review [1] included preterm infants <37 weeks' gestation and included infants with surgical conditions or intestinal failure-associated liver disease/cholestasis. Systematic review by Park <i>et al</i> [2] included neonates with parenteral nutrition associated cholestasis. Majority were between 23 and 36 weeks. The Ramiro-Cortijo [3] retrospective review of medical charts of neonates who were changed to Omegaven after the diagnosis of cholestasis while receiving SMOFlipid (i.e. a multicomponent lipid emulsion was replaced by a fish oil only lipid emulsion. Thirty-eight infants (92.1% preterm, being 44.7% born below 28 weeks' gestation), received fish oil only lipid emulsion. 1 g/kg/day. NB The usual lipid dose is 3 g/kg/day, so in addition to the change of lipid emulsion, they also had a 33% reduction in lipid emulsion, which also improves liver function. Additional experiential evidence was identified in a USA single-arm observational study using fish oil-based lipid emulsions for the treatment of intestinal failure-associated liver disease [4]. The median gestational age at birth of the 97 infants was 28 weeks (range 22.7–40 weeks). Eighty-three (86%) survived with resolution of cholestasis and 14 (14%) died.

				The median conjugated bilirubin concentration at the initiation of therapy was 4.8 mg/100mL (range 2.1–26). The median time to resolution of cholestasis was 40 days (range 3–158).	
Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with multi-component lipids (SMOFLipid)	Risk difference with HQE 1.6.b fish oil only based lipids (FOLE) (Omegaven)
Mortality - not reported	-	-	-	-	-
Adverse effects (prevention of PN associated liver disease): 1 RCT, 1 controlled trial, 2 cohort studies	1101 (4 non-randomised studies)	⊕⊕○○ Low	OR 0.56 (0.28 to 1.10)	Study population	
				51 per 1,000	22 fewer per 1,000 (36 fewer to 5 more)
Adverse effects (prevention of PN associated liver disease): retrospective chart review	0 (1 non-randomised study)	⊕○○○ Very low ^{a,b,c}	-	In 73.7% (28/38) of the neonates, the cholestasis was resolved. In 34.2% (13/38), resolution happened before FOLE discontinuation. In addition, in the rest of the neonates (15) in whom cholestasis resolved, resolution occurred after FOLE discontinuation.	
Adverse effects (recovery from PN associated liver disease): 1 RCT, 2 cohort studies	93 (3 non-randomised studies)	⊕⊕○○ Low ^d	OR 6.14 (2.27 to 16.60)	Study population	
				196 per 1,000	403 more per 1,000 (160 more to 606 more)
Faltering growth/body composition - not measured	-	-	-	-	-
Retinopathy of prematurity - not measured	-	-	-	-	-
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Neurodevelopmental impairment - not measured	-	-	-	-	-
Fully breastfed or breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Time to full enteral feeds - not measured	-	-	-	-	-
New outcome - not measured	-	-	-	-	-
Sepsis: proven or suspected: retrospective chart review	38 (1 non-randomised study)	⊕○○○ Very low ^{a,b,c}	-	No differences were found in sepsis incidence before and after initiation of FOLE ($\chi^2 = 3.014$; p -Value = 0.32).	
Necrotizing enterocolitis - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and	-	-	-	-	-

life-long cost - not measured					
Time to full sucking feeds - not measured	-	-	-	-	-

- a. Downgraded two levels for risk of bias as this is a retrospective chart review
- b. Downgraded two levels for indirectness as evidence is based on a single study with no direct comparison
- c. Downgraded three levels for risk of bias as this a retrospective chart review with no direct comparison
- d. Downgraded two levels for imprecision due to extremely large confidence intervals

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Kapoor 2019 [1]: The review included a subgroup analysis of preterm infants with surgical conditions or cholestasis. There is currently no evidence from randomised studies to determine with any certainty if fish oil only lipid emulsions offer a disadvantage in the prevention or resolution of cholestasis or in any other clinical outcome compared with multicomponent lipid emulsions in infants with liver disease. Adverse effects (prevention of intestinal failure-associated liver disease): RCT and cohort studies: No significant reduction in prevention of intestinal failure-associated liver disease (22 fewer per 1,000; 36 fewer to 5 more). [Critical] Adverse effects (prevention of intestinal failure-associated liver disease): Retrospective chart review: In 73.7% (28/38) of the neonates, the cholestasis was resolved. In 34.2% (13/38), resolution happened before fish oil only lipid emulsions discontinuation. In addition, in the rest of the neonates (15) in whom cholestasis resolved, resolution occurred after fish oil only lipid emulsion discontinuation. [Critical] Sepsis: Retrospective chart review: No differences were found in sepsis incidence before and after initiation of fish oil only lipid emulsion ($\chi^2 = 3.014$; p-Value = 0.32). Undesirable effects for Māori No evidence available	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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○ Very low ● Low ○ Moderate ○ High ○ No included studies	Low to very low certainty of evidence overall. Certainty of evidence for Māori No additional evidence available	
Outcomes	Importance	Certainty of the evidence (GRADE)
Adverse effects (prevention of PN associated liver disease): 1 RCT, 1 controlled trial, 2 cohort studies	CRITICAL	⊕⊕○○ Low
Adverse effects (prevention of PN associated liver disease): retrospective chart review	CRITICAL	⊕○○○ Very low
Adverse effects (recovery from PN associated liver disease): 1 RCT, 2 cohort studies	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition - not measured	CRITICAL	-
Retinopathy of prematurity - not measured	CRITICAL	-
Bronchopulmonary dysplasia - not measured	CRITICAL	-
Neurodevelopmental impairment - not measured	IMPORTANT	-
Fully breastfed or breastmilk feeding at hospital discharge - not measured	IMPORTANT	-
Time to full enteral feeds - not measured	IMPORTANT	-
New outcome - not measured	IMPORTANT	-
Sepsis: proven or suspected: retrospective chart review	IMPORTANT	⊕○○○ Very low
Necrotizing enterocolitis - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability. Values for Māori No additional evidence available	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Rescue therapy: Effect of fish oil only based lipids compared with multi-component lipid emulsions - Low certainty evidence Increase in recovery from intestinal failure-associated liver disease Prevention: Effect of fish oil only based lipids compared with multi-component lipid emulsions - Very low certainty evidence Uncertain effect for adverse effects (prevention of intestinal failure associated liver disease), sepsis Balance of effects for Māori No additional evidence available	There is no evidence that fish oil only based lipids compared with multi-component lipid emulsions prevent intestinal failure in preterm infants. Vote was on the effect of fish oil only based lipids compared with multi-component lipid emulsions as rescue therapy for intestinal failure

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Costs for lipid emulsions: SMOFLipid including vitamins per syringe approx. \$51 to \$71 (used for 48 hours) = \$25.50 to \$35.50 per day Omegaven, including vitamins per syringe approx. \$110 (used for 24 hours) = \$110 per day Cost difference \$74.50 to \$84.50 per day \$745 to \$845 per 10 days	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ● High ○ No included studies	The Aotearoa New Zealand costs are reasonably certain. Resourcing for Māori No additional evidence available	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No economic studies were identified to address the cost-effectiveness of the intervention or the comparison. Cost effectiveness for Māori No additional evidence available	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Influenced by the effects of colonisation, pēpi Māori are more likely to be born preterm, have more sepsis and neurodisability, both of which are associated with parenteral nutrition practices, and fewer survive. Thus, implementing standardised parenteral nutrition practices in Aotearoa New Zealand will contribute to achieving equitable health outcomes for preterm Pēpi Māori and their whānau. Equity for Pacific families Implementing standardised parenteral nutrition practices in Aotearoa New Zealand will contribute directly to reducing health disparities for all ethnicities and underrepresented groups. Equity for underrepresented groups Access to fish oil-based lipid therapy may depend on regional availability or clinician experience, which can disadvantage infants in smaller centres. Families unfamiliar with such treatments may require additional support. Equity means ensuring therapies are available across all hospitals and explained in ways that are accessible to every family.	

Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	The intervention is likely to be acceptable to stakeholders but would cost more. Acceptability for Māori There is no evidence to suggest the intervention would not be acceptable.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Fish oil only lipid emulsion is in widespread use as rescue therapy for preterm infants in Aotearoa New Zealand, so it is feasible here. Feasibility for Māori No additional evidence available	
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Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies

	JUDGEMENT						
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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References

1. Kapoor, V.; Malviya, M.N.; Soll, R. Lipid emulsions for parenterally fed preterm infants. *Cochrane Database Syst. Rev.* **2019**, *6*, CD013163, doi:10.1002/14651858.CD013163.pub2.
2. Park, H.W.; Lee, N.M.; Kim, J.H.; Kim, K.S.; Kim, S.N. Parenteral fish oil-containing lipid emulsions may reverse parenteral nutrition-associated cholestasis in neonates: a systematic review and meta-analysis. *J. Nutr.* **2015**, *145*, 277-283, doi:10.3945/jn.114.204974.
3. Ramiro-Cortijo, D.; Del Pozo Arribas, S.; Inisterra Viu, L.; Vazquez, N.G.; Saenz de Pipaon, M. Exclusive fish oil lipid emulsion rescue strategy improves cholestasis in neonates on partially fish oil-based lipid emulsion: A pilot study. *Nutrients* **2023**, *15*, doi:10.3390/nu15030509.
4. Premkumar, M.H.; Carter, B.A.; Hawthorne, K.M.; King, K.; Abrams, S.A. Fish oil-based lipid emulsions in the treatment of parenteral nutrition-associated liver disease: an ongoing positive experience. *Adv. Nutr.* **2014**, *5*, 65-70, doi:10.3945/an.113.004671.

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EtD 11. What is the recommended hang time for aqueous IV nutrition and lipid solutions for preterm infants?

POPULATION:	Preterm infants
INTERVENTION:	Parenteral nutrition aqueous phase or the lipid emulsion administration (hang) time of greater than 24 hours
COMPARISON:	Parenteral nutrition aqueous phase or the lipid emulsion administration (hang) time of 24 hours
MAIN OUTCOMES:	Critical outcomes - Mortality - Neurodevelopmental impairment - Adverse effects - Fully breastmilk feeding at hospital discharge Important but not critical - Fully breastfeeding at hospital discharge - Time to full enteral feeds - Faltering growth/body composition - Duration of initial hospital stay - Bronchopulmonary dysplasia/chronic lung disease - Necrotizing enterocolitis - Sepsis: proven or suspected - Retinopathy of prematurity - Anaemia of prematurity - Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making - Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation: population perspective
BACKGROUND:	Parenteral nutrition (PN) is a vital intervention for preterm infants, providing essential nutrients to support growth and development until enteral feeding is sufficient. The duration of PN administration, or "hang time," has significant implications for safety, nutrient intake and cost. A hang time of 24 hours is common in many settings, aiming to minimise the risk of microbial contamination and associated infections while maintaining nutritional stability. However, extending hang time beyond 24 hours may reduce preparation and administration burdens on healthcare systems, potentially increasing efficiency and lowering costs. Accessing the intravenous lines to change the PN less often may reduce the risk of infection. Conversely, longer hang times could elevate the risk of bacterial contamination and nutrient degradation, raising safety concerns. Preterm infants are particularly vulnerable to infections and nutritional deficits due to their immature immune systems and high metabolic demands.

CONFLICT OF INTERESTS: The following survey (Cormack et al, Reference 3) co-authors are on the Guideline Development Group:
Barbara Cormack, Tanith Alexander.

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS		
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence is based on a Cochrane systematic review [1] which reported on optimal timing for changing giving sets and a before-after observational study that investigated shorter vs. longer hanging time [2]. The studies that included neonates for this evidence did not provide any supporting evidence for very preterm infants and the data that is available may not be generalisable to this population. Note that in these studies the intervention is external to the infant and are researching the changing of giving sets or bags of fluid. Hang time PN solutions [2] This study looked at changing hang times of the aqueous solution bags. Lipid bags were changed daily. Adverse events: Before-After study: Hang time: Longer hang times associated with reduced central line associated bloodstream infection (24 hours vs. 48 hours hang time for central line associated bloodstream infection per 1000-line days 0.8 vs. 0.4 respectively $P<0.01$) [Critical] Sepsis: Before-After study: Hang time: Large reduction in central venous catheter-related sepsis with longer hang times (4 fewer per 1,000; 4 fewer to 4 fewer)[Important]. Cost: cost of intervention, cost of neonatal care and life-long cost: Before-After study: Annual savings (AUD) - AUD\$ 97 603.00/year with change to longer hang time (24 hours vs. 48 hours) [Important]. Set replacement [1] Adverse effects: RCT: Set replacement: Longer time between set changes had no significant reduction in infusate-related bloodstream infection at 48 hours + vs. 24 hours (25 fewer per 1,000; 45 fewer to 21 more). Longer time between set changes had no significant reduction in all-cause bloodstream infection for 48 hours + vs. 24 hours (48 fewer per 1,000; 143 fewer to 125 more) [Critical]. Desirable effects for Māori No additional evidence available	Population information for included evidence Cochrane systematic review [1]: For the two studies that included infants: One study included neonates admitted to the Neonatal Intensive Care Unit for whom intravenous lipid therapy was ordered (mean gestational age 34 weeks), the second study included neonates receiving parenteral nutrition (mean gestational age 32.8 weeks). Before-After study: Australia [2]. Median (inter-quartile range) gestational age (37 weeks (33,39) vs. 36 weeks (33,39)), mean (standard deviation) admission weight of 2442 g (101) versus 2476 g (104).		
Outcomes	Nº of participants	Certainty of the evidence	Relative effect	Anticipated absolute effects* (95% CI)

	(studies) Follow-up	(GRADE)	(95% CI)	Risk with parenteral nutrition aqueous phase or the lipid emulsion administration (hang) time of 24 hours	Risk difference with parenteral nutrition aqueous phase or the lipid emulsion administration (hang) time of greater than 24 hours
Mortality: RCT: set replacement: Lipid assessed with: 72 versus 24 hours (neonatal population only)	1189 (1 RCT)	⊕○○○ Very low ^{a,b,c}	RR 1.79 (0.97 to 3.32)	Study population 44 per 1,000	35 more per 1,000 (1 fewer to 102 more)
Neurodevelopmental impairment - not measured	-	-	-	-	-
Adverse effects: RCT: set replacement: 1 study lipids; 1 study lipid and aqueous solutions assessed with: Catheter-related bloodstream infection (48 hours + vs. 24 hours)	143 (2 RCTs)	⊕○○○ Very low ^{f,g,h}	RR 1.08 (0.07 to 16.95)	Study population 14 per 1,000	1 more per 1,000 (13 fewer to 216 more)
Adverse effects: RCT: set replacement: lipid and aqueous solutions assessed with: Infusate-related bloodstream infection (48 hours + vs. 24 hours)	341 (1 RCT)	⊕○○○ Very low ^{a,c,d}	RR 0.58 (0.25 to 1.35)	Study population 60 per 1,000	25 fewer per 1,000 (45 fewer to 21 more)
Adverse effects: RCT: set replacement: lipid and aqueous solutions assessed with: All-cause bloodstream infection (48 hours + vs. 24 hours)	148 (1 RCT)	⊕○○○ Very low ^{a,c,d}	RR 0.81 (0.44 to 1.49)	Study population 255 per 1,000	48 fewer per 1,000 (143 fewer to 125 more)
Adverse effects: Before-After study: Hang time aqueous solutions assessed with: central line-associated blood stream infection (CLABSI per 1000-line days)	260 (1 non-randomised study)	⊕○○○ Very low ^{d,h}	-	24 hours vs. 48 hours hang time for CLABSI per 1000-line days 0.8 vs. 0.4 respectively P<0.01	
Fully breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Fully breastfeeding at hospital discharge - not measured	-	-	-	-	-
Time to full enteral feeds (days) - not measured	-	-	-	-	-
Faltering growth/body composition - not measured	-	-	-	-	-
Duration of initial hospital stay - not measured	-	-	-	-	-
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Necrotizing enterocolitis - not measured	-	-	-	-	-
Sepsis: proven or suspected: Before-After study: Hang time aqueous solutions assessed with: Central venous catheter-related	1011 (1 non-randomised study)	⊕○○○ Very low ^{d,h}	not estimable	Study population 4 per 1,000	4 fewer per 1,000

sepsis					(4 fewer to 4 fewer)
Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost: Before-After study aqueous solutions assessed with: Annual savings (AUD)	260 (1 non-randomised study)	⊕○○○ Very low ^{d,h}	-	Costs including purchasing and dispensing of standard or non-standard bags 48 hours = AUD190,153 vs. 24 hours = AUD287,756. Yearly savings of AUD 97,603.00 with change to longer hang time (24 hours vs. 48 hours).	
Time to full sucking feeds - not measured	-	-	-	-	-

- a) Downgraded one level for risk of bias
b. Downgraded one level for indirectness as the evidence is unlikely to include any very or extremely preterm infants and the study reported on intravenous lipids
C) Downgraded two levels for imprecision with very wide confidence intervals that cross the line of no effect
d. Downgraded one level for indirectness as evidence is based on a single study
e. Upgraded one level for large effect
f. Downgraded two levels for inconsistency with I² = >80%
g. Downgraded two levels for indirectness. The study/studies did not report on whether the population included neonates or not

h. Downgraded two levels for risk of bias - before-after study in a single centre, no blinding, no confounding variables examined
i. Downgraded one level for imprecision as evidence is based on very few events

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Set replacement [1] Mortality: RCT: Set replacement: No significant increase in risk of neonatal mortality for longer time between set change for lipid of 72 hours or more versus 24 hours (35 more per 1,000; 1 fewer to 102 more). [Critical] Adverse effects: RCT: Set replacement: Longer time between set changes had no significant effect in risk for catheter-related bloodstream infection at 48 hours + vs. 24 hours (1 more per 1,000; 13 fewer to 216 more) [Critical] Undesirable effects for Māori No additional evidence available	In the [1] review, mortality was reported in two studies Fox 1999 and Matlow 1999. Fox 1999 did not report mortality in the study, only that “Three patients in the 48-hour group died before samples were taken”. The Cochrane review reflects that there were 3 deaths vs. 0 deaths. It does not mean there were no deaths in the 24-hour group. We have therefore not included this study for the outcome of mortality in this guideline question. The data is based on Matlow 1999 who noted that the excess deaths in the 72-hour group could not clearly be attributed to bacteraemia.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low	Very low certainty of evidence overall	

○ Low ○ Moderate ○ High ○ No included studies	Certainty of evidence for Māori No additional evidence available	
Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT: set replacement: Lipid assessed with: 72 versus 24 hours (neonatal population only)	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment - not measured	CRITICAL	-
Adverse effects: RCT: set replacement: 1 study lipids; 1 study lipid and aqueous solutions assessed with: Catheter-related bloodstream infection (48 hours + vs. 24 hours)	CRITICAL	⊕○○○ Very low
Adverse effects: RCT: set replacement: lipid and aqueous solutions assessed with: Infusate-related bloodstream infection (48 hours + vs. 24 hours)	CRITICAL	⊕○○○ Very low
Adverse effects: RCT: set replacement: lipid and aqueous solutions assessed with: All-cause bloodstream infection (48 hours + vs. 24 hours)	CRITICAL	⊕○○○ Very low
Adverse effects: Before-After study: Hang time aqueous solutions assessed with: central line-associated blood stream infection (CLABSI per 1000-line days)	CRITICAL	⊕○○○ Very low
Fully breastmilk feeding at hospital discharge - not measured	CRITICAL	-
Fully breastfeeding at hospital discharge - not measured	IMPORTANT	-
Time to full enteral feeds (days) - not measured	IMPORTANT	-
Faltering growth/body composition - not measured	IMPORTANT	-
Duration of initial hospital stay - not measured	IMPORTANT	-
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Necrotizing enterocolitis - not measured	IMPORTANT	-
Sepsis: proven or suspected: Before-After study: Hang time aqueous solutions assessed with: Central venous catheter-related sepsis	IMPORTANT	⊕○○○ Very low
Retinopathy of prematurity - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost: Before-After study aqueous solutions assessed with: Annual savings (AUD)	IMPORTANT	⊕○○○ Very low

Time to full sucking feeds - not measured	NOT IMPORTANT	-
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Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability Values for Māori No additional research available.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Longer versus shorter time between changing sets - Very low certainty evidence Lipid: Uncertain effect on mortality (lipid 72 versus 24 hours), adverse effects (catheter-related bloodstream infection, infusate-related bloodstream infection, all-cause bloodstream infection) Longer versus shorter hang time - Very low certainty evidence Reduction in sepsis Probable reduction in adverse effect (central line-associated bloodstream infection per 1000-line days) Large reduction in costs of parenteral nutrition and neonatal nursing labour Balance of effects for Māori No additional evidence	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings	Parenteral Nutrition Standard Solution Prices Aotearoa New Zealand Hospital A Aqueous solution bags \$140 per 750 mL bag SMOFLipid & Multi 12/Influvite syringe - \$50.50	

○ Varies ○ Don't know	Giving sets: Aqueous solutions (\$7.18 + \$2.77 = \$9.95) Lipid emulsion \$7.82 <i>Current Hang Time:</i> Aqueous solution bags 48 hours SMOF Lipid is 50 mL syringe 48 hours (but some hospitals change lipid after 24 hours). Aotearoa New Zealand Hospital B Aqueous solution bags costs \$117.50 SMOFLipid & Soluvit/Vitalipid syringe costs \$71.04 Giving sets: Aqueous solutions (\$7.18 + \$2.77 = \$9.95) Lipid emulsion \$7.82 <i>Current Hang Times:</i> Aqueous solution (PN) bags and lines 96 hours SMOFLipid is 50 mL syringe and lines 48 hours <i>Saving per infant to change</i> aqueous solution bags and lines after 96 hours vs. 48 is \$118 - \$140 per 4 days <i>Saving per infant to change</i> lipid emulsion bags and lines after 48 hours vs. 24 is \$117 - \$158 per 4 days Additional costs Nursing time to administer IVN and change sets	
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Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ● High ○ No included studies	Although [2] is an Australian study, it is only based on a single centre. Event rates for central line associated bloodstream infection which was the primary outcome were extremely low. There is high certainty of the local resource requirements (costs). Certainty of evidence of required resources for Māori No additional evidence available	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison	Data from a before-after study [2]: Costs including purchasing and dispensing of standard or non-	

○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	standard bags 48 hours = AUD 190,153 vs. 24 hours = AUD 287,756. Yearly savings of AUD 97 603.00 with change to longer hang time (24 hours vs. 48 hours). Nurses survey (n=50; 82% response rate)- 68.3% had decreased workload, 80.5% indicated time changing PN was reduced. Assuming infants have parenteral nutrition for a mean of 10 to 12 days, the intervention is ~\$700 to \$900 per infant cheaper than the comparison. Cost effectiveness for Māori No additional evidence available	
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Equity

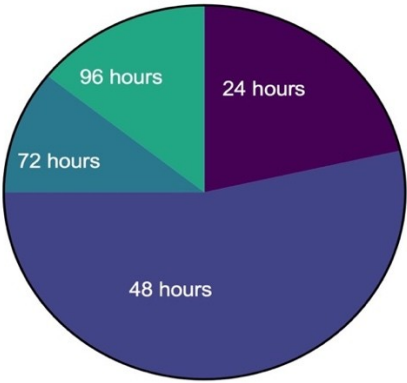
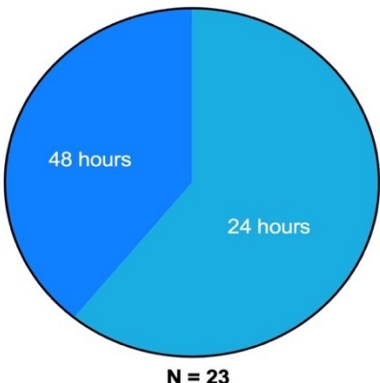
What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Influenced by the effects of colonisation, pēpi Māori are more likely to be born preterm, have more sepsis and neurodisability, both of which are associated with parenteral nutrition practices, and fewer survive. Thus, implementing standardised parenteral nutrition practices in Aotearoa New Zealand will contribute to achieving equitable health outcomes for preterm pēpi Māori and their whānau. Equity for Pacific families Implementing standardised parenteral nutrition practices in Aotearoa New Zealand will contribute directly to reducing health disparities for Pacific peoples Equity for other underrepresented groups Families from diverse backgrounds may not be informed about the safety and practical reasons behind hang time limits for parenteral nutrition. If errors occur, trust may be affected. Equity requires consistent safety protocols and proactive, inclusive communication that reassures and involves all families in understanding care procedures.	

Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	From a survey of Australasian neonatal dietitians conducted in 2024 [3]. Parenteral nutrition hang times in NZ and Australian neonatal units Glucose and amino acid solution  N = 28 Lipid emulsion  N = 23	
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Feasibility		
Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Hang times (and administration set changes) of greater than 24 hours are in widespread use, so it is feasible in Aotearoa New Zealand. Feasibility for Māori No additional evidence available	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF	Very low	Low	Moderate	High			No included studies

	JUDGEMENT						
EVIDENCE							
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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EtD 12. What is the enteral nutrition criterion (volume) to stop parenteral nutrition? What is the criterion for stopping lipids?

POPULATION:	Preterm infants receiving parenteral nutrition
INTERVENTION:	A lower volume of enteral feed (mL/kg/day)
COMPARISON:	A higher volume of enteral feed (mL/kg/day)
MAIN OUTCOMES:	Critical for making a decision Mortality Neurodevelopmental impairment Sepsis: proven or suspected Faltering growth / body composition Important but not critical Adverse effects (other than mortality, bronchopulmonary dysplasia, NEC, sepsis, anaemia of prematurity or retinopathy of prematurity) Fully breastmilk feeding at hospital discharge Fully breastfeeding at hospital discharge Duration of initial hospital stay Time to full enteral feeds Bronchopulmonary dysplasia Necrotizing enterocolitis Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Of limited importance Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical practice recommendation
BACKGROUND:	In preterm infants, the transition from parenteral nutrition to full enteral feeding is a crucial stage in supporting gut development, growth and overall clinical progress. Parenteral nutrition, which includes the provision of glucose, amino acids and lipids directly into the bloodstream, is essential for some preterm infants during the early days after birth when they are unable to tolerate sufficient volumes of milk to meet their fluid and nutritional requirements. However, there is risk of malnutrition and associated complications if parenteral feeding is stopped too early. In contrast, the longer parenteral nutrition is continued, the greater the risk of line sepsis. Each additional day of parenteral nutrition is linked to a higher risk of sepsis, which must be carefully weighed against the risk of inadequate nutrient intake, especially if the enteral feed is unfortified breastmilk. Identifying a clear enteral feed volume at which parenteral nutrition and lipid infusions can safely cease is important for standardising care. Clinical practice varies between Aotearoa New Zealand neonatal units, but parenteral nutrition is commonly weaned when enteral feeds reach approximately 120 to 140 mL/kg/day, with lipid infusions stopped around the same time. Clear, evidence-based guidance would support safe

CONFLICT OF INTERESTS:	and consistent practice across neonatal care settings.
	None

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence is based on the National Institute of Health and Care Excellence (NICE) [1] guideline that contained one RCT and 2 cohort studies; an update of trial data from the RCT in NICE guideline [2] and another RCT [3]. 100 mL/kg/day vs. 140 mL/kg/day Mortality: RCT: No significant difference in risk of death between earlier and later stopping of parenteral feeds (6 more per 1,000; 23 fewer to 84 more) [Critical]. Sepsis: RCT: There was no difference between groups for central venous catheter-associated sepsis (28 fewer per 1,000; 41 fewer to 97 more) or for “late onset sepsis–other than for central line-associated bloodstream infection (CLABSI)” (90 more per 1,000; 34 fewer to 232 more) between groups. There was no significant difference between groups for sepsis (culture proven + suspected) (100mL/kg/day 15/67 (22%) versus 140 mL/kg/day 8/70 (11%). There were no significant differences between groups for CLABSI in 100 mL/kg/day (n=106) 10.35 CLABSI rate-events/1000 catheter days versus 140 mL/kg/day (n=104) 10.20 CLABSI rate-events/1000 catheter days [Critical]. No faltering growth / body composition: RCT: No significant difference in weight at 36 weeks' post-menstrual age/discharge (MD 28.35 g higher; 61.11 lower to 117.81 higher); Z-score for weight at 36 weeks' post menstrual age (MD 0.08 points higher; 0.16 lower to 0.32 higher); weight <10th percentile at 36 weeks' post menstrual age/discharge (24 more per 1,000; 71 fewer to 146 more); growth velocity from birth to 36 weeks' postmenstrual age (MD 0.2 g/kg/day lower; 0.86 lower to 0.46 higher); length at 36 weeks' postmenstrual age/discharge (MD 0.11 cm lower; 0.68 lower to 0.45 higher); Z-score for length at 36 weeks' postmenstrual age (MD 0.16 points lower; 0.4 lower to 0.08 higher); length <10th percentile at 36 weeks' postmenstrual age/discharge (58 more per 1,000; 45 fewer to 188 more); Head circumference at 36 weeks' postmenstrual age/discharge (MD 0.1cm lower; 0.47 lower to 0.27 higher); Z-score for head circumference at 36 weeks' postmenstrual age (MD 0.1 points lower; 0.38 lower to 0.18 higher) head circumference <10th percentile at 36 weeks' post menstrual age/discharge (10 more per 1,000; 64 fewer to 125 more) [Critical]. Fully breastfeeding at hospital discharge: RCT: No significant difference in fully breastfeeding at hospital discharge (88 more per 1,000; 71 fewer to 349 more) [Important].	Full parenteral nutrition provides approximately 100 kcal/kg/day and 3.5 to 4 g/kg/day protein. 120 mL/kg/day expressed breastmilk provides 80 kcal/kg/day and 1.5 g/kg/day 140 mL/kg/day expressed breastmilk provides 92 kcal/kg/day and 1.8 g/kg/day If feeds are increased by at least 20 mL/kg/day each day, there will only be 2 days when nutrition is inadequate. Ireland [2]: RCT follow-up data: Very low birthweight infants. Poland: RCT [3]: Very low birthweight infants. We identified some additional evidence to indicate that a longer duration of parenteral nutrition is associated with increased risk of sepsis: USA [4]: Retrospective case-control study: Infants persistently infected with Coagulase-negative staphylococci were significantly

Duration of hospital stay: RCT: No significant difference in median duration of hospital stay (days) [Important]. Bronchopulmonary dysplasia (BPD) / chronic lung disease: RCT: No significant difference in bronchopulmonary dysplasia (13 more per 1,000; 49 fewer to 117 more) [Important]. Necrotizing enterocolitis (NEC): RCT: No significant difference in NEC (0 fewer per 1,000; 26 fewer to 72 more). [Important] Retinopathy of prematurity: RCT: No significant difference in retinopathy of prematurity (75 more per 1,000; 3 fewer to 284 more). [Important] 100 mL/kg/day vs. 120 mL/kg/day Sepsis: Cohort study: No significant difference for sepsis between earlier and later stopping of parenteral feeds (91 fewer per 1,000; 234 fewer to 147 more). [Critical] No faltering growth/body composition: Cohort study: Earlier stopping reduced the number of infants with weight <10th centile at 36 weeks' post conception (257 fewer per 1,000; 386 fewer to 92 fewer); length <10th centile at 36 weeks' post conception (195 fewer per 1,000; 332 fewer to 0 fewer) and head circumference <10th centile at 36 weeks' post conception (361 fewer per 1,000; 494 fewer to 180 fewer). [Critical] Duration of hospital stay: Cohort study: No significant difference in median duration of hospital stay (MD 7.9 days lower; 19.1 lower to 3.3 higher). [Important] Necrotizing enterocolitis (NEC): Cohort study: No significant difference in NEC. Unable to calculate effect estimate due to low or no event rates. [Important] Desirable effects for Māori No additional evidence available	more likely to have a greater duration of exposure to parenteral nutrition (OR 1.45 parenteral nutrition days; 95%CI 1.26 to 1.66 P<0.001). Netherlands [5]: Case-control study: Duration of parenteral feeding was identified as an independent risk factor for late onset sepsis development irrespective of the causative pathogen (OR 1.13; 95% 1.04 to 1.22; P = 0.003). South Korea [6]: Implementation study reducing number of days of central line for 195 very low birthweight infants. There was a significant reduction in blood culture-proven sepsis (25.6% vs. 10.5%, P=0.008).
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Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with a higher volume of enteral feed (mL/kg/day)	Risk difference with a lower volume of enteral feed (mL/kg/day)
Mortality: RCT: 100 mL/kg/day vs. 140 mL/kg/day	347 (2 RCTs)	⊕⊕⊕○ Moderate ^a	RR 1.15 (0.43 to 3.10)	Study population 40 per 1,000	6 more per 1,000 (23 fewer to 84 more)
Neurodevelopmental impairment - not measured	-	-	-	-	-
Sepsis: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Central line-associated bloodstream infection rate-events/1000 catheter days	210 (1 RCT)	⊕⊕○○ Low ^b	-	100mL/kg/day (n=106) 10.35 Central line-associated bloodstream infection rate-events/1000 catheter days 140 mL/kg/day (n=104) 10.20 Central line-associated bloodstream infection rate-events/1000 catheter days	
Sepsis: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Central venous catheter- associated	137 (1 RCT)	⊕⊕⊕○ Moderate ^a	RR 0.35 (0.04 to 3.27)	Study population 43 per 1,000	28 fewer per 1,000

					(41 fewer to 97 more)
Sepsis: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Late onset sepsis – other than Central line-associated bloodstream infection	210 (1 RCT)	⊕⊕○○ Low ^b	OR 1.51 (0.84 to 2.70)	Study population	
				279 per 1,000	90 more per 1,000 (34 fewer to 232 more)
Sepsis: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Culture proven and suspected sepsis	347 (1 RCT)	⊕⊕⊕⊕ High	-	100mL/kg/day 15/67 (22%) 140 mL/kg/day 8/70 (11%) Not significant	
Sepsis: proven or suspected: Observational study: 100 mL/kg/day vs. 120 mL/kg/day	87 (1 non-randomised study)	⊕○○○ Very low ^{b,c}	RR 0.79 (0.46 to 1.34)	Study population	
				432 per 1,000	91 fewer per 1,000 (234 fewer to 147 more)
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Weight (g) at 36 weeks' post menstrual age/discharge	338 (2 RCTs)	⊕⊕○○ Low ^b	-	The mean faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day was 2,289 g	MD 28.35 higher (61.11 lower to 117.81 higher)
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Z-score for weight at 36 weeks' post menstrual age	201 (1 RCT)	⊕⊕○○ Low ^{a,d}	-	The mean faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day was -1.13 points	MD 0.08 higher (0.16 lower to 0.32 higher)
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Weight < 10th percentile at 36 weeks' post menstrual age/discharge	338 (2 RCTs)	⊕⊕⊕○ Moderate ^a	RR 1.06 (0.82 to 1.37)	Study population	
				394 per 1,000	24 more per 1,000 (71 fewer to 146 more)
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Growth velocity from birth to 36 weeks' postmenstrual age (g/kg/day)	201 (1 RCT)	⊕⊕○○ Low ^{a,d}	-	The mean faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day was 13.8 g/kg/day	MD 0.2 lower (0.86 lower to 0.46 higher)
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Length (cm) at 36 weeks' postmenstrual age/discharge	323 (2 RCTs)	⊕⊕○○ Low ^{a,e}	-	The mean faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day was 43.9 cm	MD 0.11 lower (0.68 lower to 0.45 higher)
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Z-score for length at 36 weeks' postmenstrual age	186 (1 RCT)	⊕⊕○○ Low ^{a,d}	-	The mean faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day was -1.11 points	MD 0.16 points lower (0.4 lower to 0.08 higher)
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Length < 10th percentile at 36 weeks' postmenstrual age/discharge	323 (2 RCTs)	⊕⊕⊕○ Moderate ^a	RR 1.13 (0.90 to 1.42)	Study population	
				448 per 1,000	58 more per 1,000 (45 fewer to 188 more)
Faltering growth / body composition: RCT: 100	320	⊕⊕⊕○	-	The mean faltering growth / body	MD 0.1 lower

mL/kg/day vs. 140 mL/kg/day assessed with: Head circumference at 36 weeks' postmenstrual age/discharge (cm)	(2 RCTs)	Moderate ^a		composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day was 31.95 cm	(0.47 lower to 0.27 higher)
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Z-score for HC at 36 weeks' postmenstrual age	183 (1 RCT)	⊕⊕○○ Low ^{a,d}	-	The mean faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day was -0.44 Points	MD 0.1 Points lower (0.38 lower to 0.18 higher)
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Head circumference < 10th percentile at 36 weeks' postmenstrual age/discharge	320 (2 RCTs)	⊕⊕⊕○ Moderate ^a	RR 1.05 (0.68 to 1.62)	Study population	
				201 per 1,000	10 more per 1,000 (64 fewer to 125 more)
Faltering growth / body composition: Observational study: 100 mL/kg/day vs. 120 mL/kg/day assessed with: Weight gain - weight <10th centile - At 36 weeks' post conception	87 (1 non-randomised study)	⊕○○○ Very low ^{b,c}	RR 0.72 (0.58 to 0.90)	Study population	
				919 per 1,000	257 fewer per 1,000 (386 fewer to 92 fewer)
Faltering growth / body composition: Observational study: 100 mL/kg/day vs. 120 mL/kg/day assessed with: Linear growth - length <10th centile - At 36 weeks' post conception	87 (1 non-randomised study)	⊕○○○ Very low ^{b,c}	RR 0.76 (0.59 to 1.00)	Study population	
				811 per 1,000	195 fewer per 1,000 (332 fewer to 0 fewer)
Faltering growth / body composition: Observational study: 100 mL/kg/day vs. 120 mL/kg/day assessed with: Head circumference <10th centile - At 36 weeks' post conception	87 (1 non-randomised study)	⊕○○○ Very low ^{b,c}	RR 0.54 (0.37 to 0.77)	Study population	
				784 per 1,000	361 fewer per 1,000 (494 fewer to 180 fewer)
Adverse effects - not measured	-	-	-	-	-
Fully breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Fully breastfeeding at hospital discharge: RCT: 100 mL/kg/day vs. 140 mL/kg/day	112 (1 RCT)	⊕⊕○○ Low ^{a,d}	RR 1.26 (0.79 to 2.03)	Study population	
				339 per 1,000	88 more per 1,000 (71 fewer to 349 more)
Duration of initial hospital stay: RCT: 100 mL/kg/day vs. 140 mL/kg/day	137 (1 RCT)	⊕⊕⊕⊕ High	-	A RCT reported length of stay as Median 49.6 days (IQR 38.2, 69.2) n=67 for 100 mL/kg/day vs. 53.32 days (IQR 35.3) n=70 for 140 mL/kg/day (not significant).	
Duration of initial hospital stay: Observational study: 100 mL/kg/day vs. 120 mL/kg/day assessed with: Days	87 (1 non-randomised study)	⊕○○○ Very low ^{b,c}	-	The mean duration of initial hospital stay: Observational study: 100 mL/kg/day vs. 120 mL/kg/day was 76.8 days	MD 7.9 lower (19.1 lower to 3.3 higher)
Time to full enteral feeds - not measured	-	-	-	-	-
Bronchopulmonary dysplasia (BPD) / chronic lung disease: RCT: 100 mL/kg/day vs. 140 mL/kg/day	347 (2 RCTs)	⊕⊕⊕○ Moderate ^a	RR 1.09 (0.67 to 1.78)	Study population	
				149 per 1,000	13 more per 1,000 (49 fewer to 117 more)

Necrotizing enterocolitis (NEC): RCT: 100 mL/kg/day vs. 140 mL/kg/day	347 (2 RCTs)	⊕⊕⊕○ Moderate ^a	RR 1.00 (0.36 to 2.80)	Study population	
				40 per 1,000	0 fewer per 1,000 (26 fewer to 72 more)
Necrotizing enterocolitis (NEC): Observational study: 100 mL/kg/day vs. 120 mL/kg/day	87 (1 non-randomised study)	⊕○○○ Very low ^{c,f}	OR 5.82 (0.35 to 97.53)	Study population	
				0 per 1,000	0 fewer per 1,000 (0 fewer to 0 fewer)
Retinopathy of prematurity (ROP): RCT: 100 mL/kg/day vs. 140 mL/kg/day	210 (1 RCT)	⊕⊕○○ Low ^{a,d}	RR 2.55 (0.94 to 6.90)	Study population	
				48 per 1,000	75 more per 1,000 (3 fewer to 284 more)
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-

- a. Downgraded one level due to imprecision
b. Downgraded two levels for serious imprecision
c. Downgraded one level due concerns for risk of bias
d. Downgraded one level as evidence is based on a single study
e. Downgraded one level as I² > 50 but < 80%
f. Downgraded two level for imprecision due to low/no event rate

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	No evidence Undesirable effects for Māori No additional evidence available	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	High to very low certainty of evidence overall. Certainty of evidence for Māori No additional evidence available	
Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT: 100 mL/kg/day vs. 140 mL/kg/day	CRITICAL	⊕⊕⊕○ Moderate ^a
Neurodevelopmental impairment - not measured	CRITICAL	-
Sepsis: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Central line-associated bloodstream infection rate-events/1000 catheter days	CRITICAL	⊕⊕○○ Low
Sepsis: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Central venous catheter- associated	CRITICAL	⊕⊕⊕○ Moderate ^a
Sepsis: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Late onset sepsis – other than Central line-associated bloodstream infection	CRITICAL	⊕⊕○○ Low ^b
Sepsis: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Culture proven and suspected sepsis	CRITICAL	⊕⊕○○ Low
Sepsis: proven or suspected: Observational study: 100 mL/kg/day vs. 120 mL/kg/day	CRITICAL	⊕○○○ Very low ^{b,c}
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Weight (g) at 36 weeks' post menstrual age/discharge	CRITICAL	⊕⊕○○ Low ^b
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Z-score for weight at 36 weeks' post menstrual age	CRITICAL	⊕⊕○○ Low ^{a,d}
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Weight < 10th percentile at 36 weeks' post menstrual age/discharge	CRITICAL	⊕⊕⊕○ Moderate ^a
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Growth velocity from birth to 36 weeks' postmenstrual age (g/kg/day)	CRITICAL	⊕⊕○○ Low ^{a,d}
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Length (cm) at 36 weeks' postmenstrual age/discharge	CRITICAL	⊕⊕○○ Low ^{a,e}

Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Z-score for length at 36 weeks' postmenstrual age	CRITICAL	⊕⊕○○ Low ^{a,d}
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Length < 10th percentile at 36 weeks' postmenstrual age/discharge	CRITICAL	⊕⊕⊕○ Moderate ^a
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Head circumference at 36 weeks' postmenstrual age/discharge (cm)	CRITICAL	⊕⊕⊕○ Moderate ^a
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Z-score for HC at 36 weeks' postmenstrual age	CRITICAL	⊕⊕○○ Low ^{a,d}
Faltering growth / body composition: RCT: 100 mL/kg/day vs. 140 mL/kg/day assessed with: Head circumference < 10th percentile at 36 weeks' postmenstrual age/discharge	CRITICAL	⊕⊕⊕○ Moderate ^a
Faltering growth / body composition: Observational study: 100 mL/kg/day vs. 120 mL/kg/day assessed with: Weight gain - weight <10th centile - At 36 weeks' post conception	CRITICAL	⊕○○○ Very low ^{b,c}
Faltering growth / body composition: Observational study: 100 mL/kg/day vs. 120 mL/kg/day assessed with: Linear growth - length <10th centile - At 36 weeks' post conception	CRITICAL	⊕○○○ Very low ^{b,c}
Faltering growth / body composition: Observational study: 100 mL/kg/day vs. 120 mL/kg/day assessed with: Head circumference <10th centile - At 36 weeks' post conception	CRITICAL	⊕○○○ Very low ^{b,c}
Adverse effects - not measured	IMPORTANT	-
Fully breastmilk feeding at hospital discharge - not measured	IMPORTANT	-
Fully breastfeeding at hospital discharge: RCT: 100 mL/kg/day vs. 140 mL/kg/day	IMPORTANT	⊕⊕○○ Low ^{a,d}
Duration of initial hospital stay: RCT: 100 mL/kg/day vs. 140 mL/kg/day	IMPORTANT	⊕⊕⊕⊕ High
Duration of initial hospital stay: Observational study: 100 mL/kg/day vs. 120 mL/kg/day assessed with: Days	IMPORTANT	⊕○○○ Very low ^{b,c}
Time to full enteral feeds - not measured	IMPORTANT	-
Bronchopulmonary dysplasia (BPD) / chronic lung disease: RCT: 100 mL/kg/day vs. 140 mL/kg/day	IMPORTANT	⊕⊕⊕○ Moderate ^a
Necrotizing enterocolitis (NEC): RCT: 100 mL/kg/day vs. 140 mL/kg/day	IMPORTANT	⊕⊕⊕○ Moderate ^a
Necrotizing enterocolitis (NEC): Observational study: 100 mL/kg/day vs. 120 mL/kg/day	IMPORTANT	⊕○○○ Very low ^{c,f}

Retinopathy of prematurity (ROP): RCT: 100 mL/kg/day vs. 140 mL/kg/day	IMPORTANT	⊕⊕○○ Low ^{a,d}
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-

- a. Downgraded one level due to imprecision
b. Downgraded two levels for serious imprecision
c. Downgraded one level due concerns for risk of bias
d. Downgraded one level as evidence is based on a single study
e. Downgraded one level as I² > 50 but < 80%
f. Downgraded two level for imprecision due to low/no event rate

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ Important uncertainty or variability ☒ Possibly important uncertainty or variability ☐ Probably no important uncertainty or variability ☐ No important uncertainty or variability	Possibly important uncertainty or variability Values for Māori No additional evidence available	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ Favours the comparison ☐ Probably favours the comparison ☒ Does not favour either the intervention or the comparison ☐ Probably favours the intervention ☐ Favours the intervention	100 mL/kg/day vs. 140 mL/kg/day - high certainty evidence Uncertain effect on duration of hospital stay, central line associated blood infection/culture proven and suspected sepsis 100 mL/kg/day vs. 140 mL/kg/day - moderate certainty evidence Uncertain effect on mortality, weight, length and head circumference <10th percentile, head circumference, bronchopulmonary dysplasia/chronic lung disease, NEC, central venous catheter-associated sepsis 100 mL/kg/day vs. 140 mL/kg/day - low certainty evidence Uncertain effect on weight, weight z score, growth velocity, length, length z score, head circumference z score, fully breastfeeding at hospital discharge, retinopathy of prematurity, late onset sepsis other	The NICE guideline notes that the central venous catheter associated sepsis is clinically significant although it does not reach statistical significance

○ Varies ○ Don't know	than central line-associated blood infection 100 mL/kg/day vs. 120 mL/kg/day - very low certainty evidence Reduced the number of infants with weight, length and head circumference <10th centile. Uncertain effect on sepsis, duration of hospital stay, NEC Balance of effects for Māori - No additional evidence available	
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Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Assuming clinician time to prescribe standardised PN and EN and nursing time to administer and may be similar for PN and EN. Costs for parenteral nutrition: Glucose, amino acid and electrolyte standard solution (aqueous phase) Aqueous solution: Company A approx. \$140 (used for 48 hours) Company B \$118 (used for 96 hours) = \$29.50 to \$70 per day SMOFLipid, including vitamins per syringe: approx. \$51 to \$71 (used for 48 hours) = \$25.50 to \$35.50 Total \$55 to \$105 per day plus Catheter Giving sets IV Pump Parenteral nutrition is substantially more expensive than enteral nutrition, so fewer days of parenteral nutrition will save money. Resources required for Māori No additional evidence available	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Costs may vary Certainty of evidence of required resources for Māori No additional evidence available	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No studies were identified that address cost of early versus late stopping of parenteral feeds in preterm infants.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Influenced by the effects of colonisation, pēpi Māori are more likely to be born preterm, have more sepsis and neurodisability, both of which are associated with parenteral nutrition practices, and fewer survive. Thus, implementing standardised parenteral nutrition practices in Aotearoa New Zealand will contribute to achieving equitable health outcomes for preterm pēpi Māori and their whānau. Equity for Pacific families Implementing standardised parenteral nutrition practices in Aotearoa New Zealand will contribute directly to reducing health disparities for Pacific peoples Equity for other underrepresented groups Families from diverse backgrounds may not be informed about the safety and practical reasons behind minimising the number of days on parenteral nutrition. If errors occur, trust may be affected. Equity requires consistent safety protocols and proactive, inclusive communication that reassures and involves all families in understanding care procedures.	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☐ Varies ☐ Don't know	Probably acceptable	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☐ Probably yes ☒ Yes ☐ Varies ☐ Don't know	The intervention is feasible.	

Summary of Judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know

	JUDGEMENT						
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of Recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ●	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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EtD 14. Should higher parenteral protein (>4 g/kg/day) vs. Lower parenteral protein be used for preterm infants and what is the recommended protein intake by postnatal age?

POPULATION:	Preterm infants requiring parenteral nutrition
INTERVENTION:	Higher parenteral protein (>4 g/kg/day)
COMPARISON:	Lower parenteral protein ($\leq$ 4 g/kg/day)
MAIN OUTCOMES:	Critical outcomes Mortality Neurodevelopmental impairment Faltering growth/body composition Important but not critical Adverse effects Fully breastfed or breastmilk feeding at hospital discharge Time to full enteral feeds Duration of initial hospital stay Sepsis: proven or suspected Bronchopulmonary dysplasia Necrotizing enterocolitis Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation - patient perspective
BACKGROUND:	Preterm infants have high protein requirements due to their limited protein stores at birth and their rapid growth needs. Many extremely preterm infants face biochemical disturbances after birth, growth faltering and neurodevelopmental impairments during infancy and childhood, and long-term risks for cardio-metabolic diseases. For the smallest preterm infants, parenteral nutrition plays a critical role in mitigating these risks, with protein being a key nutrient supporting growth and development. Early adequate protein delivered parenterally, enhances tissue growth and promotes neurodevelopment. However, too much parenteral protein can lead to metabolic acidosis, hyperammonaemia, elevated blood urea refeeding syndrome and impaired neurodevelopment. Too little protein can result in protein deficiency, faltering growth, altered body composition and impaired neurodevelopment. Despite its importance, the optimal protein intake remains uncertain. Studies have explored intakes ranging from 2.3 to 4.5 g/kg/day, with many recommending higher intakes of 3.5–4.5 g/kg/day to support growth and development. Studies focusing on the impact of protein intake on both short-term outcomes as well as long-term growth, body composition and neurodevelopment are critical in guiding evidence-based practices.

CONFLICT OF INTERESTS:

The following Systematic Review on Protein (Das, S. et al) co-authors are on the Guideline Development Group: Barbara Cormack, Luling Lin and Frank Bloomfield and supervised the first author. Frank Bloomfield and Barbara Cormack were the ProVIDe trial investigators.

Assessment**Desirable Effects**

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	A 2024 systematic review [1] reported that seven guidelines (ESPGPR/CSPEN [critically ill neonate] guidelines, 2021; NICE 2020; Irish Society for Clinical Nutrition and Metabolism, 2020; Australasian neonatal parenteral nutrition consensus update, 2017; Turkish Neonatal Society, 2019, Portuguese Neonatal Society; ESPGHAN [parenteral] 2018) recommended a gradual increase of parenteral protein intake, ranging between 1.0–3.0 g/kg/day for the first 2 days and up to 4.0 g/kg/day subsequently. The upper limit of recommended parenteral protein intakes varied, including a maximum of 3.5 g/kg/day (strong recommendations, very low to high certainty of evidence) [ESPGHAN [critically ill neonate] guidelines, 2021; Turkish Neonatal Society, 2019]; 4 g/kg/day weak to strong recommendations, very low to high certainty of evidence) [NICE 2020; Australasian Neonatal Parenteral Nutrition Consensus Update, 2017; Turkish Neonatal Society, 2019] and >3.5 g/kg/day only as part of clinical trials (weak recommendation, low certainty of evidence) [ESPGHAN [critically ill neonate] guidelines, 2021]. NSW 2022 (1) commence parenteral protein within the first 24 hours of birth (2) commence parenteral protein at 2 g/kg/day and (3) incrementally increase protein to a maximum 4 g/kg/day by day 3-5 of life in preterm neonates. The 2022 consensus noted the latest ESPGHAN 2018 recommendation of maximum 3.5 g/kg/day of parenteral protein and NICE 2020 recommendations of maximum 4 g/kg/day. ESPGHAN 2018 R 3.1 In preterm infants the parenteral protein supply should start on the first postnatal day with at least 1.5 g/kg/day to achieve an anabolic state. (strong recommendation) R 3.2 In preterm infants the parenteral protein intake from postnatal day 2 onwards should be between 2.5 and 3.5 g/kg/day and should be accompanied by non-protein intakes >65 kcal/kg/day and adequate micronutrient intakes. (strong recommendation) R 3.3 In preterm infants, parenteral protein intakes above 3.5 g/kg/day should only be administered as part of clinical trials (conditional recommendation) Other data for this question comes from a systematic review by Osborn <i>et al</i> [2] and a relevant Aotearoa New Zealand randomised trial by Bloomfield <i>et al</i> [3]. Higher versus parenteral protein	

Mortality: RCT: No significant reduction in deaths with higher parenteral protein (13 fewer per 1,000; 41 fewer to 22 more); or early parenteral protein (1 g extra per day for 5 days) versus placebo (14 fewer per 1,000; 70 fewer to 66 more) [Critical].

Neurodevelopmental impairment: RCT: No events reported for deafness. No significant effect Bayley III score at ≥ 18 months (MD 3 points higher; 2.52 lower to 8.52 higher) and Bayley III psychomotor score at ≥ 18 months for higher dose of parenteral protein (MD 3 points higher; 6.41 lower to 12.41 higher); no significant effect on autism for higher dose of parenteral protein (0 fewer per 1,000; 58 fewer to 853 more); no significant reduction in survival without neurodisability (25 fewer per 1,000; 104 fewer to 70 more); little or no difference in blindness (1/61 (0.36%) vs. 1/63 (0.6%)) and deafness (6/161 (3.7% vs. 2/163 (1.2%)) [Critical].

No faltering growth/body composition: RCT: Very large reduction in infants with weight <10 th centile (144 fewer per 1,000; 244 fewer to 17 fewer); reduction in postnatal faltering growth at discharge [weight 2 SD below mean] (20 fewer per 1,000; 170 fewer to 200 more); no significant reduction in postnatal faltering growth post discharge (95 fewer per 1,000; 188 fewer to 90 more); fewer days to regain birthweight (MD 1.14 days lower; 1.73 lower to 0.56 lower). No significant effect on weight gain to discharge (MD 0.76 g/kg/day higher; 0.02 lower to 1.54 higher), weight change z score at discharge (MD 0.01 points higher; 0.33 lower to 0.36 higher); weight z score at discharge (MD 0.16 points higher; 0.02 lower to 0.33 higher). Small increase in head circumference to discharge (MD 0.09 cm/week higher; 0.06 higher to 0.13 higher). No significant increase in head circumference change z score to discharge (MD 0.18 points higher; 0.15 lower to 0.5 higher); head circumference z score at discharge (MD 0.04 points higher; 0.18 lower to 0.26 higher); weight z score at discharge (Adj MD 0.09 points higher; 0.08 lower to 0.26 higher); length z score at discharge (Adj MD 0.07 points higher; 0.13 lower to 0.26 higher); length z score at discharge (MD 0.12 points higher; 0.14 lower to 0.38 higher); nor head circumference z score at discharge (Adj MD 0.02 points higher; 0.16 lower to 0.2 higher)[Critical].

Adverse effects: RCT: Hyperglycaemia (plasma glucose >8.3 mmol/L). Very large reduction in hyperglycaemia (78 fewer per 1,000; 129 fewer to 10 fewer) [Important].

Fully breastfed or breastmilk feeding at hospital discharge: RCT: 87/201 (43.3%) fully breastfed or breastmilk feeding at discharge with higher parenteral protein and 82/207 (39.6%) with lower protein [Important].

Time to full enteral feeds: RCT: No significant effect on time to full enteral feeds with higher parenteral protein (MD 0.2 days lower; 1.1 lower to 0.7 higher) [Important].

Sepsis: RCT: No significant effect in late onset sepsis with higher parenteral nutrition (9 fewer per 1,000; 45 fewer to 38 more) [Important].

Necrotising enterocolitis (NEC): RCT: No significant effect on NEC with higher parenteral protein (0 fewer per 1,000; 23 fewer to 34 more) [Important].

Retinopathy of prematurity: RCT: Very large reduction in retinopathy of prematurity with higher parenteral protein (81 fewer per 1,000; 114 fewer to 10 fewer). No significant effect on retinopathy of prematurity for early parenteral protein (1 g extra per day for 5 days) versus placebo (0 fewer per 1,000; 59 fewer to 96 more) [Important].

Osborn *et al* also reported on five relevant subgroup analyses [2]. These are summarised below:

1. Higher versus lower parenteral protein intake at commencement of parenteral nutrition (>1 to ≤ 2 g/kg/day; >2 to ≤ 3 g/kg/day; >3 g/kg/day)

Mortality: RCT: No difference in mortality to discharge (RR 0.78, 95% CI 0.45 to 1.36; $n = 433$; studies = 6) and no subgroup differences: $P = 0.79$, $I^2 = 0\%$ [Critical].

Neurodevelopmental impairment: RCT: No difference in neurodevelopmental disability at two years (RR 1.04, 95% CI 0.48 to 2.23; $n = 201$; studies = 2); subgroup difference was significant: $P = 0.02$, $I^2 = 81.2\%$. Neither study reported a significant difference (high intake >2 to ≤ 3 g/kg/day; very high intake >3 g/kg/day). A single study commencing 3.6 g/kg/day versus 2.4 g/kg/day on day 2 to 6 reported no difference in cerebral palsy (RR 5.00, 95% CI 0.61 to 41.11; $n = 90$). No difference in developmental delay at ≥ 18 months (RR 1.04, 95% CI 0.35 to 3.11; $n = 201$; studies = 2); and no subgroup difference; $P = 0.53$, $I^2 = 0\%$. No infants were reported with blindness or deafness [Critical].

No faltering growth/body composition: RCT: Reduction in postnatal faltering growth at discharge (RR 0.74, 95% CI 0.56 to 0.97; n = 203; studies = 3) and no subgroup differences. No difference in days to regain birthweight (MD 0.43, 95% CI -0.51 to 1.37; n = 303; studies = 6) and no subgroup difference; P = 0.06, I² = 64.2%. No difference in weight gain to discharge (MD 1.05, 95% CI -0.55 to 2.66; n = 140; studies = 2) and no subgroup difference; P = 0.34; I² = 0%. A single study commencing 3.6 g/kg/day versus 2.4 g/kg/day on day 2 to 6 reported no difference in head circumference growth to discharge (MD 0.03, 95% CI -0.03 to 0.09; n = 96) and no difference in head circumference change z-score up to one month (MD 0.00, 95% CI -0.36 to 0.36; n = 96). No difference in head circumference change z-score up to discharge (MD 0.18, 95% CI -0.15 to 0.50; n = 207; studies = 2) and no subgroup difference; P = 0.10, I² = 62.7%. No difference in head circumference change z-score up to discharge (MD 0.25, 95% CI -0.14 to 0.64; n = 201; studies = 2) and no subgroup difference; P = 0.16, I² = 50.1%. A single study commencing 3.6 g/kg/day versus 2.4 g/kg/day on day 2 to 6 reported no difference in weight gain change z-score up to one month (MD -0.20, 95% CI -0.62 to 0.22; n = 96). No difference in weight gain change z-score up to discharge (MD 0.01, 95% CI -0.33 to 0.36; n = 207; studies = 2) and no subgroup difference; P = 0.17; I² = 48%. No difference in weight gain change z-score post-discharge (MD 0.13, 95% CI -0.26 to 0.52; n = 201; studies = 2) and no subgroup difference; P = 0.17, I² = 47.1% [Critical].

Time to full enteral feeds: RCT: No difference by commencement intake in days to full enteral feeds (MD -0.22, 95% CI -1.60 to 1.17; n = 196; studies = 4); no subgroup differences: P = 0.88, I² = 0% [Important].

Adverse effects: RCT: A single study of infants receiving very high amino acid intake (> 3 g/kg/day) reported no difference in hyperglycaemia (RR 1.47, 95% CI 0.85 to 2.53; n = 42). A single study reported no difference in hypoglycaemia among infants commencing on high amino acid intake at 3 g/kg/day (RR 1.68, 95% CI 0.83 to 3.41; n = 123) [Important].

Sepsis: RCT: No difference in late-onset sepsis (RR 0.94, 95% CI 0.65 to 1.38; n = 319; studies = 5) and no subgroup difference; P = 0.93, I² = 0% [Important].

Necrotising enterocolitis (NEC): RCT: No difference in NEC (RR 0.96, 95% CI 0.45 to 2.03; n = 340; studies = 5) and no subgroup difference; P = 0.18, I² = 44% [Important].

Bronchopulmonary dysplasia: RCT: No difference in bronchopulmonary dysplasia (RR 1.32, 95% CI 0.86 to 2.02; n = 202; studies = 4) and no subgroup difference; P = 0.90, I² = 0% [Important].

Retinopathy of prematurity: RCT: A reduction in retinopathy of prematurity (RR 0.44, 95% CI 0.21 to 0.93; n = 269; studies = 4) and no subgroup difference; P = 0.76, I² = 0%. Studies commencing with high protein intake (>2 to ≤3 g/kg/day) found a reduction in retinopathy of prematurity (RR 0.36, 95% CI 0.14 to 0.95; n = 198; studies = 2) whereas the study commencing at low protein intake (>1 to ≤2 g/kg/day) and the study commencing at very high parenteral protein intake (3.5 g/kg/day) reported no differences in retinopathy of prematurity [Important].

2. Higher versus lower protein intake at maximal intake of parenteral nutrition sub grouped by maximal intake (high amino acid intake (>3 to ≤4 g/kg/day) versus low protein intake (>2 to ≤3 g/kg/d) at maximal intake of parenteral nutrition

Mortality: RCT: No difference in mortality to discharge (RR 0.94, 95% CI 0.57 to 1.55; n = 292; studies = 2) [Critical].

No faltering growth/body composition: RCT: One trial reported an increase in head circumference growth to one month (MD 0.13 cm/week, 95% CI 0.05 to 0.20; n = 135); an increase in head circumference change z-score to one month (MD 0.37, 95% CI 0.15 to 0.59; n = 135). One trial reported a reduction in days to regain birthweight (MD -3.60 days, 95% CI -5.88 to -1.32; n = 114) [Critical].

Time to full enteral feeds: RCT: One trial reported an increase in days to full enteral feeds (MD 4.00 days, 95% CI 1.01 to 6.99; n = 114) [Important].

Sepsis: RCT: One trial reported no difference in late-onset sepsis (RR 0.94, 95% CI 0.63 to 1.41; n = 127) [Important].

Necrotising enterocolitis (NEC): RCT: No difference in NEC (RR 0.76, 95% CI 0.37 to 1.59; n = 241; studies = 2) [Important].

Bronchopulmonary dysplasia: RCT: No difference in bronchopulmonary dysplasia (RR 1.10, 95% CI 0.92 to 1.31; n = 241; studies = 2) [Important].

Retinopathy of prematurity: RCT: One trial reported no difference in severe retinopathy of prematurity (RR 2.71, 95% CI 0.75 to 9.75; n = 127) [Important].

3. Higher versus lower protein intake at commencement and maximal intake of parenteral nutrition, subgrouped by commencement intake (Very low protein intake (≤ 1 g/kg/day); Low protein intake (>1 to ≤ 2 g/kg/day); High protein intake (>2 to ≤ 3 g/kg/day); Very high protein intake (>3 g/kg/day))

Mortality: RCT: No difference in mortality to discharge (RR 0.97, 95% CI 0.66 to 1.42; n = 567; studies = 5) and no subgroup difference; P = 0.32, I² = 13.8% [Critical].

Neurodevelopmental impairment: RCT: A single study of low amino acid intake (>1 to ≤ 2 g/kg/day) reported no difference in cerebral palsy (RR 3.00, 95% CI 0.35 to 25.87; n = 32), or blindness (RR 2.00, 95% CI 0.20 to 19.91; n = 32). A single study commencing with high parenteral protein intake (2.5 g/kg/d) reported no difference in developmental delay (RR 3.25, 95% CI 0.35 to 30.19; n = 100) [Critical].

No faltering growth/body composition: RCT: A reduction in days to regain birthweight (MD -1.86, 95% CI -2.79 to -0.93; n = 496; studies = 5) and no subgroup difference; P = 0.80, I² = 0%. One study of commencing on high protein intake (>2 to ≤ 3 g/kg/day) reported no difference in weight gain to discharge (MD 0.60 g/kg/d, 95% CI -0.34 to 1.54; n = 114). Two studies commencing on high protein intake (>2 to ≤ 3 g/kg/day) reported an increase in head circumference change to discharge (MD 0.11 cm/week, 95% CI 0.07 to 0.15; n = 182) [Critical].

Time to full enteral feeds: RCT: A reduction in days to full enteral feeds with a significant subgroup effect by commencement intake (MD -1.08, 95% CI -2.42 to 0.25; n = 431; studies = 5). Two studies commencing on high protein intake (>2 to ≤ 3 g/kg/day) reported a reduction in days to full enteral feeds (MD -3.32, 95% CI -5.39 to -1.25; n = 158). Studies commencing with low parenteral protein intake (>1 to ≤ 2 g/kg/day) and very high parenteral protein intake (>3 g/kg/day) reported no difference in days to full enteral feeds [Important].

Adverse effects: RCT: A reduction in hyperglycaemia (RR 0.54, 95% CI 0.36 to 0.82; n = 463; studies = 4) and no subgroup difference; P = 0.55, I² = 0%. No difference in hypoglycaemia (RR 1.03, 95% CI 0.70 to 1.50; n = 253; studies = 2) and no subgroup difference; P = 0.76, I² = 0%.

Sepsis: RCT: No difference in late-onset sepsis (RR 0.96, 95% CI 0.72 to 1.29; n = 772; studies = 8) and no subgroup difference; P = 0.70, I² = 0% [Important].

Necrotising enterocolitis (NEC): RCT: No difference in NEC (RR 1.14, 95% CI 0.63 to 2.07; n = 683; studies = 6) and no subgroup difference; P = 0.43, I² = 0%. [Important]

Bronchopulmonary dysplasia: RCT: No difference in bronchopulmonary dysplasia (RR 0.81, 95% CI 0.55 to 1.19; n = 376; studies = 4) and no subgroup difference; P = 0.13, I² = 58% [Important].

Retinopathy of prematurity: RCT: No difference in severe retinopathy of prematurity in infants commencing on low parenteral protein intake (2 g/kg/day) (RR 1.24, 95% CI 0.49 to 3.09; n = 166; studies = 2). One study of high parenteral protein intake reported no cases of severe retinopathy of prematurity [Important].

4. Higher versus lower parenteral protein intake at commencement and maximal intake of parenteral nutrition subgrouped by maximal intake (Low protein intake (>1 to ≤ 2 g/kg/day); High protein intake (>2 to ≤ 3 g/kg/day); Very high protein intake (>3 g/kg/day))

Mortality: RCT: No difference in mortality to discharge (RR 0.97, 95% CI 0.66 to 1.42; n = 567; studies = 5) and no subgroup difference; P = 0.40, I² = 0% [Critical].

Neurodevelopmental impairment: RCT: One study (n = 32) of high maximal protein intake (4 g/kg/day) reported no difference in cerebral palsy (RR 3.00, 95% CI 0.35 to 25.87) or blindness (RR 2.00, 95% CI 0.20 to 19.91). One study of high maximal protein intake (4 g/kg/day) reported no difference in developmental delay (RR 3.25, 95% CI 0.35 to 30.19; n = 100) [Critical].

No faltering growth/body composition: RCT: A reduction in days to regain birthweight (MD -1.86, 95% CI -2.79 to -0.93; n = 496; studies = 5) and no subgroup difference; P = 0.67, I² = 0%. One study of high protein intake (>3 to ≤ 4 g/kg/day) reported no difference in weight gain to discharge (MD 0.60 g/kg/day, 95% CI -0.34 to 1.54; n = 114). Two studies of high maximal protein intake (>3 to ≤ 4 g/kg/day) reported an increase in head circumference growth to discharge (MD 0.11, 95% CI 0.07 to 0.15; n = 182) [Critical].

Time to full enteral feeds: RCT: Five studies of high maximal protein intake (>3 to ≤ 4 g/kg/day) reported a reduction in days to full

enteral feeds (MD -1.08, 95% CI -2.42 to 0.25; n = 431) [Important]. Adverse effects: RCT: A reduction in hyperglycaemia (RR 0.54, 95% CI 0.36 to 0.82; n = 463; studies = 4) and no subgroup difference; P = 0.28, I² = 15.8%. No difference in hypoglycaemia (RR 1.03, 95% CI 0.70 to 1.50; n = 253; studies = 2) and no subgroup difference; P = 0.76, I² = 0% [Important]. Sepsis: RCT: No difference in late-onset sepsis (RR 0.96, 95% CI 0.72 to 1.29; n = 772; studies = 8) and no subgroup difference; P = 0.55, I² = 0% [Important]. Necrotising enterocolitis (NEC): RCT: Six studies of high maximal protein intake (>3 to ≤4 g/kg/day) reported no difference in NEC (RR 1.14, 95% CI 0.63 to 2.07; n = 683) [Important]. Bronchopulmonary dysplasia: RCT: Four studies of high maximal protein intake (>3 to ≤4 g/kg/day) reported no difference in bronchopulmonary dysplasia (RR 0.81, 95% CI 0.55 to 1.19; n = 376) [Important]. Retinopathy of prematurity: RCT: Three studies of high maximal amino acid intake (>3 to ≤4 g/kg/day) reported no difference in severe retinopathy of prematurity (RR 1.24, 95% CI 0.49 to 3.09; n = 280) [Important]. 5. Higher versus lower parenteral protein intake in parenteral nutrition, very preterm or low birthweight infants (Studies that enrolled infants ≤1500 g and/or at ≤32 weeks' gestation). Mortality: RCT: No difference in mortality (RR 0.90, 95% CI 0.69 to 1.17; n = 1407; studies = 14). Neurodevelopmental impairment: RCT: No difference in neurodevelopmental disability at two years (RR 1.04, 95% CI 0.48 to 2.23; n = 201; studies = 2). No difference in cerebral palsy (RR 4.00, 95% CI 0.89 to 17.97; n = 122; studies = 2) or in developmental delay (RR 1.35, 95% CI 0.52 to 3.53; n = 301; studies = 3) or in blindness (RR 2.00, 95% CI 0.20 to 19.91; n = 122; studies = 2). One study reported no difference in infants with deafness in either group. No faltering growth/body composition: RCT: A reduction in postnatal faltering growth at discharge (RR 0.74, 95% CI 0.56 to 0.97; n = 203; studies = 3). One study reported no difference in faltering at two years (RR 0.66, 95% CI 0.33 to 1.32; n = 111). A significant reduction in days to regain birthweight (MD -0.78, 95% CI -1.46 to -0.11; n = 800; studies = 10). A reduction in weight gain to one month (MD -1.50, 95% CI -2.56 to -0.44; n = 373; studies = 4) and no difference in weight gain to discharge (MD 0.72, 95% CI -0.09 to 1.52; n = 254; studies = 3). A reduction in linear growth to one month (MD -0.16, 95% CI -0.26 to -0.06; n = 245; studies = 2). No difference in head circumference growth to one month (MD 0.01, 95% CI -0.04 to 0.06; n = 476; studies = 4) and an increase in head circumference growth to discharge (MD 0.08, 95% CI 0.05 to 0.12; n = 182; studies = 2). One study reported no difference in weight change in z-score to one month (MD -0.20, 95% CI -0.62 to 0.22; n = 96). No difference in weight change in z-score to discharge (MD 0.01, 95% CI -0.33 to 0.36; n = 207; studies = 2) and no difference in weight change in z-score post-discharge (MD 0.13, 95% CI -0.26 to 0.52; n = 201; studies = 2). An increase in head circumference change in z-score to one month (MD 0.27, 95% CI 0.08 to 0.46; n = 231; studies = 2). No difference in head circumference change in z-score to discharge (MD 0.18, 95% CI -0.15 to 0.50; n = 207; studies = 2) and no difference in head circumference change in z-score post-discharge (MD 0.25, 95% CI -0.14 to 0.64; n = 201; studies = 2). Time to full enteral feeds: RCT: No difference in days to full enteral feeds (MD -0.19, 95% CI -1.07 to 0.70; n = 778; studies = 11). Adverse effects: RCT: A reduction in hyperglycaemia (RR 0.66, 95% CI 0.45 to 0.96; n = 409; studies = 4). No difference in hypoglycaemia (RR 1.17, 95% CI 0.84 to 1.63; n = 376; studies = 3). Sepsis: RCT: No difference in late-onset sepsis (RR 0.96, 95% CI 0.79 to 1.18; n = 1255; studies = 15). Necrotising enterocolitis (NEC): RCT: No difference in NEC (typical RR 1.00, 95% CI 0.68 to 1.47; n = 1301; studies = 14). Bronchopulmonary dysplasia: RCT: No difference in bronchopulmonary dysplasia (RR 1.04, 95% CI 0.89 to 1.23; n = 819; studies = 10). Retinopathy of prematurity: RCT: A reduction in retinopathy of prematurity (RR 0.44, 95% CI 0.21 to 0.93; n = 269; studies = 4).					
Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with lower parenteral protein	Risk difference with higher parenteral protein

Mortality: RCT: higher versus lower protein intake assessed with: Mortality to hospital discharge	1407 (13 RCTs)	 Very low ^{a,b,c}	RR 0.90 (0.69 to 1.17)	Study population	
				131 per 1,000	13 fewer per 1,000 (41 fewer to 22 more)
Mortality: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Death	434 (1 RCT)	 Moderate ^b	Adj RR 0.93 (0.64 to 1.34)	Study population	
				194 per 1,000	14 fewer per 1,000 (70 fewer to 66 more)
Neurodevelopmental impairment: RCT: higher versus lower parenteral protein intake assessed with: neurodevelopmental disability	201 (2 RCTs)	 Very low ^{a,b,d}	RR 1.04 (0.48 to 2.23)	Study population	
				118 per 1,000	5 more per 1,000 (61 fewer to 145 more)
Neurodevelopmental impairment: RCT: higher versus lower parenteral protein intake assessed with: Developmental delay at ≥ 18 months	301 (3 RCTs)	 Very low ^{a,e}	RR 1.35 (0.52 to 3.53)	Study population	
				45 per 1,000	16 more per 1,000 (22 fewer to 115 more)
Neurodevelopmental impairment: RCT: higher versus lower parenteral protein intake assessed with: Cerebral palsy	122 (2 RCTs)	 Very low ^{a,f}	RR 4.00 (0.89 to 17.97)	Study population	
				33 per 1,000	98 more per 1,000 (4 fewer to 556 more)
Neurodevelopmental impairment: RCT: higher versus lower parenteral protein intake assessed with: Blindness	122 (2 RCTs)	 Very low ^{f,g,h}	RR 2.00 (0.20 to 19.91)	Study population	
				16 per 1,000	16 more per 1,000 (13 fewer to 310 more)
Neurodevelopmental impairment: RCT: higher versus lower parenteral protein intake assessed with: Deafness	90 (1 RCT)	 Very low ^{h,i,j}	not estimable	Study population	
				0 per 1,000	0 fewer per 1,000 (0 fewer to 0 fewer)
Neurodevelopmental impairment: RCT: higher versus lower parenteral protein intake assessed with: Bayley III motor development at ≥ 18 months	105 (2 RCTs)	 Very low ^{a,e}	-	The mean neurodevelopmental impairment: RCT: higher versus lower amino acid intake: Bayley III Motor Development score was 79.8 points	MD 4.18 lower (8.53 lower to 0.17 higher)
Neurodevelopmental impairment: RCT: higher versus lower parenteral protein intake assessed with: Bayley score at ≥ 18 months	100 (1 RCT)	 Very low ^{e,i,j}	-	The mean neurodevelopmental impairment: RCT: higher versus lower amino acid intake: Bayley score was 94 points	MD 3 higher (2.52 lower to 8.52 higher)
Neurodevelopmental impairment: RCT: higher versus lower parenteral protein intake assessed with: Bayley II psychomotor score at ≥ 18 months	32 (1 RCT)	 Very low ^{f,i,j}	-	The mean neurodevelopmental impairment: RCT: higher versus lower amino acid intake: Bayley II Psychomotor score was 64 points	MD 3 higher (6.41 lower to 12.41 higher)
Neurodevelopmental impairment: RCT: higher versus lower parenteral protein intake assessed with: Autism	32 (1 RCT)	 Very low ^{f,i,j}	RR 1.00 (0.07 to 14.64)	Study population	
				63 per 1,000	0 fewer per 1,000 (58 fewer to 853 more)
Neurodevelopmental impairment: RCT: early parenteral	408		Adj RR 0.95	Study population	

protein intake (1 g extra per day for 5 days) versus placebo assessed with: Survival without neurodisability	(1 RCT)	⊕⊕⊕⊕○ Moderate ^b	(0.79 to 1.14)	498 per 1,000	25 fewer per 1,000 (104 fewer to 70 more)
Neurodevelopmental impairment: RCT: early parenteral protein intake (1 g extra per day for 5 days) versus placebo assessed with: Neurodisability	327 (1 RCT)	⊕⊕⊕⊕○ Moderate ^b	Adj RR 1.16 (0.90 to 1.50)	Study population 374 per 1,000	60 more per 1,000 (37 fewer to 187 more)
Neurodevelopmental impairment: RCT: protein assessed with: Blindness	324 (1 RCT)	⊕⊕⊕⊕○ Moderate ^h	not estimable	Study population 6 per 1,000	6 fewer per 1,000 (6 fewer to 6 fewer)
Neurodevelopmental impairment: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Deafness	324 (1 RCT)	⊕⊕⊕⊕○ Moderate ^h	not estimable	Study population 12 per 1,000	12 fewer per 1,000 (12 fewer to 12 fewer)
Neurodevelopmental impairment: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Cerebral palsy	324 (1 RCT)	⊕⊕⊕⊕○ Moderate ^b	Adj RR 1.47 (0.64 to 3.39)	Study population 55 per 1,000	26 more per 1,000 (20 fewer to 132 more)
Neurodevelopmental impairment: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Bayley III Cognitive score at 2 years	321 (1 RCT)	⊕○○○ Very low ^{b,k,h}	-	The mean neurodevelopmental impairment: RCT: early amino acid (1 g per day for 5 days) versus placebo: Bayley III cognitive score was 96 points	Adj MD 2.13 lower (5.29 lower to 1.02 higher)
Neurodevelopmental impairment: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Bayley III Motor score at 2 years	321 (1 RCT)	⊕○○○ Very low ^{eb,h,k}	-	The mean neurodevelopmental impairment: RCT: early amino acid (1 g per day for 5 days) versus placebo: Bayley III Motor score was 96 points	Adj MD 1.88 lower (4.9 lower to 1.14 higher)
Neurodevelopmental impairment: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Bayley III Language score at 2 years	321 (1 RCT)	⊕⊕○○ Low ^{h,k}	-	The mean neurodevelopmental impairment: RCT: early amino acid (1 g per day for 5 days) versus placebo: Bayley III Language score was 93 points	Adj MD 3.86 lower (7.43 lower to 0.29 lower)
Faltering growth/body composition: RCT: higher versus lower parenteral protein intake assessed with: Weight <10th centile	203 (3 RCTs)	⊕⊕⊕⊕○ Moderate ^a	RR 0.74 (0.56 to 0.97)	Study population 554 per 1,000	144 fewer per 1,000 (244 fewer to 17 fewer)
Faltering growth/body composition: RCT: higher versus lower parenteral protein intake assessed with: Postnatal faltering growth at discharge (weight 2 SD below mean)	114 (1 RCT)	⊕⊕⊕⊕○ Moderate ^b	RR 0.96 (0.66 to 1.40)	Study population 500 per 1,000	20 fewer per 1,000 (170 fewer to 200 more)
Faltering growth/body composition: RCT: higher versus lower parenteral protein assessed with: Postnatal faltering growth post-discharge.	111 (1 RCT)	⊕⊕○○ Low ^{a,b}	RR 0.66 (0.33 to 1.32)	Study population 281 per 1,000	95 fewer per 1,000 (188 fewer to 90 more)
Faltering growth/body composition: RCT: higher versus lower parenteral protein intake assessed with: Days to regain birthweight	950 (13 RCTs)	⊕⊕○○ Low ^{a,i}	-	The mean faltering growth/body composition: RCT: higher versus lower amino acid intake was 12.49 days	MD 1.14 lower (1.73 lower to 0.56 lower)

Faltering growth/body composition: RCT: higher versus lower parenteral protein intake assessed with: Weight gain to discharge (g/kg/day)	291 (4 RCTs)	⊕⊕⊕⊕ Moderate ^a	-	The mean faltering growth/body composition: RCT: higher versus lower amino acid intake was 19.33 days	MD 0.76 higher (0.02 lower to 1.54 higher)
Faltering growth/body composition: RCT: higher versus lower parenteral protein intake assessed with: Weight change z score at discharge	207 (2 RCTs)	⊕⊕○○ Low ^{a,b}	-	The mean faltering growth/body composition: RCT: higher versus lower amino acid intake was -0.3 points	MD 0.01 higher (0.33 lower to 0.36 higher)
Faltering growth/body composition: RCT: higher versus lower parenteral protein intake assessed with: Weight z score at discharge	352 (3 RCTs)	⊕⊕⊕○ Moderate ^a	-	The mean faltering growth/body composition: RCT: higher versus lower amino acid intake was -1.67 points	MD 0.16 higher (0.02 lower to 0.33 higher)
Faltering growth/body composition: RCT: higher versus lower parenteral protein intake assessed with: Linear growth cm/week	245 (2 RCTs)	⊕⊕○○ Low ^d	-	The mean faltering growth/body composition: RCT: higher versus lower amino acid intake was 0.7 cm/week	MD 0.16 lower (0.26 lower to 0.06 lower)
Faltering growth/body composition: RCT: higher versus lower parenteral protein intake assessed with: Head circumference to discharge (cm/week)	315 (4 RCTs)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT: higher versus lower amino acid intake was 0.8 cm/week	MD 0.09 higher (0.06 higher to 0.13 higher)
Faltering growth/body composition: RCT: higher versus lower parenteral protein intake assessed with: Head circumference change z score to discharge	207 (2 RCTs)	⊕○○○ Very low ^{a,b,j}	-	The mean faltering growth/body composition: RCT: higher versus lower amino acid intake was 0.2 points	MD 0.18 higher (0.15 lower to 0.5 higher)
Faltering growth/body composition: RCT: higher versus lower parenteral protein intake assessed with: Head circumference z score at discharge	354 (3 RCTs)	⊕○○○ Very low ^{a,b,j}	-	The mean faltering growth/body composition: RCT: higher versus lower amino acid intake was -1.2 points	MD 0.04 higher (0.18 lower to 0.26 higher)
Faltering growth/body composition: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Weight z score at discharge	434 (1 RCT)	⊕⊕⊕○ Moderate ^b	-	The mean faltering growth/body composition: RCT: early amino acid (1 g per day for 5 days) versus placebo was 0	Adj MD 0.09 higher (0.08 lower to 0.26 higher)
Faltering growth/body composition: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Weight z score at 2 years	434 (1 RCT)	⊕⊕⊕○ Moderate ^b	-	The mean faltering growth/body composition: RCT: early amino acid (1 g per day for 5 days) versus placebo was -0.05 points	Adj MD 0.19 lower (0.41 lower to 0.02 higher)
Faltering growth/body composition: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Length z score at discharge	434 (1 RCT)	⊕⊕⊕○ Moderate ^b	-	The mean faltering growth/body composition: RCT: early amino acid (1 g per day for 5 days) versus placebo was 0	Adj MD 0.07 higher (0.13 lower to 0.26 higher)
Faltering growth/body composition: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Length z score at 2 years	434 (1 RCT)	⊕⊕⊕○ Moderate ^b	-	The mean faltering growth/body composition: RCT: early amino acid (1 g per day for 5 days) versus placebo was -0.41 points	Adj MD 0.16 lower (0.4 lower to 0.08 higher)
Faltering growth/body composition: RCT: higher versus lower parenteral protein intake assessed with: Length z score at discharge	228 (2 RCTs)	⊕⊕○○ Low ^{a,b}	-	The mean faltering growth/body composition: RCT: higher versus lower amino acid intake was -2.25 points	MD 0.12 higher (0.14 lower to 0.38 higher)

Faltering growth/body composition: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Head circumference z score at discharge	434 (1 RCT)	⊕⊕⊕⊕ Moderate ^b	-	The mean faltering growth/body composition: RCT: early amino acid (1 g per day for 5 days) versus placebo was -0.55 points	Adj MD 0.02 higher (0.16 lower to 0.2 higher)
Faltering growth/body composition: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Head circumference z score at 2 years	434 (1 RCT)	⊕⊕⊕⊕ Moderate ^b	-	The mean faltering growth/body composition: RCT: early amino acid (1 g per day for 5 days) versus placebo was 0.13 points	Adj MD 0.26 lower (0.53 lower to 0.002 higher)
Adverse effects: RCT: higher versus lower parenteral protein intake assessed with: Hypoglycaemia	376 (3 RCTs)	⊕⊕⊕⊕ Low ^{a,b}	RR 1.17 (0.84 to 1.63)	Study population	
				238 per 1,000	40 more per 1,000 (38 fewer to 150 more)
Adverse effects: RCT: higher versus lower parenteral protein intake assessed with: Hyperglycaemia (plasma glucose > 8.3 mmol/L)	505 (5 RCTs)	⊕⊕⊕⊕ Low ^{a,i}	RR 0.69 (0.49 to 0.96)	Study population	
				253 per 1,000	78 fewer per 1,000 (129 fewer to 10 fewer)
Adverse effects: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Refeeding syndrome	338 (1 RCT)	⊕⊕⊕⊕ Low ^{i,g}	Adj RR 1.64 (1.09 to 2.45)	Study population	
				157 per 1,000	100 more per 1,000 (14 more to 227 more)
Fully breastfed or breastmilk feeding at hospital discharge: RCT: early protein (1 g extra per day for 5 days) versus placebo assessed with: Exclusively breastfed or breastmilk fed	408 (1 RCT)	⊕⊕⊕⊕ Very low ^{a,h}	not estimable	Study population	
				396 per 1,000	396 fewer per 1,000 (396 fewer to 396 fewer)
Time to full enteral feeds: RCT: higher versus lower parenteral protein intake assessed with: Days to full enteral feeds	778 (11 RCTs)	⊕⊕⊕⊕ Low ^{a,b}	-	The mean time to full enteral feeds: RCT: higher versus lower amino acid intake was 16.75 days	MD 0.19 lower (1.07 lower to 0.7 higher)
Time to full enteral feeds: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Days after birth full enteral feed was reached	377 (1 RCT)	⊕⊕⊕⊕ Moderate ^b	-	The mean time to full enteral feeds: RCT: early amino acid (1 g per day for 5 days) versus placebo was 16.6 days	Adj HR 0.86 higher (0.69 higher to 1.06 higher)
Duration of initial hospital stay - not measured	-	-	-	-	-
Sepsis: proven or suspected: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Culture proven late onset	422 (1 RCT)	⊕⊕⊕⊕ Moderate ^b	Adj RR 1.19 (0.91 to 1.56)	Study population	
				308 per 1,000	58 more per 1,000 (28 fewer to 172 more)
Sepsis: proven or suspected: RCT: higher versus lower parenteral protein intake assessed with: Late onset sepsis	1255 (15 RCTs)	⊕⊕⊕⊕ Low ^{a,b}	RR 0.96 (0.79 to 1.18)	Study population	
				213 per 1,000	9 fewer per 1,000 (45 fewer to 38 more)
Bronchopulmonary dysplasia: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo	363 (1 RCT)	⊕⊕⊕⊕ Moderate ^b	Adj RR 1.10 (0.96 to 1.24)	Study population	
				696 per 1,000	70 more per 1,000 (28 fewer to 167 more)

Bronchopulmonary dysplasia: RCT: higher versus lower parenteral protein intake assessed with: Bronchopulmonary dysplasia at ≥ 36 weeks' PMA	819 (10 RCTs)	 Low ^{a,b}	RR 1.04 (0.89 to 1.23)	Study population	
				353 per 1,000	14 more per 1,000 (39 fewer to 81 more)
Necrotising enterocolitis: RCT: higher versus lower parenteral protein intake	1301 (13 RCTs)	 Low ^{a,b}	RR 1.00 (0.68 to 1.47)	Study population	
				73 per 1,000	0 fewer per 1,000 (23 fewer to 34 more)
Necrotising enterocolitis: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo assessed with: Bell stage ≥ II	423 (1 RCT)	 Moderate ^b	Adj RR 1.06 (0.65 to 1.74)	Study population	
				124 per 1,000	7 more per 1,000 (44 fewer to 92 more)
Retinopathy of prematurity: RCT: higher versus lower parenteral protein intake	269 (4 RCTs)	 Moderate ^a	RR 0.44 (0.21 to 0.93)	Study population	
				144 per 1,000	81 fewer per 1,000 (114 fewer to 10 fewer)
Retinopathy of prematurity: RCT: early parenteral protein (1 g extra per day for 5 days) versus placebo	376 (1 RCT)	 Moderate ^b	Adj RR 1.00 (0.63 to 1.60)	Study population	
				160 per 1,000	0 fewer per 1,000 (59 fewer to 96 more)
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-

- a. Downgraded one level for concerns of risk of bias
- b. Downgraded one level for imprecision as confidence intervals cross the line of no effect
- c. Downgraded one level as funnel plot suggested publication/reporting bias
- d. Downgraded two levels for inconsistency with I²>80%
- e. Downgraded two levels for imprecision with very wide confidence intervals crossing the line of no effect
- f. Downgraded three levels for imprecision with extremely wide confidence intervals crossing the line of no effect
- g. Downgraded for imprecision due to low event rates
- h. Downgraded one level for indirectness as evidence is based on a single study
- i. Downgraded one level for imprecision due to wide confidence intervals
- j. Downgraded one level for inconsistency with I² >50% but <80%
- k. Downgraded one level for imprecision as a result of low sample size

Desirable effects for Māori

In the Aotearoa New Zealand randomised trial, the ProVIDe trial (5), 102 of the 434 enrolled preterm infants (24%) were pēpi Māori. The study investigated whether an additional 1 gram of parenteral amino acids daily for 5 days improved neurodevelopmental outcomes in extremely low birthweight infants. Pēpi Māori were well represented in both the intervention and placebo groups. The trial found no overall benefit in survival without neurodisability at 2 years and suggested a possible increase in moderate-to-severe neurodisability in the intervention group.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Higher versus lower parenteral protein Neurodevelopmental impairment: RCT: Higher dose of parenteral protein showed no significant effect on neurodevelopmental disability (5 more per 1,000; 61 fewer to 145 more); on developmental delay at ≥18 months (16 more per 1,000; 22 fewer to 115 more); cerebral palsy (98 more per 1,000; 4 fewer to 556 more); blindness (16 more per 1,000; 13 fewer to 310 more); Bayley III Motor development score at ≥18 months (MD 4.18 points lower; 8.53 lower to 0.17 higher); Bayley III Cognitive score at 2 years (Adj MD 2.13 lower; 5.29 lower to 1.02 higher), the Bayley III Motor score at 2 years (Adj MD 1.88 lower; 4.9 lower to 1.14 higher). There was a reduction in Bayley III Language score at 2 years (Adj MD 3.86 lower; 7.43 lower to 0.29 lower). No significant increase in neurodisability (60 more per 1,000; 37 fewer to 187 more); or in cerebral palsy (26 more per 1,000; 20 fewer to 132 more) [Critical]. Faltering growth/body composition: RCT: Small reduction in linear growth with higher dose of parenteral nutrition (MD 0.16 cm/week lower; 0.26 lower to 0.06 lower). No significant effect on weight z score at 2 years (Adj MD 0.19 points lower; 0.41 lower to 0.02 higher); length z score at 2 years (Adj MD 0.16 points lower; 0.4 lower to 0.08 higher) or head circumference z score at 2 years (Adj MD 0.26 points lower; 0.53 lower to 0.002 higher) [Critical]. Adverse effects: RCT: No significant increase in hypoglycaemia with higher parenteral protein (40 more per 1,000; 38 fewer to 150 more). Very large increase in refeeding syndrome (100 more per 1,000; 14 more to 227 more) [Important]. Time to full enteral feeds: RCT: Small increase in time to full enteral feeds with higher parenteral protein (Adj HR 0.86 days higher; 0.69 higher to 1.06 higher) [Important]. Sepsis: RCT: No significant increase in culture proven late onset sepsis with higher parenteral nutrition (58 more per 1,000; 28 fewer to 172 more). [Important] Bronchopulmonary dysplasia: RCT: No significant increase in bronchopulmonary dysplasia (70 more per 1,000; 28 fewer to 167 more) or bronchopulmonary dysplasia (14 more per 1,000; 39 fewer to 81 more) with higher parenteral protein [Important]. Necrotising enterocolitis (NEC): RCT: No significant effect on NEC with higher parenteral protein (7 more per 1,000; 44 fewer to 92 more) [Important]. Undesirable effects for Māori No additional evidence available	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Moderate to very low certainty of evidence overall	

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT: higher versus lower amino acid intake assessed with: Mortality to hospital discharge	CRITICAL	⊕○○○ Very low

Mortality: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Death	CRITICAL	⊕⊕⊕⊕ Moderate
Neurodevelopmental impairment: RCT: higher versus lower amino acid intake assessed with: neurodevelopmental disability	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: higher versus lower amino acid intake assessed with: Developmental delay at ≥ 18 months	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: higher versus lower amino acid intake assessed with: Cerebral palsy	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: higher versus lower amino acid intake assessed with: Blindness	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: higher versus lower amino acid intake assessed with: Deafness	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: higher versus lower amino acid intake assessed with: Bayley motor development at ≥ 18 months	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: higher versus lower amino acid intake assessed with: Bayley III score at ≥ 18 months	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: higher versus lower amino acid intake assessed with: Bayley psychomotor score at ≥ 18 months	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: higher versus lower amino acid intake assessed with: Autism	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Survival without neurodisability	CRITICAL	⊕⊕⊕⊕ Moderate
Neurodevelopmental impairment: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Neurodisability	CRITICAL	⊕⊕⊕⊕ Moderate
Neurodevelopmental impairment: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Blindness	CRITICAL	⊕⊕⊕⊕ Moderate
Neurodevelopmental impairment: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Deafness	CRITICAL	⊕⊕⊕⊕ Moderate
Neurodevelopmental impairment: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Cerebral palsy	CRITICAL	⊕⊕⊕⊕ Moderate
Neurodevelopmental impairment: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Bayley III Cognitive score at 2 years	CRITICAL	⊕⊕⊕⊕ Moderate
Neurodevelopmental impairment: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Bayley III Motor score at 2 years	CRITICAL	⊕⊕⊕⊕

		Moderate
Neurodevelopmental impairment: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Bayley III Language score at 2 years	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT: higher versus lower amino acid intake assessed with: Weight < 10th centile	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT: higher versus lower amino acid intake assessed with: Postnatal growth failure at discharge (weight 2 SD below mean)	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT: higher versus lower amino acid intake assessed with: Postnatal growth failure post discharge.	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT: higher versus lower amino acid intake assessed with: Days to regain birthweight	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT: higher versus lower amino acid intake assessed with: Weight gain to discharge (g/kg/day)	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT: higher versus lower amino acid intake assessed with: Weight change z score at discharge	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT: higher versus lower amino acid intake assessed with: Weight z score at discharge	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT: higher versus lower amino acid intake assessed with: Linear growth cm/week	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT: higher versus lower amino acid intake assessed with: Head circumference to discharge (cm/week)	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT: higher versus lower amino acid intake assessed with: Head circumference change z score to discharge	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT: higher versus lower amino acid intake assessed with: Head circumference z score at discharge	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Weight z score at discharge	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Weight z score at 2 years	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Length z score at discharge	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Length z score at 2 years	CRITICAL	⊕⊕⊕○ Moderate

Faltering growth/body composition: RCT: higher versus lower amino acid intake assessed with: Length z score at discharge	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Head circumference z score at discharge	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Head circumference z score at 2 years	CRITICAL	⊕⊕⊕○ Moderate
Adverse effects: RCT: higher versus lower amino acid intake assessed with: Hypoglycaemia	IMPORTANT	⊕⊕○○ Low
Adverse effects: RCT: higher versus lower amino acid intake assessed with: Hyperglycaemia (plasma glucose > 8.3 mmol/L)	IMPORTANT	⊕⊕○○ Low ^{a,l}
Adverse effects: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Refeeding syndrome	IMPORTANT	⊕⊕○○ Low
Fully breastfed or breastmilk feeding at hospital discharge: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Exclusively breastfed or breastmilk fed	IMPORTANT	⊕○○○ Very low
Time to full enteral feeds: RCT: higher versus lower amino acid intake assessed with: Days to full enteral feeds	IMPORTANT	⊕⊕○○ Low
Time to full enteral feeds: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Days after birth full enteral feed was reached	IMPORTANT	⊕⊕⊕○ Moderate
Duration of initial hospital stay - not measured	IMPORTANT	-
Sepsis: proven or suspected: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Culture proven late onset	IMPORTANT	⊕⊕⊕○ Moderate
Sepsis: proven or suspected: RCT: higher versus lower amino acid intake assessed with: Late onset sepsis	IMPORTANT	⊕⊕○○ Low
Bronchopulmonary dysplasia RCT: early amino acid (1 g per day for 5 days) versus placebo	IMPORTANT	⊕⊕⊕○ Moderate
Bronchopulmonary dysplasia: RCT: higher versus lower amino acid intake assessed with: Bronchopulmonary dysplasia at ≥ 36 weeks' PMA	IMPORTANT	⊕⊕○○ Low
Necrotizing enterocolitis: RCT: higher versus lower amino acid intake	IMPORTANT	⊕⊕○○ Low
Necrotising enterocolitis: RCT: early amino acid (1 g per day for 5 days) versus placebo assessed with: Bell stage ≥II	IMPORTANT	⊕⊕⊕○ Moderate
Retinopathy of prematurity: RCT: higher versus lower amino acid intake	IMPORTANT	⊕⊕⊕○ Moderate

Retinopathy of prematurity: RCT: early amino acid (1 g per day for 5 days) versus placebo	IMPORTANT	⊕⊕⊕○ Moderate
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-

Certainty of evidence for Māori

No additional evidence available

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	Probably no important uncertainty or variability Values for Māori No additional research available.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ● Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Higher versus lower parenteral protein - moderate certainty evidence Reduction in faltering growth/body composition (weight <10th centile), retinopathy of prematurity Uncertain effect on mortality, neurodevelopmental impairment, faltering growth/body composition, sepsis, NEC, bronchopulmonary dysplasia, retinopathy of prematurity Increase in neurodevelopmental impairment (Lower Bayley III Language score at 2 years), increase in time to full enteral feeds, Higher versus lower parenteral protein - low certainty evidence Reduced days to regain birthweight, reduced hyperglycaemia Reduction in linear growth Increase in adverse effects (refeeding syndrome) Uncertain effect on faltering growth/body composition, adverse effects (hypoglycaemia), time to full enteral feeds, sepsis, bronchopulmonary dysplasia, NEC Higher versus lower parenteral protein - very low certainty evidence	

	Reduction in faltering growth/body composition (Increase in head circumference) Uncertain effect on mortality, neurodevelopmental impairment, faltering growth/body composition, fully breastfed or breastmilk feeding at hospital discharge Balance of effects for Māori No additional evidence
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Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Costs for PN: Additional protein (amino acids) added to a standard parenteral nutrition solution has a minimal effect on the total cost of the solution. Resourcing for Māori No additional evidence available	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ● High ○ No included studies	The certainty of resource requirements is high. Certainty of evidence of required resources for Māori No additional evidence available	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention	None of the evidence reported on cost-effectiveness of different intravenous protein intakes. Cost effectiveness for Māori No additional evidence available	

○ Varies ● No included studies		
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Influenced by the effects of colonisation, pēpi Māori are more likely to be born preterm, have more sepsis and neurodisability, both of which are associated with parenteral nutrition practices, and fewer survive. Thus, implementing standardised parenteral nutrition practices in Aotearoa New Zealand will contribute to achieving equitable health outcomes for preterm pēpi Māori and their whānau. Equity for Pacific families Implementing standardised parenteral nutrition practices in Aotearoa New Zealand will contribute directly to reducing health disparities for all ethnicities and underrepresented groups. Equity for underrepresented groups Understanding the importance of parenteral protein may be difficult for parents with language or health literacy barriers. If explanations are lacking, these families may disengage or feel mistrust. Equity requires culturally appropriate communication and consistent clinical practice to ensure all infants receive adequate protein regardless of background.	
Acceptability Is the intervention acceptable to key interest-holders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	The intervention is probably acceptable. Acceptability for Māori is unknown	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes	A specified parenteral protein intake would not be difficult to implement if there were clear guidance and protocols available.	

- Varies
- Don't know

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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References

1. Meiliana, M.; Alexander, T.; Bloomfield, F.H.; Cormack, B.E.; Harding, J.E.; Walsh, O.; Lin, L. Nutrition guidelines for preterm infants: A systematic review. *JPEN J. Parenter. Enteral Nutr.* **2024**, *48*, 11-26, doi:10.1002/jpen.2568.

2. Osborn, D.A.; Schindler, T.; Jones, L.J.; Sinn, J.K.; Bolisetty, S. Higher versus lower amino acid intake in parenteral nutrition for newborn infants. *Cochrane Database Syst. Rev.* **2018**, *3*, CD005949, doi:10.1002/14651858.CD005949.pub2.

3. Bloomfield, F.H.; Jiang, Y.; Harding, J.E.; Crowther, C.A.; Cormack, B.E.; ProVIDe Trial Group. Early amino acids in extremely preterm infants and neurodisability at 2 years. *N Engl J Med* **2022**, *387*, 1661-1672, doi:10.1056/NEJMoa2204886.

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EtD 15. What is the recommended vitamin intake by postnatal age? Fat-soluble vitamins (vitamin A, E, D, K), Water soluble vitamins (B vitamins, vitamin C, choline)?

POPULATION:	Preterm infants
INTERVENTION:	Higher vitamin intake
COMPARISON:	No/lower vitamin intake
MAIN OUTCOMES:	Critical outcomes Mortality Neurodevelopmental impairment Important but not critical Adverse effects (prevention of unnecessary blood tests) Faltering growth/body composition Retinopathy of prematurity Bronchopulmonary dysplasia Fully breastfed or breastmilk feeding at hospital discharge Time to full enteral feeds Duration of initial hospital stay Sepsis: proven or suspected Necrotising enterocolitis Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation - population perspective
BACKGROUND:	Preterm infants face numerous challenges because they are born with immature metabolic, immune, and organ systems, and often have little to no subcutaneous fat, glycogen, minerals, or vitamin stores. These infants are at heightened risk of malnutrition and suboptimal neurodevelopmental and health outcomes later in life. Adequate nutrition, including essential vitamins, is critical in the neonatal period to support growth, immune function, metabolic processes, and brain maturation. Vitamins are essential micronutrients that cannot be synthesised by the human body in sufficient quantities. They serve diverse roles, such as acting as cofactors in enzymatic reactions, regulating gene expression, and supporting energy metabolism and immune responses. Vitamin deficiencies in preterm infants can result in severe or fatal consequences. However, determining the optimal PN vitamin requirements for preterm infants remains a significant challenge. Current recommendations for both fat-soluble and water-soluble vitamins in preterm infants are based on estimations rather than robust evidence. Some guidelines provide very wide intake ranges for specific vitamins, reflecting

CONFLICT OF INTERESTS:	the lack of conclusive research. These disparities in guidelines may lead to either under- or over-supplementation, potentially impacting health outcomes. Until more high-quality evidence is available, vitamin supplementation practices will continue to rely on estimations and clinical judgment, emphasising the need for close monitoring to ensure that vitamin intake meets but does not exceed requirements.
	The following vitamin systematic review (Bronnert <i>et al</i>) co-authors are on the Guideline Development Group: Barbara Cormack, Frank Bloomfield and Luling Lin and on the Guideline Development Group: Barbara Cormack, Luling Lin and Frank Bloomfield and supervised the first author. The following systematic review on Guidelines (Meiliana M, <i>et al</i>) co-authors are on the Guideline Development Group: Barbara Cormack, Tanith Alexander, Luling Lin and Frank Bloomfield and supervised the first author.

Assessment

Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence from a systematic review (Bronnert <i>et al</i>) [1] and a systematic review (Meiliana <i>et al</i>) which summarised guideline recommendations [2]. ESPGHAN recommendations for vitamins [3,4]: Vitamin A ESPGHAN (enteral) 2022 All preterm: 1,333-3,333 IU.Kg-1.day-1 (Strong) ESPGHAN (parenteral) 2018 All preterm: 700-1,500 IU.Kg-1.day-1 (Weak) Vitamin E ESPGHAN (enteral) 2022 All preterm: 2.2-11 IU.Kg-1.day-1 (Strong) ESPGHAN (parenteral) 2018 All preterm: 2.8-3.5 IU.Kg-1.day-1, ≤11 mg/day (Strong) Vitamin D ESPGHAN (enteral) 2022 All preterm: 400-700 IU.day-1 (Strong) ESPGHAN (parenteral) 2018 All preterm: 200-1,000 IU.day-1 (Strong) Vitamin K ESPGHAN (enteral) 2022 All preterm: 4.4-28 µg.Kg-1.day-1 (Strong) ESPGHAN (parenteral) 2018 All preterm: 10 µg.Kg-1.day-1 (Strong) Vitamin C ESPGHAN (enteral) 2022 All preterm: 17-43 mg.Kg-1.day-1 (Weak) ESPGHAN (parenteral) 2018 All preterm: 15-25 mg.Kg-1.day-1 (Strong) Vitamin B1	Population information for included evidence Bronnert systematic review was on very low birthweight and very preterm infants

ESPGHAN (enteral) 2022 All preterm: 140-290 µg.Kg-1.day-1 (Weak) ESPGHAN (parenteral) 2018 All preterm: 350-500 µg.Kg-1.day-1 (Weak) Vitamin B2 ESPGHAN (enteral) 2022 All preterm: 200-430 µg.Kg-1.day-1 (Weak) ESPGHAN (parenteral) 2018 All preterm: 150-200 µg.Kg-1.day-1 (Weak) Vitamin B3 ESPGHAN (enteral) 2022 All preterm: 1.1-5.7 mg.Kg-1.day-1 (Weak) ESPGHAN (parenteral) 2018 All preterm: 4.0-6.8 mg.Kg-1.day-1 (Weak) Vitamin B5 ESPGHAN (enteral) 2022 All preterm: 0.6-2.2 mg.Kg-1.day-1 (Weak) ESPGHAN (parenteral) 2018 All preterm: 2.5 mg.Kg-1.day-1 (Weak) Vitamin B6 ESPGHAN (enteral) 2022 All preterm: 70-290 µg.Kg-1.day-1 (Weak) ESPGHAN (parenteral) 2018 All preterm: 150-200 µg.Kg-1.day-1 (Weak) Vitamin B7 ESPGHAN (enteral) 2022 All preterm: 3.5-15 µg.Kg-1.day-1 (Weak) ESPGHAN (parenteral) 2018 All preterm: 5.0-8.0 µg.Kg-1.day-1 (Weak) Vitamin B9 ESPGHAN (enteral) 2022 All preterm: 23-100 µg.Kg-1.day-1 (Weak) ESPGHAN (parenteral) 2018 All preterm: 56 µg.Kg-1.day-1 (Strong) Vitamin B12 ESPGHAN (enteral) 2022 All preterm: 0.1-0.6 µg.Kg-1.day-1 (Weak) ESPGHAN (parenteral) 2018 All preterm: 0.3 µg.Kg-1.day-1 (Weak) Choline - ESPGHAN (enteral) 2022 All preterm: 8-55 mg.Kg-1.day-1 (Weak) Vitamin C No faltering growth/body composition: RCT: No significant effect in weight with increased dose (MD 0.2 g/day higher; 4.42 lower to 4.82 higher) [Important]. Retinopathy of prematurity: RCT: No significant reduction in retinopathy of prematurity with higher dose (4 fewer per 1,000; 166 fewer to 279 more) [Important]. Bronchopulmonary dysplasia/chronic lung disease: RCT: Very large reduction in bronchopulmonary	
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dysplasia with higher dose (176 fewer per 1,000; 270 fewer to 30 fewer) [Important].
Sepsis: RCT: No significant reduction in culture proven sepsis with higher dose (156 fewer per 1,000; 316 fewer to 188 more) [Important].

Vitamin E

Mortality: RCT: No significant effect on mortality with higher dose (4 fewer per 1,000; 35 fewer to 35 more) [Critical].
Retinopathy of prematurity: RCT: No significant reduction in retinopathy of prematurity with higher dose (49 fewer per 1,000; 131 fewer to 53 more) [Important].
Bronchopulmonary dysplasia: RCT: No significant reduction in bronchopulmonary dysplasia with higher dose (16 fewer per 1,000; 55 fewer to 31 more) [Important].
Anaemia of prematurity: RCT: No significant effect in the number of transfusions per infant (MD 0.2 transfusions lower; 1.18 lower to 0.78 higher) [Important].

Vitamin D

Neurodevelopmental impairment: RCT: No significant reduction in neurodevelopmental impairment (120 fewer per 1,000; 270 fewer to 135 more); cognitive impairment (63 fewer per 1,000; 216 fewer to 228 more) or language impairment (129 fewer per 1,000; 302 fewer to 129 more) at 22-26 months [Critical].
No faltering growth/body composition: RCT: No significant increase in weight with increased dose (MD 2.0 g/day higher; 2.38 lower to 6.38 higher) [Important].
Retinopathy of prematurity: RCT: No significant reduction in retinopathy of prematurity with higher dose (105 fewer per 1,000; 265 fewer to 165 more) [Important].
Bronchopulmonary dysplasia: RCT: Very large reduction in bronchopulmonary dysplasia with higher dose (169 fewer per 1,000; 237 fewer to 68 fewer) [Important].
Sepsis: RCT: No significant reduction in culture proven sepsis with higher dose (156 fewer per 1,000; 316 fewer to 188 more) [Important].

Vitamin A

Mortality: RCT: No significant effect in mortality for larger dose (3 fewer per 1,000; 23 fewer to 21 more) [Critical].
Neurodevelopmental impairment: RCT: No significant reduction in neurodevelopmental impairment (53 fewer per 1,000; 125 fewer to 38 more); cognitive impairment (66 fewer per 1,000; 132 fewer to 16 more); motor impairment (50 fewer per 1,000; 110 fewer to 30 more) and cerebral palsy (31 fewer per 1,000; 77 fewer to 36 more) [Critical].
Retinopathy of prematurity: RCT: Very large reduction of retinopathy of prematurity with larger dose (98 fewer per 1,000; 166 fewer to 9 fewer) [Important].
Bronchopulmonary dysplasia: RCT: No significant reduction in bronchopulmonary dysplasia with larger dose (65 fewer per 1,000; 130 fewer to 6 more) [Important].
Sepsis: RCT: Very large reduction in culture proven sepsis (28 fewer per 1,000; 54 fewer to 0 fewer) and

culture proven or suspected sepsis with larger dose (30 fewer per 1,000; 56 fewer to 3 fewer) [Important]. Necrotising enterocolitis (NEC): RCT: No significant reduction in NEC with larger dose (13 fewer per 1,000; 31 fewer to 10 more) [Important]. Vitamin K Necrotising enterocolitis (NEC): RCT: No significant reduction in NEC with larger dose (35 fewer per 1,000; 87 fewer to 281 more) [Important]. Vitamin B12 and folic acid Necrotising enterocolitis (NEC): RCT: No significant reduction in NEC with larger dose (59 fewer per 1,000; 87 fewer to 203 more). [Important] Anaemia of prematurity: RCT: No significant reduction in anaemia requiring transfusion (76 fewer per 1,000; 206 fewer to 215 more) [Important]. Desirable effects for Māori No additional evidence available	
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Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with no/lower vitamin intake	Risk difference with higher vitamin intake
Mortality: RCT: Vitamin C	130 (2 RCTs)	⊕○○○ Very low ^{a,b,c,d}	RR 1.99 (0.36 to 11.12)	Study population	
				30 per 1,000	30 more per 1,000 (19 fewer to 307 more)
Mortality: RCT: Vitamin E	1602 (10 RCTs)	⊕⊕⊕○ Moderate ^e	RR 0.98 (0.80 to 1.20)	Study population	
				177 per 1,000	4 fewer per 1,000 (35 fewer to 35 more)
Mortality: RCT: Vitamin D	187 (2 RCTs)	⊕○○○ Very low ^{a,c,f}	RR 1.43 (0.32 to 6.39)	Study population	
				38 per 1,000	17 more per 1,000 (26 fewer to 207 more)
Mortality: RCT: Vitamin A	2971 (14 RCTs)	⊕⊕⊕○ Moderate ^e	RR 0.97 (0.80 to 1.18)	Study population	
				115 per 1,000	3 fewer per 1,000 (23 fewer to 21 more)
Mortality: RCT: Vitamin B ₁₂ and folic acid	64 (1 RCT)	⊕○○○ Very low ^{a,f,g}	RR 1.60 (0.29 to 8.92)	Study population	
				61 per 1,000	36 more per 1,000 (43 fewer to 480 more)
Mortality: RCT: Vitamin K	75		RR 1.43	Study population	

	(1 RCT)	⊕○○○ Very low ^{a,f,g}	(0.25 to 8.20)	59 per 1,000	25 more per 1,000 (44 fewer to 424 more)
Neurodevelopmental impairment: RCT: Vitamin D assessed with: 22-26 months	78 (1 RCT)	⊕○○○ Very low ^{e,g,h}	RR 0.76 (0.46 to 1.27)	Study population	
				500 per 1,000	120 fewer per 1,000 (270 fewer to 135 more)
Neurodevelopmental impairment: RCT: Vitamin D assessed with: Cognitive impairment (22-26 months)	70 (1 RCT)	⊕○○○ Very low ^{e,g,h}	RR 0.84 (0.45 to 1.58)	Study population	
				393 per 1,000	63 fewer per 1,000 (216 fewer to 228 more)
Neurodevelopmental impairment: RCT: Vitamin D assessed with: Language impairment (22-26 months)	69 (1 RCT)	⊕○○○ Very low ^{e,g,h}	RR 0.80 (0.53 to 1.20)	Study population	
				643 per 1,000	129 fewer per 1,000 (302 fewer to 129 more)
Neurodevelopmental impairment: RCT: Vitamin A assessed with: 18-22 months	538 (1 RCT)	⊕○○○ Very low ^{c,e,g}	RR 0.89 (0.74 to 1.08)	Study population	
				481 per 1,000	53 fewer per 1,000 (125 fewer to 38 more)
Neurodevelopmental impairment: RCT: Vitamin A (assessed with: 18-22 months) assessed with: Cognitive impairment	539 (1 RCT)	⊕○○○ Very low ^{ec,e,g}	RR 0.83 (0.66 to 1.04)	Study population	
				388 per 1,000	66 fewer per 1,000 (132 fewer to 16 more)
Neurodevelopmental impairment: RCT: Vitamin A (assessed with: 18-22 months) assessed with: Motor impairment	534 (1 RCT)	⊕○○○ Very low ^{c,e,g}	RR 0.83 (0.63 to 1.10)	Study population	
				297 per 1,000	50 fewer per 1,000 (110 fewer to 30 more)
Neurodevelopmental impairment: RCT: Vitamin A (assessed with: 18-22 months) assessed with: bilateral blindness	577 (1 RCT)	⊕○○○ Very low ^{d,g}	RR 4.98 (0.24 to 103.33)	Study population	
				0 per 1,000	0 fewer per 1,000 (0 fewer to 0 fewer)
Neurodevelopmental impairment: RCT: Vitamin A (assessed with: 18-22 months) assessed with: Deafness	578 (1 RCT)	⊕○○○ Very low ^{d,g}	RR 1.24 (0.34 to 4.58)	Study population	
				14 per 1,000	3 more per 1,000 (9 fewer to 50 more)
Neurodevelopmental impairment: RCT: Vitamin A (assessed with: 18-22 months) assessed with: Cerebral palsy	570 (1 RCT)	⊕○○○ Very low ^{c,e,g}	RR 0.83 (0.57 to 1.20)	Study population	
				180 per 1,000	31 fewer per 1,000 (77 fewer to 36 more)
Adverse effects (prevention of unnecessary blood tests) - not measured	-	-	-	-	-
Faltering growth/body composition : RCT: Vitamin D assessed with: Weight (g.d-1)	81 (1 RCT)	⊕○○○	-	The mean faltering growth/body composition : RCT: Vitamin D was not	MD 2 higher

		Very low ^{c,e,g}		reported	(2.38 lower to 6.38 higher)
Faltering growth/body composition : RCT: Vitamin C assessed with: Weight (g.d-1)	50 (1 RCT)	⊕○○○ Very low ^{a,d,g}	-	The mean faltering growth/body composition : RCT: Vitamin C was not reported	MD 0.2 higher (4.42 lower to 4.82 higher)
Retinopathy of prematurity: RCT: Vitamin A	1989 (11 RCTs)	⊕⊕○○ Low ^{a,k}	RR 0.77 (0.61 to 0.98)	Study population	
				426 per 1,000	98 fewer per 1,000 (166 fewer to 9 fewer)
Retinopathy of prematurity: RCT: Vitamin E	822 (5 RCTs)	⊕⊕○○ Low ^{a,e}	RR 0.90 (0.73 to 1.11)	Study population	
				485 per 1,000	49 fewer per 1,000 (131 fewer to 53 more)
Retinopathy of prematurity: RCT: Vitamin C	86 (1 RCT)	⊕○○○ Very low ^{a,c,e}	RR 0.99 (0.57 to 1.72)	Study population	
				387 per 1,000	4 fewer per 1,000 (166 fewer to 279 more)
Retinopathy of prematurity: RCT: Vitamin D	100 (1 RCT)	⊕○○○ Very low ^{c,e,g}	RR 0.79 (0.47 to 1.33)	Study population	
				500 per 1,000	105 fewer per 1,000 (265 fewer to 165 more)
Bronchopulmonary dysplasia: RCT: Vitamin C	160 (2 RCTs)	⊕○○○ Very low ^{a,b,c}	RR 0.59 (0.37 to 0.93)	Study population	
				429 per 1,000	176 fewer per 1,000 (270 fewer to 30 fewer)
Bronchopulmonary dysplasia: RCT: Vitamin E	1255 (6 RCTs)	⊕○○○ Very low ^{e,j}	RR 0.94 (0.79 to 1.12)	Study population	
				261 per 1,000	16 fewer per 1,000 (55 fewer to 31 more)
Bronchopulmonary dysplasia: RCT: Vitamin A	2618 (12 RCTs)	⊕⊕○○ Low ^{a,e}	RR 0.89 (0.78 to 1.01)	Study population	
				589 per 1,000	65 fewer per 1,000 (130 fewer to 6 more)
Bronchopulmonary dysplasia: RCT: Vitamin D	244 (3 RCTs)	⊕⊕○○ Low ⁱ	RR 0.58 (0.41 to 0.83)	Study population	
				402 per 1,000	169 fewer per 1,000 (237 fewer to 68 fewer)
Fully breastfed or breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Time to full enteral feeds - not measured	-	-	-	-	-
Duration of initial hospital stay - not measured	-	-	-	-	-

Sepsis: proven or suspected: RCT: Vitamin A assessed with: Culture proven	2244 (6 RCTs)	 Low ^{e,i}	RR 0.88 (0.77 to 1.00)	Study population	
				237 per 1,000	28 fewer per 1,000 (54 fewer to 0 fewer)
Sepsis: proven or suspected: RCT: Vitamin A assessed with: culture proven or suspected	2552 (8 RCTs)	 Moderate ^a	RR 0.88 (0.78 to 0.99)	Study population	
				254 per 1,000	30 fewer per 1,000 (56 fewer to 3 fewer)
Sepsis: proven or suspected: RCT: Vitamin E assessed with: Proven	1031 (6 RCTs)	 Low ^{a,e}	RR 1.34 (0.99 to 1.80)	Study population	
				126 per 1,000	43 more per 1,000 (1 fewer to 101 more)
Sepsis: proven or suspected: RCT: Vitamin E	1121 (7 RCTs)	 Low ^{a,e}	RR 1.15 (0.91 to 1.47)	Study population	
				184 per 1,000	28 more per 1,000 (17 fewer to 87 more)
Sepsis: proven or suspected: RCT: Vitamin C assessed with: Culture proven	47 (1 RCT)	 Very low ^{a,c,f}	RR 0.66 (0.31 to 1.41)	Study population	
				458 per 1,000	156 fewer per 1,000 (316 fewer to 188 more)
Sepsis: proven or suspected: RCT: Vitamin D assessed with: Proven	100 (1 RCT)	 Very low ^{c,e,g}	RR 0.68 (0.31 to 1.50)	Study population	
				139 per 1,000	44 fewer per 1,000 (96 fewer to 69 more)
Necrotising enterocolitis: RCT: Vitamin B12 and folic acid	66 (1 RCT)	 Very low ^{a,f,g}	RR 0.35 (0.04 to 3.23)	Study population	
				91 per 1,000	59 fewer per 1,000 (87 fewer to 203 more)
Necrotising enterocolitis: RCT: Vitamin K	75 (1 RCT)	 Very low ^{a,f,g}	RR 0.64 (0.11 to 3.87)	Study population	
				98 per 1,000	35 fewer per 1,000 (87 fewer to 281 more)
Necrotising enterocolitis: RCT: Vitamin C	119 (1 RCT)	 Very low ^{a,f,g}	RR 1.27 (0.17 to 9.25)	Study population	
				25 per 1,000	7 more per 1,000 (21 fewer to 206 more)
Necrotising enterocolitis: RCT: Vitamin D	100 (1 RCT)	 Very low ^{d,g}	RR 1.63 (0.20 to 13.39)	Study population	
				28 per 1,000	17 more per 1,000 (22 fewer to 344 more)
Necrotising enterocolitis: RCT: Vitamin E	1331 (8 RCTs)	 Low ^{a,e}	RR 1.29 (0.90 to 1.85)	Study population	
				71 per 1,000	21 more per 1,000

					(7 fewer to 61 more)
Necrotising enterocolitis: RCT: Vitamin A	2626 (9 RCTs)	⊕⊕○○ Low ^{a,e}	RR 0.87 (0.69 to 1.10)	Study population	
				100 per 1,000	13 fewer per 1,000 (31 fewer to 10 more)
Anaemia of prematurity: RCT: Vitamin E assessed with: Number of transfusion per infant	30 (1 RCT)	⊕○○○ Very low ^{e,g,i,j,k,u}	-	The mean anaemia of prematurity: RCT: Vitamin E was not reported	MD 0.2 lower (1.18 lower to 0.78 higher)
Anaemia of prematurity: RCT: Vitamin C assessed with: Number of transfusion per infant	51 (1 RCT)	⊕○○○ Very low ^{a,c,g}	-	The mean anaemia of prematurity: RCT: Vitamin C was not reported	MD 0.1 higher (1.36 lower to 1.56 higher)
Anaemia of prematurity: RCT: Vitamin C assessed with: Number of infants requiring transfusions	81 (1 RCT)	⊕○○○ Very low ^{d,g}	RR 1.86 (0.50 to 6.92)	Study population	
				77 per 1,000	66 more per 1,000 (38 fewer to 455 more)
Anaemia of prematurity: RCT: Vitamin B12 and folic acid assessed with: Anaemia of infants who required transfusion	64 (1 RCT)	⊕○○○ Very low ^{a,e,g}	RR 0.75 (0.32 to 1.71)	Study population	
				303 per 1,000	76 fewer per 1,000 (206 fewer to 215 more)
Cost: cost of intervention, cost of neonatal care and life- long cost - not measured	-	-	-	-	-
Time to full sucking feeds (<0.5 days) - not measured	-	-	-	-	-

- a. Downgraded one level for concerns about risk of bias
b. Downgraded one level for inconsistency
c. Downgraded one level for indirectness as population may not be generalisable
d. Downgraded three levels for imprecision with extremely wide confidence intervals crossing the line of no effect
e. Downgraded one level for imprecision due to confidence intervals crossing the line of no effect
f. Downgraded two levels for imprecision with very wide confidence intervals crossing the line of no effect
g. Downgraded one level for indirectness as evidence based on a single study
h. Downgraded one level for imprecision due to low event rates and/or small sample size
i. Downgraded one level as evidence is based on a single study
j. Downgraded two levels for concerns of risk of bias
k. Downgraded one level for inconsistency as I² >50%
l. Downgraded one level for indirectness as the mode of administration is not generalisable

a)

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial	Vitamin A	

○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Neurodevelopmental impairment: RCT: No significant effect in bilateral blindness (RR 4.98; 0.24 to 103.33; unable to calculate absolute risk due to low events) and in deafness (3 more per 1,000; 9 fewer to 50 more) [Critical]. Vitamin E Sepsis: RCT: No significant increase in proven or suspected sepsis (28 more per 1,000; 17 fewer to 87 more) and proven sepsis with higher dose (43 more per 1,000; 1 fewer to 101 more) [Important]. Necrotising enterocolitis (NEC): RCT: No significant increase in NEC with higher dose (21 more per 1,000; 7 fewer to 61 more) [Important]. Vitamin C Mortality: RCT: No significant increase in mortality with higher dose (30 more per 1,000; 19 fewer to 307 more) [Critical]. Necrotising enterocolitis: RCT: No significant increase in NEC with higher dose (7 more per 1,000; 21 fewer to 206 more) [Important]. Anaemia of prematurity: RCT: No significant effect on the number of transfusions per infant with higher dose (MD 0.1 transfusions higher; 1.36 lower to 1.56 higher) [Important]. Anaemia of prematurity: RCT: No significant increase in number of infants requiring transfusions with higher dose (66 more per 1,000; 38 fewer to 455 more) [Important]. Vitamin D Mortality: RCT: No significant increase in mortality with higher dose (17 more per 1,000; 26 fewer to 207 more) [Critical]. Necrotising enterocolitis: RCT: No significant increase in NEC with higher dose (17 more per 1,000; 22 fewer to 344 more) [Important]. Vitamin K Mortality: RCT: No significant increase in mortality with higher dosage (25 more per 1,000; 44 fewer to 424 more) [Critical]. Vitamin B₁₂ and folic acid Mortality: RCT: No significant increase in mortality with higher dosage (36 more per 1,000; 43 fewer to 480 more) [Critical]. Undesirable effects for Māori No additional evidence available	
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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Moderate to very low certainty of evidence overall Certainty of evidence for Māori No additional evidence available	
Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT: Vitamin C	CRITICAL	⊕○○○ Very low
Mortality: RCT: Vitamin E	CRITICAL	⊕⊕⊕○ Moderate
Mortality: RCT: Vitamin D	CRITICAL	⊕○○○ Very low
Mortality: RCT: Vitamin A	CRITICAL	⊕⊕⊕○

		Moderate
Mortality: RCT: Vitamin B ₁₂ and folic acid	CRITICAL	⊕○○○ Very low
Mortality: RCT: Vitamin K	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: Vitamin D assessed with : 22-26 months	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: Vitamin D assessed with: Cognitive impairment (22-26 months)	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: Vitamin D assessed with: Language impairment (22-26 months)	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: Vitamin A assessed with: 18-22 months	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: Vitamin A (assessed with: 18-22 months) assessed with: Cognitive impairment	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: Vitamin A (assessed with: 18-22 months) assessed with: Motor impairment	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: Vitamin A (assessed with: 18-22 months) assessed with: bilateral blindness	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: Vitamin A (assessed with: 18-22 months) assessed with: Deafness	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: Vitamin A (assessed with: 18-22 months) assessed with: Cerebral palsy	CRITICAL	⊕○○○ Very low
Adverse effects (prevention of unnecessary blood tests) - not measured	IMPORTANT	-
Faltering growth/body composition: RCT: Vitamin D assessed with: Weight (g.d-1)	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT: Vitamin C assessed with: Weight (g.d-1)	IMPORTANT	⊕○○○ Very low
Retinopathy of prematurity: RCT: Vitamin A	IMPORTANT	⊕⊕○○ Low
Retinopathy of prematurity: RCT: Vitamin E	IMPORTANT	⊕⊕○○

		Low
Retinopathy of prematurity: RCT: Vitamin C	IMPORTANT	⊕○○○ Very low
Retinopathy of prematurity: RCT: Vitamin D	IMPORTANT	⊕○○○ Very low
Bronchopulmonary dysplasia: RCT: Vitamin C	IMPORTANT	⊕○○○ Very low
Bronchopulmonary dysplasia: RCT: Vitamin E	IMPORTANT	⊕○○○ Very low
Bronchopulmonary dysplasia: RCT: Vitamin A	IMPORTANT	⊕⊕○○ Low
Bronchopulmonary dysplasia: RCT: Vitamin D	IMPORTANT	⊕⊕○○ Low
Fully breastfed or breastmilk feeding at hospital discharge - not measured	IMPORTANT	-
Time to full enteral feeds - not measured	IMPORTANT	-
Duration of initial hospital stay - not measured	IMPORTANT	-
Sepsis: proven or suspected: RCT: Vitamin A assessed with: Culture proven	IMPORTANT	⊕⊕○○ Low
Sepsis: proven or suspected: RCT: Vitamin A assessed with: culture proven or suspected	IMPORTANT	⊕⊕⊕○ Moderate
Sepsis: proven or suspected: RCT: Vitamin E assessed with: Proven	IMPORTANT	⊕⊕○○ Low
Sepsis: proven or suspected: RCT: Vitamin E	IMPORTANT	⊕⊕○○ Low
Sepsis: proven or suspected: RCT: Vitamin C assessed with: Culture proven	IMPORTANT	⊕○○○ Very low
Sepsis: proven or suspected: RCT: Vitamin D assessed with: Proven	IMPORTANT	⊕○○○ Very low
Necrotising enterocolitis: RCT: Vitamin B12 and folic acid	IMPORTANT	⊕○○○ Very low
Necrotising enterocolitis: RCT: Vitamin K	IMPORTANT	⊕○○○

		Very low
Necrotising enterocolitis: RCT: Vitamin C	IMPORTANT	⊕○○○ Very low
Necrotising enterocolitis: RCT: Vitamin D	IMPORTANT	⊕○○○ Very low
Necrotising enterocolitis: RCT: Vitamin E	IMPORTANT	⊕⊕○○ Low
Necrotising enterocolitis: RCT: Vitamin A	IMPORTANT	⊕⊕○○ Low
Anaemia of prematurity: RCT: Vitamin E assessed with: Number of transfusion per infant	IMPORTANT	⊕○○○ Very low
Anaemia of prematurity: RCT: Vitamin C assessed with: Number of transfusion per infant	IMPORTANT	⊕○○○ Very low
Anaemia of prematurity: RCT: Vitamin C assessed with: Number of infants requiring transfusions	IMPORTANT	⊕○○○ Very low
Anaemia of prematurity: RCT: Vitamin B12 and folic acid assessed with: Anaemia of infants who required transfusion	IMPORTANT	⊕○○○ Very low
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds (<0.5 days) - not measured	NOT IMPORTANT	-

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or	There is a high prevalence of maternal vitamin D deficiency in Aotearoa New Zealand. Because the prevalence of vitamin D deficiency is higher in Pacific people, supplementation might especially benefit Pacific infants. Values for Māori	Critical outcomes Mortality (<1 per 1000) Neurodevelopmental impairment (<10 per 1000)

variability	No evidence available.	
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Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Vitamin C Higher versus no/lower dosage - very low certainty evidence Reduction in bronchopulmonary dysplasia Uncertain effect on mortality, faltering growth/body composition, retinopathy of prematurity, sepsis, necrotising enterocolitis, anaemia of prematurity Vitamin A Higher versus no/lower dosage - moderate certainty evidence Reduced sepsis Uncertain effect on mortality Higher versus no/lower dosage - low certainty evidence Reduced retinopathy of prematurity Uncertain effect on bronchopulmonary dysplasia, necrotising enterocolitis, bronchopulmonary dysplasia, sepsis Higher versus no/lower dosage - very low certainty evidence Uncertain effect on neurodevelopmental impairment, cognitive impairment, motor impairment, bilateral blindness, deafness, cerebral palsy Vitamin E Higher versus no/lower dosage - moderate certainty evidence Uncertain effect on mortality Higher versus no/lower dosage - low certainty evidence Uncertain effect on retinopathy of prematurity, sepsis Higher versus no/lower dosage - very low certainty evidence Uncertain effect on anaemia of prematurity Vitamin D Higher versus no/lower dosage - low certainty evidence Reduction in bronchopulmonary dysplasia Higher versus no/lower dosage - very low certainty evidence Uncertain effect on mortality; neurodevelopmental impairment, cognitive and language	

	impairment, faltering growth/body composition, retinopathy of prematurity, sepsis, necrotising enterocolitis Vitamin K Higher versus no/lower dosage - very low certainty evidence Uncertain effect on mortality, necrotising enterocolitis Vitamin B12 and folic acid Higher versus no/lower dosage - very low certainty evidence Uncertain effect on mortality, necrotising enterocolitis, anaemia of prematurity Balance of effects for Māori No additional evidence	
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Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Vitamin A 2 drops/kg/day (2 to 3 drops Optimus Vitamin A) \$0.14 Vitamin D 1 drop/kg/day (2 to 3 drops Clinicians Vitamin D) \$0.30 Vitamin E 7 mg/kg/day (7 to 10 mg) \$0.12 Vitamin B1 Thiamine 200 µg/kg/day (200 to 300 µg) \$0.05 Cost are small.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Costs are reasonably certain. Certainty of evidence of required resources for Māori No additional evidence available	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No economic studies were identified to address the cost-effectiveness of the higher or lower vitamin intake. Cost effectiveness for Māori No evidence available.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Our health system privileges whiteness with significant advantage experienced by non-Māori. Pēpi Māori are more likely to be born preterm, admitted to NICU, born at ELBW, and fewer survive. Preterm pēpi Māori are more likely to be vitamin deficient due to both biological and systemic factors, due to the social determinants of health and nutrition (e.g. colonisation, racism, income, education, employment and housing). Having more pigmented skin decreases the effectiveness of ultraviolet-induced vitamin D production, leading to lower vitamin D status compared with people with fairer skin. Neonatal and maternal plasma vitamin D concentration is significantly lower in infants with late-onset sepsis and with NEC, meaning that addressing vitamin D status has the potential to improve equity. Less is known about the deficiency of other vitamins in Māori. Equity for Pacific families A study of the nutritional status of 413 Auckland children aged 6-23 months found the prevalence of vitamin D deficiency varied with ethnicity: Pacific 24%, Māori 11%, European 3% and other ethnic groups 16%. Because the prevalence of vitamin D deficiency is higher in Pacific people, supplementation might especially benefit Pacific infants. While specific, up-to-date vitamin deficiency data in infants is limited, strong evidence from clinical and population health research points consistently to Māori and Pacific infants being disproportionately affected due to a combination of biological, social, and systemic factors. Pacific Island infants are over-represented in the preterm infant population and also at higher nutrient deficiency risk. Equity for other underrepresented groups	

	Indian infants are over-represented in the preterm infant population and also at higher nutrient deficiency risk. Based on presentations to Starship Child Health, a group at particular risk of symptomatic vitamin deficiency are Indian children from vegan families. Equity requires system-wide availability and clear, inclusive protocols that ensure every infant receives what they need from day one.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☐ Probably yes ☐ Yes ☒ Varies ☐ Don't know	The addition of some vitamins to enteral feeds is standard practice in Aotearoa New Zealand. Intramuscular vitamin A injections may not be acceptable to staff and parents. Acceptability for Māori No evidence available.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☐ Probably yes ☐ Yes ☒ Varies ☐ Don't know	The addition of some vitamins to enteral feeds is already standard practice in Aotearoa New Zealand. Intramuscular vitamin A injections may not be available to Aotearoa New Zealand hospitals. Feasibility for Māori No additional evidence available	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know

	JUDGEMENT						
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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Appendix H.2 – Evidence to Decision: Enteral Nutrition

EtD 18. Should we give infant formula/donor milk vs. wait for mother's own milk be used for moderate-to-late preterm infants whose mothers' breastmilk is not available at birth?

POPULATION:	Moderate-to-late preterm infants whose mothers' breastmilk is not available at birth
INTERVENTION:	Infant formula/donor milk
COMPARISON:	Wait for mother's own milk
MAIN OUTCOMES:	Critical outcomes Mortality Neurodevelopmental impairment Fully breastfed or breastmilk feeding at hospital discharge Important but not critical Adverse effects Time to full enteral feeds Duration of initial hospital stay Sepsis: proven or suspected Bronchopulmonary dysplasia Necrotising enterocolitis Retinopathy of prematurity Anaemia of prematurity Faltering growth/body composition Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation: population perspective
BACKGROUND:	The choice of nutrition support for moderate-to-late preterm infants when mothers' breastmilk is not yet available may have a significant impact on short- and long-term outcomes. Parenteral nutrition (PN) ensures the direct provision of essential nutrients into the bloodstream. While PN supports early growth and prevents malnutrition, it is invasive and poses risks such as catheter-related infections, biochemical imbalances and liver dysfunction. Parenteral 10% glucose is often used temporarily to prevent dehydration and hypoglycaemia in the absence of enteral nutrition, but it does not provide the protein, fat, and micronutrients necessary for growth and development. Use for more than a few days leads to nutrient deficits. Infant formula is nutritionally complete and supports growth when human breastmilk is unavailable. However, it lacks the bioactive components of human breastmilk, increasing the risk of feeding intolerance and necrotising enterocolitis (NEC). Donor breastmilk, when available, is preferred to infant formula because it provides bioactive factors that promote immunity, gut maturation, and neurodevelopment while lowering the risk of NEC. However, the protein and energy content may be lower than infant formula, necessitating additional fortification. Selecting the optimal feeding method involves balancing the

	immediate fluid and nutritional needs of the infant with the long-term benefits of waiting for mother's own breastmilk to promote breastfeeding, optimal neurodevelopment and long-term health.
CONFLICT OF INTERESTS:	The following DIAMOND study investigators and co-authors (references 1, 2 and 3) are on the Guideline Development Group: Tanith Alexander and Frank Bloomfield

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	[1,2] Mortality: RCT: Little or no effect on mortality between milk supplement and mother's own milk (0/261 for supplement milk vs. 1/271 for mother's own milk) [Critical]. Duration of initial hospital stay: RCT: Little or no effect on duration of hospital stay (adj MD 0.17 days higher; 1.43 lower to 1.77 higher) [Important]. Sepsis: RCT: Little or no effect between milk supplementation and mother's own milk for incidence of sepsis (1/261 for supplement milk vs. 3/271 for mother's own milk) [Important]. Necrotising enterocolitis (NEC): RCT: Little or no effect between milk supplementation and mother's own milk for incidence of NEC (0/261 for supplement milk vs. 1/271) No faltering growth/body composition: RCT: Little or no effect in body-fat percentage at 4 months of corrected gestational age for supplemental milk (Adj MD 0.65 % higher; 0.45 lower to 1.74 higher); fat mass z score at discharge (Adj MD 0.1 points higher; 0.1 lower to 0.4 higher); day 7 weight z score (Adj MD 0.02 points higher; 0.02 lower to 0.05 higher); day 14 weight z score (Adj MD 0.03 points higher; 0.03 lower to 0.08 higher); day 21 weight z score (Adj MD 0.04 points higher; 0.03 lower to 0.12 higher); day 28 weight z score (Adj MD 0.1 points higher; 0.02 lower to 0.23 higher); discharge weight z score (Adj MD 0.01 points lower; 0.08 lower to 0.06 higher); 4 months corrected age weight z score (Adj MD 0.05 points higher; 0.14 lower to 0.24 higher); day 7 length z score (Adj MD 0 points; 0.1 lower to 0.12 higher); day 14 length z score (Adj MD 0 points; 0.12 lower to 0.11 higher); day 21 length z score (Adj MD 0.13 points lower; 0.28 lower to 0.01 higher); day 28 length z score (Adj MD 0.15 points lower; 0.35 lower to 0.06 higher); discharge length z score (Adj MD 0.05 points lower; 0.18 lower to 0.07 higher); 4 months corrected age length z score (Adj MD 0.07 points lower; 0.26 lower to 0.12 higher); day 7 head circumference z score (Adj MD 0.03 points higher; 0.07 lower to 0.13 higher); day 14 circumference z score (Adj MD 0.08 points higher; 0.02 lower to 0.18 higher); day 21 circumference z score (Adj MD 0.04 points higher; 0.08 lower to 0.16 higher); day 28 circumference z score (Adj MD 0.09 points higher; 0.08 lower to 0.25 higher); discharge circumference z score (Adj MD 0.02 points lower; 0.12 lower to 0.08 higher); 4 months corrected age circumference z score (Adj MD 0.05 points lower; 0.23 lower to 0.14 higher) [Important]. Time to achieve full sucking feeds: RCT: Small effect for longer time to achieve full sucking feeds for supplemental milk (Adj HR 0.91 days higher; 0.69 higher to 1.19 higher) [Not important].	Population information for included evidence New Zealand: RCT (DIAMOND trial) [1,2] Population were moderate- to late-preterm infants. Note that only a small proportion of infants in this study received donor EBM. New Zealand [3]: Conference proceedings: Neurosensory impairment was similar at 2 years in milk supplement and mother's EBM (DIAMOND trial)

	Desirable effects for Māori No additional evidence available				
Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with mother's own milk	Risk difference with infant formula/donor milk
Mortality	532 (1 RCT)	⊕○○○○ Very low ^{a,b}	-	0/261 for supplement milk vs. 1/271 for mother's own milk	
Neurodevelopmental impairment - not measured	-	-	-	-	-
Fully breastfed or breastmilk feeding at hospital discharge: RCT	528 (1 RCT)	⊕⊕○○○ Low ^a	OR 0.96 (0.65 to 1.40)	Study population	
				708 per 1,000	9 fewer per 1,000 (96 fewer to 64 more)
Adverse effects - not measured	-	-	-	-	-
Time to full enteral feeds: RCT assessed with: Days	526 (1 RCT)	⊕⊕○○○ Low ^a	-	The mean time to full enteral feeds: RCT was 5.8 days	Adj HR 1.13 higher (0.88 higher to 1.34 higher)
Duration of initial hospital stay: RCT assessed with: Days	532 (1 RCT)	⊕○○○○ Very low ^{a,c}	-	The mean duration of initial hospital stay: RCT was 24.7 days	adj MD 0.17 higher (1.43 lower to 1.77 higher)
Sepsis: proven or suspected: RCT assessed with: Culture-proven late-onset sepsis	532 (1 RCT)	⊕○○○○ Very low ^{a,b}	-	1/261 for supplement milk vs. 3/271 for mother's own milk	
Sepsis: proven or suspected: RCT assessed with: Probable late-onset sepsis	532 (1 RCT)	⊕○○○○ Very low ^{a,b}	-	1/261 for supplement milk vs. 3/271 for mother's own milk	
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Necrotising enterocolitis: RCT	532 (1 RCT)	⊕○○○○ Very low ^{a,b}	-	0/261 for supplement milk vs. 1/271 for mother's own milk	
Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Faltering growth/body composition: RCT assessed with: Body-fat percentage at 4 months of corrected gestational age	324 (1 RCT)	⊕⊕○○○ Low ^a	-	The mean faltering growth/body composition: RCT was 25.8%	Adj MD 0.65 higher (0.45 lower to 1.74 higher)
Faltering growth/body composition: RCT assessed with: Discharge: Fat mass z score	324 (1 RCT)	⊕⊕○○○ Low ^a	-	The mean faltering growth/body composition: RCT was -0.5 points	Adj MD 0.1 higher (0.1 lower to 0.4 higher)

Faltering growth/body composition: RCT assessed with: Day 7: Weight z score	493 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -0.87 points	Adj MD 0.02 higher (0.02 lower to 0.05 higher)
Faltering growth/body composition: RCT assessed with: Day 14: Weight z score	428 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -0.93 points	Adj MD 0.03 higher (0.03 lower to 0.08 higher)
Faltering growth/body composition: RCT assessed with: Day 21: Weight z score	309 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -0.84 points	Adj MD 0.04 higher (0.03 lower to 0.12 higher)
Faltering growth/body composition: RCT assessed with: Day 28: Weight z score	182 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -0.77 points	Adj MD 0.1 higher (0.02 lower to 0.23 higher)
Faltering growth/body composition: RCT assessed with: Discharge: Weight z score	514 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -0.76 points	Adj MD 0.01 lower (0.08 lower to 0.06 higher)
Faltering growth/body composition: RCT assessed with: 4 months' corrected age: Weight z score	401 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -0.05 points	Adj MD 0.05 higher (0.14 lower to 0.24 higher)
Faltering growth/body composition: RCT assessed with: Day 7: Length z score	469 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -0.19 points	Adj MD 0 (0.1 lower to 0.12 higher)
Faltering growth/body composition: RCT assessed with: Day 14: Length z score	415 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -0.31 points	Adj MD 0 (0.12 lower to 0.11 higher)
Faltering growth/body composition: RCT assessed with: Day 21: Length z score	299 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -0.26 points	Adj MD 0.13 lower (0.28 lower to 0.01 higher)
Faltering growth/body composition: RCT assessed with: Day 28: Length z score	178 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -0.34 points	Adj MD 0.15 lower (0.35 lower to 0.06 higher)
Faltering growth/body composition: RCT assessed with: Discharge: Length z score	495 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -0.17 points	Adj MD 0.05 lower (0.18 lower to 0.07 higher)
Faltering growth/body composition: RCT assessed with: 4 months' corrected age: Length z score	401 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was 0.57 points	Adj MD 0.07 lower (0.26 lower to 0.12 higher)
Faltering growth/body composition: RCT assessed with: Day 7: Head circumference z score	472 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -0.27 points	Adj MD 0.03 higher (0.07 lower to 0.13 higher)
Faltering growth/body composition: RCT assessed with: Day 14: Head circumference z score	420 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -0.28 points	Adj MD 0.08 higher (0.02 lower to 0.18 higher)
Faltering growth/body composition: RCT assessed with: Day 21: Head circumference z score	299 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -0.12 points	Adj MD 0.04 higher (0.08 lower to 0.16 higher)
Faltering growth/body composition: RCT assessed with: Day 28: Head circumference z score	178 (1 RCT)	⊕○○○ Very low ^{a,c}	-	The mean faltering growth/body composition: RCT was -0.02 points	Adj MD 0.09 higher (0.08 lower to 0.25 higher)

Faltering growth/body composition: RCT assessed with: Discharge: Head circumference z score	500 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was 0.03 points	Adj MD 0.02 lower (0.12 lower to 0.08 higher)
Faltering growth/body composition: RCT assessed with: 4 months' corrected age: Head circumference z score	401 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was 0.74 points	Adj MD 0.05 lower (0.23 lower to 0.14 higher)
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds: RCT	519 (1 RCT)	⊕⊕○○ Low ^a	-	The mean time to full sucking feeds: RCT was 22.2 days	Adj HR 0.91 higher (0.69 higher to 1.19 higher)

- a. Downgraded one level for indirectness as evidence is based on a single trial.
b. Downgraded two levels for imprecision as unable to provide effect estimate and only one study with extremely low or no events
c. Downgraded one level for imprecision with wide confidence intervals that cross the line of no effect
d. Downgraded one level for imprecision with confidence intervals that cross the line of no effect

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Fully breastfed or breastmilk feeding at hospital discharge: RCT: No significant effect on breastfeeding at discharge for infants receiving milk supplement (9 fewer per 1,000; 96 fewer to 64 more) [Critical]. Time to full enteral feeds: RCT: No significant effect on time to achieve full enteral feeds between groups (Adj HR 1.13 days earlier; 0.88 earlier to 1.34 later) [Important]. Undesirable effects for Māori No additional evidence available	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Low to very low certainty of evidence overall mainly due to the body of evidence being from a single trial, albeit well conducted. Certainty of evidence for Māori No additional evidence available	

Outcomes	Importance	Certainty of the evidence
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		(GRADE)
Mortality	CRITICAL	⊕○○○ Very low ^{a,b}
Neurodevelopmental impairment - not measured	CRITICAL	-
Fully breastfed or breastmilk feeding at hospital discharge: RCT	CRITICAL	⊕⊕○○ Low ^a
Adverse effects - not measured	IMPORTANT	-
Time to full enteral feeds: RCT assessed with: Days	IMPORTANT	⊕⊕○○ Low ^a
Duration of initial hospital stay: RCT assessed with: Days	IMPORTANT	⊕○○○ Very low ^{a,c}
Sepsis: proven or suspected: RCT assessed with: Culture-proven late-onset sepsis	IMPORTANT	⊕○○○ Very low ^{a,b}
Sepsis: proven or suspected: RCT assessed with: Probable late-onset sepsis	IMPORTANT	⊕○○○ Very low ^{a,b}
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Necrotising enterocolitis: RCT	IMPORTANT	⊕○○○ Very low ^{a,b}
Retinopathy of prematurity - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Faltering growth/body composition: RCT assessed with: Body-fat percentage at 4 months of corrected gestational age	IMPORTANT	⊕⊕○○ Low ^a
Faltering growth/body composition: RCT assessed with: Discharge: Fat mass z score	IMPORTANT	⊕⊕○○ Low ^a
Faltering growth/body composition: RCT assessed with: Day 7: Weight z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Faltering growth/body composition: RCT assessed with: Day 14: Weight z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Faltering growth/body composition: RCT assessed with: Day 21: Weight z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Faltering growth/body composition: RCT	IMPORTANT	⊕○○○

assessed with: Day 28: Weight z score		Very low ^{a,d}
Faltering growth/body composition: RCT assessed with: Discharge: Weight z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Faltering growth/body composition: RCT assessed with: 4 months' corrected age: Weight z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Faltering growth/body composition: RCT assessed with: Day 7: Length z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Faltering growth/body composition: RCT assessed with: Day 14: Length z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Faltering growth/body composition: RCT assessed with: Day 21: Length z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Faltering growth/body composition: RCT assessed with: Day 28: Length z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Faltering growth/body composition: RCT assessed with: Discharge: Length z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Faltering growth/body composition: RCT assessed with: 4 months' corrected age: Length z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Faltering growth/body composition: RCT assessed with: Day 7: Head circumference z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Faltering growth/body composition: RCT assessed with: Day 14: Head circumference z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Faltering growth/body composition: RCT assessed with: Day 21: Head circumference z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Faltering growth/body composition: RCT assessed with: Day 28: Head circumference z score	IMPORTANT	⊕○○○ Very low ^{a,c}
Faltering growth/body composition: RCT assessed with: Discharge: Head circumference z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Faltering growth/body composition: RCT assessed with: 4 months' corrected age: Head circumference z score	IMPORTANT	⊕○○○ Very low ^{a,d}
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds: RCT	IMPORTANT	⊕⊕○○

- a. Downgraded one level for inconsistency as evidence is based on a single trial.
 b. Downgraded two levels as unable to provide effect estimate and only one study with extremely low or no events
 c. Downgraded one level for imprecision with wide confidence intervals that cross the line of no effect
 d. Downgraded one level for imprecision with confidence intervals that cross the line of no effect

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability Values for Māori No additional information	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Infant formula/donor milk compared with mother's own milk moderate-to-late preterm infants whose mother's breastmilk is not available at birth - low certainty evidence Uncertain effect on fully breastfed or breastmilk feeding at hospital discharge; faltering growth/body composition (Body-fat percentage at 4 months of corrected gestational age; fat mass z score at discharge Achieved full enteral feeds earlier Longer time to achieve full sucking feeds Infant formula/donor milk compared with mother's own milk moderate-to-late preterm infants whose mother's breastmilk is not available at birth - very low certainty evidence Little or no effect on mortality, sepsis (proven or suspected); NEC, faltering growth/body composition (day 7, 14, 21, 28, discharge and 4 months' corrected age weight z score, length z score and head circumference z score), duration of hospital stay Balance of effects for Māori No additional evidence	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Enteral nutrition costs at 180 mL/kg/day \$2 to \$62 per day, depending on feed type (small) Term infant formula \$2 to \$5 per day Preterm infant formula \$6 to \$15 per day Pasteurised donor milk from a milk bank (\$16 per 100 mL) \$29 to \$43 per day Fortified donor milk from a milk bank (\$23 per 100 mL) \$42 to \$62 per day Expressing and storage equipment Enteral feed warmers Lactation consultant time Bottles and nasogastric tubes Costs for Formula <i>The cost of fortified mother's own expressed breastmilk and preterm infant formula is similar over the course of a neonatal care admission.</i> Resources required for Māori No additional evidence available	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ● High ○ No included studies	A formal assessment of the certainty of evidence of the cost was not undertaken. Certainty of evidence of required sources for Māori No additional evidence available	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	There are no studies that assess the specific cost-effectiveness of infant formula/donor milk versus mother's own milk, particularly in the context of preterm infants. Cost effectiveness for Māori No additional evidence available	
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Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Influenced by the effects of colonisation, pēpi Māori are more likely to be born preterm, admitted to NICU, born at extremely low birthweight and fewer survive. There is also a greater burden for Māori of morbidities associated with nutrition practices such as intraventricular haemorrhage, sepsis, bronchopulmonary dysplasia and neurodisability. Pēpi Māori may also experience different nutritional transitions in early life. In one recent Aotearoa New Zealand study, pēpi Māori transitioned off parenteral fluids more quickly than other ethnicities but were less likely to achieve a successful transition to mother's own milk only, with just 43% reaching this compared to 74% of Pacific and 70% of European infants. By day three, 55% of pēpi Māori had received alternative nutrition that was not mother's own milk, which was substantially higher than Pacific at 22%, European at 20% and Asian at 28%. Furthermore, pēpi Māori were significantly less likely to be exclusively breastmilk fed at discharge compared with European infants. These data highlight an urgent need for quality initiatives to support and encourage mothers of moderate- and late-preterm infants in their lactation. (2) Equity for Pacific families Implementing standardised parenteral nutrition practices in Aotearoa New Zealand will	

	contribute directly to reducing health disparities across all ethnicities and under-represented groups. While Pacific infants were more likely to successfully transition to mother's own milk only by comparison to Māori and European pēpi, 74% versus 43% and 70% respectively, they still had a high rate of receiving alternative nutrition by day three, with 22% affected. These findings highlight that variation in early nutrition practices affects all groups and addressing these differences through consistent care will promote more equitable outcomes for all preterm pēpi and their families. Equity for underrepresented groups Families who are migrants, live rurally or lack transport may find it difficult to provide breastmilk. Without flexible visiting policies or logistical support, participation may be limited. Equity calls for inclusive NICU policies and resources to ensure all families can benefit from lactation consultant support if needed. In the DIAMOND RCT, Asian infants also showed varied access to exclusive breastfeeding. These differences reflect broader systemic inequities in healthcare delivery and cultural support.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know	The acceptability of intravenous interventions, donor milk or infant formula to parents and health professionals may vary. Acceptability for Māori No additional data	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	The feasibility of intravenous interventions, donor milk or infant formula will vary depending on the neonatal unit. Feasibility for Māori No data available	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
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References

1. Alexander, T.; Meyer, M.; Harding, J.E.; Alsweiler, J.M.; Jiang, Y.; Wall, C.; Muelbert, M.; Bloomfield, F.H.; Group, D.S. Nutritional management of moderate- and late-preterm infants commenced on intravenous fluids pending mother's own milk: Cohort analysis from the DIAMOND trial. *Front Pediatr* **2022**, *10*, 817331, doi:10.3389/fped.2022.817331.
2. Alexander, T.; Asadi, S.; Meyer, M.; Harding, J.E.; Jiang, Y.; Alsweiler, J.M.; Muelbert, M.; Bloomfield, F.H.; Group, D.T. Nutritional support for moderate-to-late-preterm infants - A randomized trial. *N Engl J Med* **2024**, *390*, 1493-1504, doi:10.1056/NEJMoa2313942.
3. Das, S.; Bloomfield, F.; Alexander, T.; Jiang, Y.; Gamble, G.; Lin, L.; Harding, J.E. Effect of different feeding strategies on neurosensory impairment at 2 years' corrected age in children born moderate-and-late preterm: Follow-up of the DIAMOND randomised trial. In Proceedings of PSANZ conference proceedings; pp. 6-40.

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EtD 20. Should donor breastmilk vs. infant formula be used for preterm infants for whom there is insufficient mother's own breastmilk?

POPULATION:	Preterm infants for whom there is insufficient mother's own breastmilk
INTERVENTION:	Donor breastmilk
COMPARISON:	Infant formula
MAIN OUTCOMES:	Critical outcomes Mortality Necrotising enterocolitis Fully breastfed or breastmilk feeding at hospital discharge Time to full enteral feeds Faltering growth/body composition Duration of initial hospital stay Important but not critical Neurodevelopmental impairment Adverse effects Sepsis: proven or suspected Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	Mother's own breastmilk is the ideal nutrition for preterm infants, offering essential nutrients, growth factors, and immune protection that support gut maturation, reduce the risk of necrotising enterocolitis and promote neurodevelopment. When insufficient, substitutes such as donor breastmilk or infant formula are used to meet nutritional needs. For very low birthweight (VLBW, <1500 g) infants, both the American Academy of Pediatrics and European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) recommend donor breastmilk over infant formula, primarily due to lower necrotising enterocolitis rates. However, donor breastmilk, especially if pasteurised, is associated with slower postnatal weight gain compared to preterm formula. This is because donor breastmilk has nutritional deficits due to storage and pasteurisation for safety and its origin from mothers of older infants because expressed breastmilk from mothers of more mature infants has lower amounts of key nutrients. For example, protein, immunoglobulin, lactoferrin and insulin concentrations are lower in donor breastmilk. While moderate-to-late preterm infants are less fragile than VLBW infants, they may still benefit from donor breastmilk over formula, highlighting its potential role in improving outcomes across the preterm population. In Aotearoa, donor breastmilk is increasingly being used for preterm infants instead of infant formula. However, the macro- and micronutrient composition of donor breastmilk is largely unknown and represents a critical knowledge gap for healthcare providers for preterm infants.

CONFLICT OF INTERESTS:

The following DIAMOND study authors are on the Guideline Development Group: Tanith Alexander and Frank Bloomfield
The following McClintock *et al* systematic review co-authors are on the Guideline Development Group: Luling Lin and Frank Bloomfield

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know	Evidence taken from 2 systematic reviews [1,2] Bayley II Mental Development Index. Neither review looked at gestational age or birthweight as a subgroup Necrotising enterocolitis: RCT: Very large reduction in NEC for donor EBM (33 fewer per 1,000; 45 fewer to 17 fewer) [Critical]. The risk was reduced whether the donor milk was the entire diet or supplemented mother's own milk. Fully breastfed or breastmilk feeding at hospital discharge: Cohort: No clear difference between donor EBM supplementation and infant formula supplementation on exclusive breastfeeding rates at hospital discharge (5 cohort studies). There was possible benefit of donor EBM on the rates of any breastfeeding at hospital discharge (1 cohort study) [Critical]. No faltering growth/body composition: RCT: No difference between donor EBM supplementation and infant formula supplementation for weight at 18 months (MD 0.1 kg lower; 0.35 lower to 0.15 higher). No difference between donor EBM supplementation and infant formula supplementation for head circumference at 18 months (MD 0.1 cm lower; 0.39 lower to 0.19 higher) [Critical]. One additional pilot RCT reported outcomes related to infant growth. At 6–8 weeks chronological age, there was no difference in weight and length of both groups except for higher head circumference z-score in the infant formula group (Donor EBM -0.4 (1.3) vs. infant formula 0.4 (0.9), $p = 0.04$). Neurodevelopmental outcomes: RCT: Donor EBM has no significant effect on Bayley Mental Development Indices at 18 months (MD 1.24 points lower; 5.09 lower to 2.62 higher); Psychomotor Development Indices at 18 months (MD 0.32 points higher; 2.79 lower to 3.43 higher); Bayley-III assessments at 18 to 22 months' corrected age: Cognitive (MD 0.84 points lower), language (MD 0.53 points lower) and motor (MD 0.92 points lower). Donor EBM has no significant effect on cerebral palsy (1 fewer per 1,000; 28 fewer to 38 more); hearing impairment (1 fewer per 1,000; 24 fewer to 78 more); visual impairment (not estimable as no events); and severe neurodevelopmental disability as assessed by the Amiel-Tison 1986 classification (15 fewer per 1000; 50 fewer to 53 more) [Important]. Desirable effects for Māori The benefits of breastfeeding are well established and efforts to encourage women to breastfeed exclusively or partially should be encouraged.	Population information for included evidence McClintock <i>et al</i> [1] healthy infants, most studies included infants >35 weeks and some included term infants. In Quigley <i>et al</i> the population is very preterm or very low birthweight infants [2]. The trials associated with growth outcomes with donor milk as the sole diet are very old trials with 4/5 being conducted in the '70s and '80s. Sample sizes in these studies are also very small. Caution may be advised when interpreting these data.

Outcomes	N of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with infant formula	Risk difference with donor breastmilk
Mortality-All cause RCT	2116 (9 RCTs)	⊕⊕⊕○ Moderate ^a	RR 1.00 (0.76 to 1.31)	Study population 87 per 1,000	0 fewer per 1,000 (21 fewer to 27 more)
Necrotising enterocolitis RCT	2261 (10 RCTs)	⊕⊕⊕⊕ High	RR 0.53 (0.37 to 0.76)	Study population 71 per 1,000	33 fewer per 1,000 (45 fewer to 17 fewer)
Fully breastfed or breastmilk feeding at hospital discharge cohort	1966 (5 non-randomised studies)	⊕○○○ Very low ^{b,c}	-	No clear difference between donor breastmilk supplementation and infant formula supplementation on exclusive breastfeeding rates at hospital discharge (5 cohort studies). There was possible benefit of donor breastmilk on the rates of any breastfeeding at hospital discharge (1 cohort study).	
Time to full enteral feeds - not measured	-	-	-	-	-
Faltering growth/body composition RCT assessed with: In-hospital rate of weight gain (g/kg/day) until term equivalent	1360 (9 RCTs)	⊕⊕○○ Low ^d	-	The mean faltering growth/body composition RCT was 21.5 g/kg/day	MD 3.55 lower (4.21 lower to 2.89 lower)
Faltering growth/body composition RCT assessed with: In-hospital rate of head circumference growth (mm/week) until term equivalent	1261 (9 RCTs)	⊕⊕○○ Low ^e	-	The mean faltering growth/body composition RCT was 9.5 mm/wk	MD 0.69 lower (1.01 lower to 0.36 lower)
Faltering growth/body composition RCT assessed with: Weight at 18 months post term (kg)	438 (2 RCTs)	⊕⊕○○ Low ^{a,f}	-	The mean faltering growth/body composition RCT was 10.05 kg	MD 0.1 lower (0.35 lower to 0.15 higher)
Faltering growth/body composition RCT assessed with: Head circumference at 18 months post term (cm)	438 (2 RCTs)	⊕⊕○○ Low ^{a,f}	-	The mean faltering growth/body composition RCT was 47.95 cm	MD 0.1 lower (0.39 lower to 0.19 higher)
Duration of initial hospital stay Cohort	156 (1 non-randomised studies)	⊕○○○ Very low ^{b,c}	-	The mean duration of hospital stay cohort 2.86 days	MD 0.09 higher (0.32 lower to 0.50 higher)
Neurodevelopmental impairment RCT assessed with: Bayley II Mental Development Index at 18 months Scale from: 1 to 100	387 (2 RCTs)	⊕⊕○○ Low ^{a,f}	-	The mean neurodevelopmental impairment RCT: Bayley II Mental Development Index was 99.55 points	MD 1.24 lower (5.09 lower to 2.62 higher)
Neurodevelopmental impairment RCT assessed with: Bayley II Psychomotor Development Index at 18 months Scale from: 1 to 100	387 (2 RCTs)	⊕⊕○○ Low ^{a,f}	-	The mean neurodevelopmental impairment RCT: Bayley Psychomotor Developmental Index was 94.35 points	MD 0.32 higher (2.79 lower to 3.43 higher)

Neurodevelopmental impairment assessed with: Cerebral Palsy	1124 (4 RCTs)	 Low ^{a,f}	RR 0.99 (0.66 to 1.46)	Study population	
				82 per 1,000	1 fewer per 1,000 (28 fewer to 38 more)
Neurodevelopmental impairment assessed with: Hearing impairment	299 (1 RCT)	 Low ^{a,g}	RR 0.98 (0.29 to 3.32)	Study population	
				34 per 1,000	1 fewer per 1,000 (24 fewer to 78 more)
Neurodevelopmental impairment assessed with: Visual impairment	299 (1 RCT)	 Low ^{a,h}	not estimable - no events	Study population	
				0 per 1,000	0 fewer per 1,000 (0 fewer to 0 fewer)
Neurodevelopmental impairment assessed with: Neurodevelopmental disability at 18 months	400 (2 RCTs)	 Low ^{a,f}	RR 0.83 (0.43 to 1.60)	Study population	
				88 per 1,000	15 fewer per 1,000 (50 fewer to 53 more)
Adverse effects - not measured	-	-	-	-	
Sepsis proven or suspected - not measured	-	-	-	-	-
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-

- a. Downgraded one level due to imprecision with confidence intervals that cross the line of no effect, indicating potential benefit and harm.
b. Downgraded one level for risk of bias as included data from poorer designed retrospective cohort studies.
c. Downgraded one level as unable to judge as data were not pooled.
d. Downgraded two levels due to extremely high heterogeneity I² >80%
e. Downgraded two levels as I² = 76% and was high for both subgroups of donor milk as entire diet or as supplement to mothers own milk.
f. Downgraded one level for risk of bias due to lack of clarity on methodology including randomisation and blinding
g. Downgraded one level for indirectness as evidence is based on a single study with low event rates.
h. Downgraded one level for imprecision as there were no events recorded

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large	Evidence taken from 2 systematic reviews [1,2] Mortality: RCT: No significant effect on all-cause mortality (0 fewer per 1,000; 21 fewer to 27 more) [Critical]. Faltering growth/body composition: RCT: Donor EBM results in slower in-hospital weight gain	

○ Varies ○ Don't know	until term equivalent (MD 3.55 g/kg/day lower; 4.21 lower to 2.89 lower); donor breastmilk results in slower head circumference growth until term equivalent (MD 0.69 mm/week lower; 1.01 lower to 0.36 lower) [Critical]. Duration of initial hospital stay: Cohort: Little or no difference between donor EBM supplementation and infant formula supplementation on admission to NICU and length of hospital stay (MD 0.09 days higher; 0.32 lower to 0.50 higher. [Critical]) Undesirable effects for Māori The benefits of breastfeeding are well established and efforts to encourage women to breastfeed exclusively or partially should be encouraged.	
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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Some of the evidence is based on observational studies and some is based on older studies conducted over 40 years ago. High to very low certainty evidence overall Certainty of evidence for Māori There was no specific evidence relating to Māori but the overall the certainty of the evidence is very low.	

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality-All cause RCT	CRITICAL	⊕⊕⊕⊕ Moderate ^a
Necrotising enterocolitis RCT	CRITICAL	⊕⊕⊕⊕ High
Fully breastfed or breastmilk feeding at hospital discharge cohort	CRITICAL	⊕○○○ Very low ^{b,c}
Time to full enteral feeds - not measured	CRITICAL	-
Faltering growth/body composition RCT assessed with: In-hospital rate of weight gain (g/kg/day) until term equivalent	CRITICAL	⊕⊕○○ Low ^d
Faltering growth/body composition RCT assessed with: In-hospital rate of head circumference growth (mm/week) until term equivalent	CRITICAL	⊕⊕○○ Low ^e

Faltering growth/body composition RCT assessed with: Weight at 18 months post term (kg)	CRITICAL	⊕⊕○○ Low ^{a,f}
Faltering growth/body composition RCT assessed with: Head circumference at 18 months post term (cm)	CRITICAL	⊕⊕○○ Low ^{a,f}
Duration of initial hospital stay Cohort	CRITICAL	⊕○○○ Very low ^{b,c}
Neurodevelopmental impairment RCT assessed with: Bayley Mental Development Index at 18 months Scale from: 1 to 100	IMPORTANT	⊕⊕○○ Low ^{a,f}
Neurodevelopmental impairment RCT assessed with: Bayley Psychomotor Development Index at 18 months Scale from: 1 to 100	IMPORTANT	⊕⊕○○ Low ^{a,f}
Neurodevelopmental impairment assessed with: Cerebral Palsy	IMPORTANT	⊕⊕○○ Low ^{a,f}
Neurodevelopmental impairment assessed with: Hearing impairment	IMPORTANT	⊕⊕○○ Low ^{a,g}
Neurodevelopmental impairment assessed with: Visual impairment	IMPORTANT	⊕⊕○○ Low ^{a,h}
Neurodevelopmental impairment assessed with: Neurodevelopmental disability at 18 months	IMPORTANT	⊕⊕○○ Low ^{a,f}
Adverse effects - not measured	IMPORTANT	-
Sepsis proven or suspected - not measured	IMPORTANT	-
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Retinopathy of prematurity - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-

- a. Downgraded one level due to imprecision with confidence intervals that cross the line of no effect, indicating potential benefit and harm.
b. Downgraded one level as included data from poorer designed retrospective cohort studies.
c. Downgraded one level as unable to judge as data were not pooled.
d. Downgraded two levels due to extremely high heterogeneity I² >80%
e. Downgraded two levels as I² = 76% and was high for both subgroups of donor milk as entire diet or as supplement to mother's own milk.
f. Downgraded one level due to lack of clarity on methodology including randomisation and blinding
g. Downgraded one level as evidence is based on a single study with low event rates.
h. Downgraded one level as there were no events recorded

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability Values for Māori No additional research available	Critical outcomes Mortality Necrotising enterocolitis Fully breastfed or breastmilk feeding at hospital discharge Time to full enteral feeds Faltering growth/body composition Duration of initial hospital stay

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

Judgement	Research evidence	Additional considerations
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies	Donor EBM compared with infant formula - high certainty of evidence Large reduction in NEC Donor EBM compared with infant formula - moderate certainty of evidence Uncertain effect on mortality Donor EBM compared with infant formula - low certainty of evidence Uncertain effect on fully breastfed or breastmilk feeding at hospital discharge, weight gain and head circumference at 18 months, neurodevelopmental impairment, hypoglycaemia Reduction in weight gain and head circumference until term equivalent Donor EBM compared with infant formula - very low certainty of evidence Uncertain effect on duration of hospital stay.	

○ Don't know	Balance of effects for Māori No additional data	
Resources required		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	There are six active human breastmilk banks (all non-profit) in Aotearoa New Zealand, none of which are in Auckland (the largest, most populated city with two tertiary neonatal intensive care units). Screened unpasteurised EBM from peer-to-peer donation is available at both Auckland City and Middlemore Hospitals. Women may also rely on or rely on peer-to-peer donation via informal social networks. Donor EBM supplies (formal and informal) and milk banks are required. Other resources required include expressing and storage equipment, lactation consultant time Evidence from a mixed-method national survey (including 7.6% Māori) found that informal screening processes undertaken by parents and health professionals before informal human breastmilk donation were lifestyle including smoking status, medication, drug and alcohol intake (44% and 36%, respectively) (Harris 2024) [3]. No cost data available. Costs (for up to 100-120 days) Preterm infant formula \$3.24 per 100 mL (\$6 to \$15 per day, approx. \$500 to \$1500 per infant per admission of 100 days) Term infant formula \$1.16 to \$1.56 per 100 mL (\$2.08 to \$4.20 per day, approx. \$208 to \$420 per infant per admission of 100 days) Pasteurised donor milk from a Milk Bank is \$16 per 100 mL (\$29 to \$43 per day, approx. \$2,900 to \$4,300 per infant per admission of 100 days) Fortified donor breastmilk from a Milk Bank is \$23 per 100 mL (\$42 to \$62 per day, approx. \$4,200 to \$6,200 per infant per admission of 100 days) Cost difference for preterm formula vs. fortified pasteurised donor breastmilk is \$3,700 to \$4,700 per infant per admission (large) Cost difference for preterm formula vs. fortified unpasteurised donor breastmilk is negligible. Resources required by Māori Need for wāhine Māori women to donate milk and access to donated breastmilk for wāhine Māori.	Pasteurised Donor EBM estimated cost is \$16.00 per 100 mL (Christchurch Women's Hospital Milk Bank) Breastmilk fortifier \$3.75 per 100 mL Preterm infant formula (Liquid ready to feed) \$3.24 per 100 mL Term infant formula (Liquid ready to feed) \$1.56 per 100 mL
Certainty of evidence of required resources		

What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Costs are moderately certain. Certainty of evidence of resource requirements for Māori No evidence available.	Evidence from a mixed-method national survey found that costs associated with breastmilk donation are covered by a combination of health services, donor and recipient parents (5).
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No economic studies were identified to address the cost-effectiveness of the intervention or the comparison; however, the costs associated with one case of NEC requiring surgery and the potential ongoing consequences are substantial Cost effectiveness for Māori No evidence available.	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced	Equity for Māori There is inequity in access to donor milk for Māori, especially if they do not live in centres where there is a breastmilk bank. Whānau Māori in smaller, rural, or under-resourced regions, where	

○ Probably no impact ○ Probably increased ● Increased ○ Varies ○ Don't know	Māori make up a significant proportion of the population, are less likely to have access to donor milk. Urban tertiary NICUs may have milk banks but may not offer consistent or equitable eligibility criteria across ethnicities or income levels. In the DIAMOND trial, which investigated nutrition interventions to support moderate-late preterm infants pending full breastmilk feeding in Aotearoa New Zealand NICUs, pēpi Māori received infant formula more frequently and earlier than European infants, despite an intention to breastfeed being an entry criterion to the trial. By 3 days after birth, almost 50% of preterm pēpi Māori had received infant formula compared with 25% of European infants, indicating divergent treatment by ethnicity. Equity for Pacific families Pacific families also face inequities in access to donor breastmilk, and other ethnic minority groups may experience similar challenges, though data is sparse. Language barriers, lack of culturally appropriate information and systemic bias likely affect access for infants of other ethnicities, especially refugee and migrant communities. These families may experience clinicians defaulting to formula due to time/resource constraints, lack of clear discussion about donor milk as an option, cultural misunderstandings or stigma. Equity for underrepresented groups Migrant, refugee and rural families often lack access to hospital donor milk due to distance or low resourcing. Language barriers can hinder understanding of its safety and benefits. Equity means making donor milk universally available and ensuring families receive information in their own language to make informed, confident decisions.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Evidence from a mixed-method Aotearoa New Zealand national survey found that there was a high level of support for donor breastmilk among health professionals and donors. Almost all parents (98%) and health professionals (98%) supported the use of donor breastmilk in hospitals. Support for the use of donor breastmilk in the community was more common among parents (92%) than health professionals (87%), yet not statistically different (Harris 2024). There may be benefits to the donor for altruism (Harris 2024) [3]. The composition of donor breastmilk in Aotearoa New Zealand is unknown in relation to macro- and micronutrients.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Human breastmilk donation is already implemented in Aotearoa New Zealand so it is feasible but there are no national and standardised guidelines for milk sharing with informal breastmilk donation. Some regions have better access than others.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies

	JUDGEMENT						
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ●
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References

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3. Harris, S.; Bloomfield, F.H.; Muelbert, M. Formal and informal human milk donation in New Zealand: a mixed-method national survey. *Int Breastfeed J* **2024**, *19*, 61, doi:10.1186/s13006-024-00667-4.

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EtD 21. Should slower feed advancement vs. faster feed advancement be used for preterm infants who require enteral feeding?

POPULATION:	Preterm infants who require enteral feeding
INTERVENTION:	Slower feed advancement
COMPARISON:	Faster feed advancement
MAIN OUTCOMES:	Critical outcomes Mortality Necrotising enterocolitis Time to full enteral feeds Duration of initial hospital stay Fully breastfed or breastmilk feeding at hospital discharge Adverse effects – feed intolerance Important but not critical Neurodevelopmental impairment Faltering growth/body composition – especially length growth Sepsis: proven or suspected Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	Enteral feeding is essential to provide the necessary nutrients for growth and development. However, determining the optimal rate of feed advancement for preterm infants remains a significant clinical challenge. The speed of advancing feeds must balance the risk of gastrointestinal complications, such as feed intolerance and necrotising enterocolitis, with the benefits of earlier nutritional adequacy, reduced parenteral nutrition exposure and a shorter hospital stay. Faster feed advancement can reduce the time to achieve full enteral feeds and minimise reliance on parenteral nutrition, which is associated with risks such as infection and liver dysfunction. However, rapid progression may overwhelm the immature gastrointestinal system, increasing the risk of necrotising enterocolitis—a life-threatening condition that remains a leading cause of morbidity and mortality in preterm infants. Slower feed advancement is thought to reduce the risk of gastrointestinal complications by allowing the gut more time to adapt to enteral feeding. However, prolonged reliance on parenteral nutrition and increased risk of sepsis, and delayed achievement of full enteral feeds can all result in nutritional deficits, growth faltering and extended neonatal intensive care stays. While each infant needs individualised prescription of advances in enteral feeding based on the infant's clinical condition, gestational age, and tolerance to feeds, standardised feeding protocols on which to base these decisions are helpful and when used, have been shown to reduce necrotising

CONFLICT OF INTERESTS:	enterocolitis rates.
	None

Assessment

Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence based on a Cochrane systematic review [1], another systematic review [2], an additional RCT report from the SIFT trial [3] and an economic evaluation of the SIFT trial [4]. Note that the data as slow advancement being the intervention versus faster advancement as the comparator. Mortality: RCT: No difference in all-cause mortality in the slow-rate-of-advancement group (7 more per 1000; from 8 fewer to 27 more) [Critical]. Necrotising enterocolitis: RCT: Little or no effect on risk of NEC (3 more per 1000, 9 fewer to 20 more). Sensitivity analysis did not show any effect in extremely preterm or ELBW infants [Critical]. Time to full enteral feeds: RCT: Eleven trials reported that it took longer to establish full enteral feeds in infants in the slow-rate-of-advancement group (meta-analysis not possible) [Critical]. Neurodevelopmental impairment: RCT: No significant effect on moderate to severe disability (31 per 1,000 fewer; 64 fewer to 6 more). No significant reduction in neurodevelopmental impairment (slow advancement of enteral feed volumes) for cognitive impairment (19 per 1,000 fewer; 50 fewer to 19 more), in hearing impairment (16 per 1,000 fewer; 27 fewer to 1 more), or in visual impairment (5 per 1,000 fewer; 11 fewer to 8 more). No significant reduction in survival without moderate or severe neurodevelopmental disability at 24 months (26 fewer per 1,000; 59 fewer to 13 more) [Important]. Large reduction in risk of cerebral palsy (21 per 1,000 fewer; 33 fewer to 5 fewer). No faltering growth/body composition: RCT: Little or no effect on weight z-scores at hospital discharge (MD 0.00 points; 0.08 lower to 0.08 higher) or head circumference z-scores at hospital discharge (MD 0.00 points; 0.13 lower to 0.13 higher). Slow-rate-of-advancement group took a longer time to regain birthweight (meta-analysis not possible) [Important]. Desirable effects for Māori	Population information for included evidence The Cochrane review [1] included 14 RCTs that assessed effects of slow (up to 24 mL/kg/day) versus faster rates of advancement of enteral feed volumes in very preterm or VLBW infants. Trials typically defined slow advancement as daily increments of 15 to 24 mL/kg/day, and faster advancement as daily increments of 30 to 40 mL/kg/day. The other systematic review [2] included 12 RCTs. Slow feed advancement was defined as <30 mL/kg per day and compared with fast feed advancement ≥30 mL/kg per day. No additional studies identified. UK [3]: RCT: included very preterm or very-low-birth-weight infants.

	No additional data				
Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with faster feed advancement	Risk difference with slower feed advancement
Mortality: RCT assessed with: All-cause mortality prior to hospital discharge	3860 (13 RCTs)	⊕⊕⊕⊕ Moderate ^a	RR 1.10 (0.88 to 1.38)	Study population 71 per 1,000	7 more per 1,000 (8 fewer to 27 more)
Necrotising enterocolitis: RCT	4026 (14 RCTs)	⊕⊕⊕⊕ Moderate ^a	RR 1.06 (0.83 to 1.37)	Study population 54 per 1,000	3 more per 1,000 (9 fewer to 20 more)
Time to full enteral feeds: RCT	n not reported (11 RCTs)	⊕⊕○○ Low ^{a,b}	-	Eleven trials reported that it took longer to establish full enteral feeds in infants in the slow-rate-of-advancement group (meta-analysis not possible)	
Duration of initial hospital stay (RCT)	n not reported (10 RCTs)	⊕○○○ Very low ^{a,b}	-	Six trials reported no difference in duration of hospital stay between groups. Four trials reported that duration of hospital stay was longer amongst infants in the slow-rate-of-advancement group (meta-analysis not possible).	
Fully breastfed or breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Adverse effects (feed intolerance): RCT assessed with: Feed intolerance (causing interruption of enteral feeding)	719 (8 RCTs)	⊕⊕○○ Low ^{a,c}	RR 1.18 (0.95 to 1.46)	Study population 282 per 1,000	51 more per 1,000 (14 fewer to 130 more)
Survival without severe neurodevelopmental disability: RCT follow-up: 24 months	2470 (1 RCT)	⊕⊕○○ Low ^{a,d}	RR 0.96 (0.91 to 1.02)	Study population 655 per 1,000	26 fewer per 1,000 (59 fewer to 13 more)
Neurodevelopmental impairment: RCT assessed with: Cognitive impairment	2326 (1 RCT)	⊕○○○ Very low ^{a,c,d}	RR 0.93 (0.81 to 1.07)	Study population 266 per 1,000	19 fewer per 1,000 (50 fewer to 19 more)
Neurodevelopmental impairment: RCT assessed with: Hearing impairment	2315 (1 RCT)	⊕⊕○○ Low ^{a,d}	RR 0.69 (0.47 to 1.02)	Study population 51 per 1,000	16 fewer per 1,000 (27 fewer to 1 more)
Neurodevelopmental impairment: RCT assessed with: Visual impairment	2327 (1 RCT)	⊕○○○ Very low ^{a,c,d}	RR 0.75 (0.39 to 1.43)	Study population 18 per 1,000	5 fewer per 1,000 (11 fewer to 8 more)

Neurodevelopmental impairment: RCT assessed with: cerebral palsy	2183 (1 RCT)	 Low ^{a,d}	RR 0.60 (0.39 to 0.90)	Study population	
				54 per 1,000	21 fewer per 1,000 (33 fewer to 5 fewer)
Neurodevelopmental impairment: RCT assessed with: moderate or severe disability	2325 (1 RCT)	 Low ^{a,d}	RR 0.90 (0.79 to 1.02)	Study population	
				306 per 1,000	31 fewer per 1,000 (64 fewer to 6 more)
Faltering growth/body composition: RCT assessed with: Weight z score at hospital discharge	2602 (1 RCT)	 Low ^{a,d}	-	The mean faltering growth/body composition: RCT was -1.5 points	MD 0 (0.08 lower to 0.08 higher)
Faltering growth/body composition: RCT assessed with: Head circumference z score at hospital discharge	2286 (1 RCT)	 Very low ^{a,c,d}	-	The mean faltering growth/body composition: RCT was -0.8 points	MD 0 (0.13 lower to 0.13 higher)
Faltering growth/body composition: RCT assessed with: Time to regain birthweight	n not reported (10 RCTs)	 Low ^a	-	Ten trials reported that infants in the slow-rate-of-advancement group took a longer time to regain birthweight (meta-analysis not possible).	
Sepsis - not measured	-	-	-	-	-
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost: RCT assessed with: Total costs (£) of health service use after initial discharge from hospital and up to 24 months corrected age	2470 (1 RCT)	 Very low ^{a,c}	-	The mean cost: cost of intervention, cost of neonatal care and life-long cost: RCT was GBP 109,783 (total cost divided by sample size of arm)	MD 267 lower (6928 lower to 8117 higher)
Cost: cost of intervention, cost of neonatal care and life-long cost: RCT assessed with: Costs (£) of initial hospital care	2470 (1 RCT)	 Very low ^{a,d}	-	The mean cost: cost of intervention, cost of neonatal care and life-long cost: RCT was GBP 101,744 (total cost divided by sample size of arm)	MD 242 higher (6307 lower to 6251 higher)
Time to full sucking feeds (<0.5 days) - not measured	-	-	-	-	-

a. Downgraded one level for methodological concerns/risk of bias.

b. Downgraded one level for indirectness as studies had inconsistent reporting of no effect or increased duration of hospital stay.

c. Downgraded one level for imprecision with confidence intervals crossing the line of no effect

d. Downgraded one level for indirectness. Although this is a large study it is only based in the UK and results may not be generalisable to other settings

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Duration of hospital stay: RCT: Six trials reported no difference in duration of hospital stay between groups. Four trials reported that duration of hospital stay was longer amongst infants in the slow-rate-of-advancement group (meta-analysis not possible) [Critical]. Adverse effects (Feed intolerance): RCT: No significant increase in feed intolerance for slow advancement of enteral feed volumes (51 per 1,000 more; 14 fewer to 130 more) [Critical]. Cost: RCT: No significant increase in costs for slow advancement feeds compared with faster feeds (mean difference £247 higher; 6307 lower to 6251 higher) for costs of initial hospital care. No significant reduction in costs for slow advancement feeds compared with faster feeds (mean difference £267 lower; 6928 lower to 8117 higher) for total costs of health service use after initial discharge from hospital and up to 24 months corrected age [Important]. Undesirable effects for Māori	
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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	We have some concerns about the economic evaluation that was based on UK cost data only so may not be generalisable to Aotearoa New Zealand context. Some resource uses were self-reported by parents/caregivers but the proportion of responders was 69.5% which may have influenced the data. The use of self-reported parental data may also influence the findings. The confidence intervals associated with the costs are extremely wide and no statistical analysis of the data were conducted. The available trial data indicate that advancing enteral feed volumes slowly (daily increments up to 24 mL/kg/day) compared with faster rates probably does not reduce the risk of NEC, death, or feed intolerance in very preterm or VLBW infants. Advancing the volume of enteral feeds at faster rates (typically 30 to 40 mL/kg/day) shortens by several days the time taken to regain birthweight and establish full enteral feeds, and may slightly reduce the risk of late-onset invasive infection (low-certainty evidence) Moderate to very low certainty of evidence overall. Certainty of evidence for Māori	

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT assessed with: All-cause mortality prior to hospital discharge	CRITICAL	⊕⊕⊕○ Moderate ^a
Mortality: RCT assessed with: Survival without moderate or severe neurodevelopmental disability at 24 months	CRITICAL	⊕⊕○○ Low ^{a,b}
Necrotising enterocolitis: RCT	CRITICAL	⊕⊕⊕○ Moderate ^a
Time to full enteral feeds: RCT	CRITICAL	⊕⊕○○ Low ^{a,c}
Duration of initial hospital stay (RCT)	CRITICAL	⊕○○○ Very low ^{a,c,d}
Fully breastfed or breastmilk feeding at hospital discharge - not measured	CRITICAL	-
Adverse effects (feed intolerance): RCT assessed with: Feed intolerance (causing interruption of enteral feeding)	CRITICAL	⊕⊕○○ Low ^{a,e}
Survival without severe neurodevelopmental disability: RCT follow-up: 24 months	IMPORTANT	⊕⊕○○ Low ^{a,b}
Neurodevelopmental impairment: RCT assessed with: Cognitive impairment	IMPORTANT	⊕○○○ Very low ^{a,b,e}
Neurodevelopmental impairment: RCT assessed with: Hearing impairment	IMPORTANT	⊕⊕○○ Low ^{a,b}
Neurodevelopmental impairment: RCT assessed with: Visual impairment	IMPORTANT	⊕○○○ Very low ^{a,b,e}
Neurodevelopmental impairment: RCT assessed with: cerebral palsy	IMPORTANT	⊕⊕○○ Low ^{a,b}
Neurodevelopmental impairment: RCT assessed with: moderate or severe disability	IMPORTANT	⊕⊕○○ Low ^{a,b}
Faltering growth/body composition: RCT assessed with: Weight z score at hospital discharge	IMPORTANT	⊕⊕○○ Low ^{a,b}
Faltering growth/body composition: RCT assessed with: Head circumference z score at hospital discharge	IMPORTANT	⊕○○○ Very low ^{a,b,e}
Faltering growth/body composition: RCT	IMPORTANT	⊕⊕○○

assessed with: Time to regain birthweight		Low ^{a,c}
Sepsis - not measured	IMPORTANT	-
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Retinopathy of prematurity - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost: RCT assessed with: Total costs of health service use after initial discharge from hospital and up to 24 months corrected age	IMPORTANT	⊕○○○ Very low ^{a,e}
Time to full sucking feeds (<0.5 days) - not measured	NOT IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost: RCT assessed with: Costs of initial hospital care		⊕○○○ Very low ^{a,b}

- a. Downgraded one level for methodological concerns/risk of bias.
b. Downgraded one level for imprecision. Although this is a large study it is only based in the UK and results may not be generalisable to other settings
c. Downgraded as unable to judge as meta-analysis not possible.
d. Downgraded one level as studies had inconsistent reporting of no effect or increased duration of hospital stay.
e. Downgraded one level for imprecision with confidence intervals crossing the line of no effect

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ Important uncertainty or variability ☒ Possibly important uncertainty or variability ☐ Probably no important uncertainty or variability ☐ No important uncertainty or variability	Possibly important uncertainty or variability. Values for Māori No data available	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Slow advancement of enteral feed volumes - moderate certainty of evidence Uncertain effect for all-cause mortality Probably has little or no effect on NEC Slow advancement of enteral feed volumes - low certainty of evidence Reduction in cerebral palsy Longer time to full enteral feeds, longer time to regain birthweight Uncertain effect on adverse effects (feeding intolerance); neurodevelopmental impairment (hearing impairment); survival without severe neurodevelopmental disability at 24 months No effect on faltering growth/body composition (weight z score at discharge) Slow advancement of enteral feed volumes - very low certainty of evidence Uncertain effect on duration of initial hospital stay, neurodevelopmental impairment (cognitive impairment, visual impairment), No effect on faltering growth/body composition (head circumference z score discharge) Balance of effects for Māori No additional data	Low certainty evidence of an increased risk of neurodevelopmental impairment at 24 months in the 1 trial (the SIFT trial) that reported this outcome. Additionally, the SIFT trial found an increased risk of moderate to severe motor impairment in the faster feed advancement group. These findings need to be interpreted with extra caution for three reasons. Both fast and slow groups in the SIFT trial had about 200 participants that were lost to follow-up and did not complete the neurodevelopment assessment. As the neurodevelopment status of this substantial portion of participants was unavailable, we should be careful in interpreting the finding and drawing conclusions. There was no significant difference in the primary outcome of survival without moderate or severe neurodevelopmental disability at 24 months in the SIFT trial. These findings are from a single trial and may have occurred by chance as it was 1 of many secondary outcomes assessed and was not a prespecified trial outcome.

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Parenteral nutrition costs \$55 to \$105 per day, depending on region and policies for hang time. Enteral nutrition costs at 180 mL/kg/day \$2 to \$62 per day, depending on feed type Term infant formula \$2 to \$5 per day Preterm infant formula \$6 to \$15 per day Fortified mother's own milk (fortifier \$3.75 per 100 mL) \$5.80 to \$9 per day Pasteurised donor milk from a Milk Bank (\$16 per 100 mL) \$29 to \$43 per day Fortified donor milk from a Milk Bank (\$23 per 100 mL) \$42 to \$62 per day Slower feed advancement costs \$10 to \$103 per extra day on parenteral nutrition, depending on feed type Resources required for Māori	

	No additional data	
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	A formal assessment of the certainty of evidence of the cost was not undertaken. Certainty of evidence of required resources for Māori No additional data	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	There are no studies that assess the specific cost-effectiveness of slower compared with faster feed advancement, particularly in the context of preterm infants. Cost effectiveness for Māori No additional data	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact	Equity for Māori Whānau Māori want the very best health outcomes for their pēpi. Whānau Māori experience racism within the health system. When healthcare professionals need to	

○ Probably increased ○ Increased ○ Varies ○ Don't know	provide observations, it is important to ensure that this is communicated with whānau Māori in a mana-enhancing way. Equity for Pacific families Pacific infants may experience inconsistent feeding approaches across hospitals, particularly where clinical staffing or guidelines vary. Pacific families may not receive clear explanations about the reasons for feed advancement decisions. Equity requires consistent protocols and culturally inclusive communication that empowers Pacific families to understand and support feeding progression. Equity for underrepresented groups Families from migrant or rural communities may be unfamiliar with the concept of feed advancement and its risks or benefits. Without accessible information or consistent care, they may feel anxious or excluded. Standardised guidelines and inclusive education are essential to ensure all infants benefit equally from safe and timely feeding practices.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Some parents are concerned when feeds increase at a rate that they perceive as too slow or fast. Acceptability for Māori No additional data	

Feasibility

Is the intervention feasible to implement?

Judgement	Research evidence	Additional considerations
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Faster advancement of enteral feeds requires the production of sufficient expressed breastmilk. Feasibility for Māori No additional data	

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Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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2. Yang, W.C.; Fogel, A.; Lauria, M.E.; Ferguson, K.; Smith, E.R. Fast feed advancement for preterm and low birth weight infants: A systematic review and meta-analysis. *Pediatrics* **2022**, *150*, doi:10.1542/peds.2022-057092G.
3. Dorling, J.; Abbott, J.; Berrington, J.; Bosiak, B.; Bowler, U.; Boyle, E.; Embleton, N.; Hewer, O.; Johnson, S.; Juszczak, E., et al. Controlled trial of two incremental milk-feeding rates in preterm infants. *N Engl J Med* **2019**, *381*, 1434-1443, doi:10.1056/NEJMoa1816654.
4. Tahir, W.; Monahan, M.; Dorling, J.; Hewer, O.; Bowler, U.; Linsell, L.; Partlett, C.; Berrington, J.E.; Boyle, E.; Embleton, N., et al. Economic evaluation alongside the Speed of Increasing milk Feeds Trial (SIFT). *Arch Dis Child Fetal Neonatal Ed* **2020**, *105*, 587-592, doi:10.1136/archdischild-2019-318346.

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EtD 22. Should routine gastric aspiration before feeds vs. no routine gastric aspiration before feeds be used for preterm infants who require enteral feeding?

POPULATION:	Preterm infants who require enteral feeding
INTERVENTION:	Routine gastric aspiration before feeds
COMPARISON:	No routine gastric aspiration before feeds
MAIN OUTCOMES:	Critical outcomes Mortality Necrotising enterocolitis Time to full enteral feeds Duration of initial hospital stay Fully breastfed or breastmilk feeding at hospital discharge Faltering growth/body composition Sepsis: proven or suspected Adverse effects Important but not critical Neurodevelopmental impairment Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	In neonatal care, it is common to check how much milk remains in an infant's stomach before their next feed by aspirating it through a feeding tube. This is done to see if the infant is tolerating their feeds, as a large volume of leftover milk or unusual coloured aspirate might indicate feeding problems or necrotising enterocolitis, a serious condition in preterm infants. If concerns arise, feeds may be reduced or stopped to lower these risks. However, this practice is debated. Stomach contents can vary a lot and don't always reliably signal feed intolerance or necrotising enterocolitis. Routine gastric aspiration may disrupt the gastrointestinal tract's natural processes, delay the progression of enteral feeds and increase the risk of infection due to frequent handling of feeding tubes. Additionally, withholding feeds based on aspiration findings could prolong dependence on parenteral nutrition, increasing the risks of associated complications such as infection and liver dysfunction. It is also unclear whether the gastric aspirate should be returned to the infant's stomach or discarded. The absence of routine gastric aspiration has been associated with more rapid advancement to full enteral feeding and earlier discharge in some studies. However, concerns remain about the

	potential for missed early signs of necrotising enterocolitis in the absence of routine aspiration.
CONFLICT OF INTERESTS:	None

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence is based on two Cochrane systematic reviews [1,2]. Re-feeding gastric residual compared with discarding the gastric residual Mortality: RCT: No significant reduction on all-cause mortality before hospital discharge for re-feeding gastric residuals (83 fewer deaths per 1,000; 143 fewer to 142 more) [Critical]. Necrotising enterocolitis: RCT: No significant reduction on risk of necrotising enterocolitis stage ≥ 2 or spontaneous intestinal perforation with re-feeding gastric residuals (56 fewer per 1,000; 146 fewer to 202 more) [Critical]. Time to reach full enteral feeds: RCT: No significant reduction in time to establish enteral feeds ≥ 120 mL/kg/day for re-feeding gastric residuals (MD 1.3 days lower; 2.93 lower to 0.33 higher) [Critical]. Duration of initial hospital stay: RCT: No significant reduction in duration of hospital stay with re-feeding gastric residuals (MD 1.9 days lower; 25.27 lower to 21.47 higher) [Critical]. No faltering growth/body composition: RCT: No significant effect in time to regain birthweight for re-feeding gastric residuals may result in (MD 0.4 days higher; 2.89 lower to 3.69 higher) [Critical]. Quality and volume of gastric aspirate compared with quality alone Time to reach full enteral feeds: RCT: Little or no effect on time to establish full enteral feeds between using quality and volume of gastric aspirate compared with quality alone (MD -0.10 days, 0.91 lower to 0.71 higher) [Critical].	Population information for included evidence Routine monitoring versus no routine monitoring of gastric residual in preterm infants [2]. Cochrane systematic review. Three studies were performed in infants with birthweight of $<1,500$ g, while one study included infants with birthweight between 750 g and 2,000 g. The trials were unmasked but were otherwise of good methodological quality. Quality and volume of gastric residual compared to quality of gastric residual alone for feed interruption in preterm infants [2]. Cochrane systematic review. One trial with 87 preterm infants met the inclusion criteria for this comparison. The trial included infants with 1,500 g to 2,000 g birthweight. Re-feeding versus discarding gastric residuals in preterm infants [1]. Systematic review: Preterm infants (23 to 28 weeks' gestation).

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with the absence of regular gastric aspiration before feeds	Risk difference with routine gastric aspiration before feeds
Mortality: RCT: assessed with: All-cause mortality before hospital discharge: Refeed/discard	72 (1 RCT)	⊕○○○ Very low ^{a,b}	RR 0.50 (0.14 to 1.85)	Study population	
				167 per 1,000	83 fewer per 1,000

					(143 fewer to 142 more)
Mortality: RCT assessed with: All-cause mortality before discharge: Quality + Volume/quality	87 (1 RCT)	⊕○○○ Very low ^{a,c}	RR 3.21 (0.13 to 76.67)	Study population	
				0 per 1,000	Not estimable
Mortality: RCT assessed with: All-cause mortality before discharge: Monitor/not monitor	80 (1 RCT)	⊕○○○ Very low ^{b,d}	RR 1.25 (0.36 to 4.32)	Study population	
				100 per 1,000	25 more per 1,000 (64 fewer to 332 more)
Necrotising enterocolitis: RCT assessed with: Refeed/discard	72 (1 RCT)	⊕○○○ Very low ^{a,b}	RR 0.71 (0.25 to 2.04)	Study population	
				194 per 1,000	56 fewer per 1,000 (146 fewer to 202 more)
Necrotising enterocolitis: RCT assessed with: Quality + Volume/quality	87 (1 RCT)	⊕○○○ Very low ^{a,e}	RR 5.35 (0.26 to 108.27)	Study population	
				0 per 1,000	Not estimable
Necrotising enterocolitis: RCT assessed with: Monitor/not monitor	141 (2 RCTs)	⊕○○○ Very low ^{d,e}	RR 3.07 (0.50 to 18.77)	Study population	
				14 per 1,000	29 more per 1,000 (7 fewer to 250 more)
Time to full enteral feeds: RCT assessed with: Time to establish full enteral feeds (120 mL/kg/day) Days: Refeed/discard	59 (1 RCT)	⊕○○○ Very low ^{a,b}	-	The mean time to full enteral feeds: RCT was 11.3 days	MD 1.3 lower (2.93 lower to 0.33 higher)
Time to full enteral feeds: RCT assessed with: Days; monitoring/no monitoring	141 (2 RCTs)	⊕⊕⊕○ Moderate ^d	-	The mean time to full enteral feeds: RCT was 17.05 days	MD 3.92 higher (2.06 higher to 5.77 higher)
Time to full enteral feeds: RCT assessed with: Days; Quality + Volume/quality	87 (1 RCT)	⊕○○○ Very low ^{a,b}	-	The mean time to full enteral feeds: RCT was 7.1 days	MD 0.1 lower (0.91 lower to 0.71 higher)
Duration of initial hospital stay: RCT assessed with: Days: Refeed/discard	59 (1 RCT)	⊕○○○ Very low ^{a,c}	-	The mean duration of initial hospital stay: RCT was 93.5 days	MD 1.9 lower (25.27 lower to 21.47 higher)
Duration of initial hospital stay: RCT assessed with: Days: Monitoring/no monitoring	80 (1 RCT)	⊕○○○ Very low ^{a,c,d}	-	The mean duration of initial hospital stay: RCT was 31.3 days	MD 3.2 higher (4.45 lower to 10.85 higher)
Fully breastfed or breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Faltering growth/body composition: RCT: Refeed/discard assessed with: Time to regain birthweight (days)	59 (1 RCT)	⊕○○○ Very low ^{a,c}	-	The mean faltering growth/body composition: RCT: Refeed/discard was 14.5 days	MD 0.4 higher (2.89 lower to 3.69 higher)
Faltering growth/body composition assessed with: Time to regain birthweight (days); monitoring/no monitoring	80 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition was 9.8 days	MD 1.7 higher (0.01 higher to 3.39 higher)

Faltering growth/body composition assessed with: Time to regain birthweight (days); Quality + Volume/quality	87 (1 RCT)	⊕○○○ Very low ^{a,b}	-	The mean faltering growth/body composition was 11 days	MD 1 higher (0.37 lower to 2.37 higher)
Sepsis: proven or suspected - not measured	-	-	-	-	-
Adverse effects - not measured	-	-	-	-	-
Neurodevelopmental impairment - not measured	-	-	-	-	-
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-

- a. Downgraded one level for indirectness as evidence is based on a single trial
b. Downgraded one level for imprecision with confidence intervals crossing the line of no effect
c. Downgraded two levels for extremely wide confidence intervals that cross the line of no effect
d. Downgraded one level for concerns for risk of bias
e. Downgraded two levels for imprecision due to extremely wide confidence intervals that cross the line of no effect; downgraded one level for imprecision due to very low/no event rates

Desirable effects for Māori

No additional evidence available

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	Routine monitoring compared with no monitoring Mortality: RCT: No significant increase for all-cause mortality before hospital discharge for routine monitoring of gastric residual (25 more deaths per 1,000; 64 fewer to 332 more) [Critical]. Necrotising enterocolitis: RCT: No significant increase in risk of NEC for routine monitoring of gastric residual (19 more per 1,000; 7 fewer to 250 more) [Critical]. Time to reach full enteral feeds: RCT: Large increase in the time to establish full enteral feeds for routine monitoring of gastric residual (MD 3.92 days higher, 2.063 higher to 5.77 higher) [Critical]. Duration of initial hospital stay: RCT: No significant increase in duration of hospital stay	Abiramalatha 2023b Routine monitoring versus no routine monitoring of gastric residual in preterm infants Four RCTs with 336 preterm infants met the inclusion criteria for this comparison. Three studies were performed in infants with birthweight of <1500 g, while one study included infants with birthweight between 750 g and 2000 g. The trials were unmasked but were otherwise of good methodological quality.

	with monitoring (MD 3.2 higher; 4.45 lower to 10.85 higher) [Critical]. No faltering growth/body composition: RCT: Increased time to regain birthweight for routine monitoring of gastric residual (MD 1.7 days, 0.01 higher to 3.39 higher) [Critical]. Quality and volume of gastric aspirate compared with quality alone Mortality: RCT: Little or no effect for using quality and volume of gastric aspirate compared with quality alone may result in little or no difference in all-cause mortality before hospital discharge (Unable to calculate absolute effect due to low or no events) [Critical]. Necrotising enterocolitis: RCT: Little or no difference in the incidence of NEC between quality and volume of gastric aspirate compared with quality alone (Unable to calculate absolute effect due to low or no events) [Critical]. Undesirable effects for Māori No additional evidence available	Abiramalatha 2023b Quality and volume of gastric residual compared to quality of gastric residual alone for feed interruption in preterm infants One trial with 87 preterm infants met the inclusion criteria for this comparison. The trial included infants with 1,500 g to 2,000 g birthweight.
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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Re-feeding gastric residual compared with discarding - Very low certainty evidence overall Quality and volume of gastric aspirate compared with quality alone - Very low certainty evidence overall Routine monitoring compared with no monitoring - Moderate to very low certainty evidence overall	Further RCTs are warranted to assess the effect on long-term growth and neurodevelopmental outcomes.

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT: assessed with: All-cause mortality before hospital discharge: Refeed/discard	CRITICAL	⊕○○○ Very low ^{a,b}
Mortality: RCT assessed with: All-cause mortality before discharge: Quality + Volume/quality	CRITICAL	⊕○○○ Very low ^{a,c}
Mortality: RCT assessed with: All-cause mortality before discharge: Monitor/not monitor	CRITICAL	⊕○○○ Very low ^{b,d}
Necrotising enterocolitis: RCT assessed with: Refeed/discard	CRITICAL	⊕○○○ Very low ^{a,b}
Necrotising enterocolitis: RCT	CRITICAL	⊕○○○

assessed with: Quality + Volume/quality		Very low ^{a,e}
Necrotising enterocolitis: RCT assessed with: Monitor/not monitor	CRITICAL	⊕○○○ Very low ^{d,e}
Time to full enteral feeds: RCT assessed with: Time to establish full enteral feeds (120 mL/kg/day) Days: Refeed/discard	CRITICAL	⊕○○○ Very low ^{a,b}
Time to full enteral feeds: RCT assessed with: Days; monitoring/no monitoring	CRITICAL	⊕⊕⊕○ Moderate ^d
Duration of initial hospital stay: RCT assessed with: Days: Refeed/discard	CRITICAL	⊕○○○ Very low ^{a,c}
Fully breastfed or breastmilk feeding at hospital discharge - not measured	CRITICAL	-
Faltering growth/body composition: RCT: Refeed/discard assessed with: Time to regain birthweight (days)	CRITICAL	⊕○○○ Very low ^{a,c}
Faltering growth/body composition assessed with: Time to regain birthweight (days); monitoring/no monitoring	CRITICAL	⊕○○○ Very low ^{a,d}
Faltering growth/body composition assessed with: Time to regain birthweight (days); Quality + Volume/quality	CRITICAL	⊕○○○ Very low ^{a,b}
Sepsis: proven or suspected - not measured	CRITICAL	-
Adverse effects - not measured	CRITICAL	-
Neurodevelopmental impairment - not measured	IMPORTANT	-
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Retinopathy of prematurity - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-
a. Downgraded one level as evidence is based on a single trial b. Downgraded one level for imprecision with confidence intervals crossing the line of no effect c. Downgraded two levels for extremely wide confidence intervals that cross the line of no effect d. Downgraded one level for concerns for risk of bias e. Downgraded two levels for imprecision due to extremely wide confidence intervals that cross the line of no effect; downgraded one level for imprecision due to very low/no event rates Certainty of evidence for Māori No additional evidence available		

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability Values for Māori No additional evidence available	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ● Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Re-feeding gastric residual compared with discarding - Very low certainty evidence Uncertain effect for all-cause mortality before hospital discharge, faltering growth/body composition (time to regain birthweight), NEC, time to full enteral feeds, duration of initial hospital stay Quality and volume of gastric aspirate compared with quality alone - Very low certainty evidence Uncertain effect for all-cause mortality before hospital discharge, necrotising enterocolitis, time to full enteral feeds, faltering growth/body composition (regain birthweight) Routine monitoring compared with no monitoring - Moderate certainty evidence Increases time to establish full enteral feeds Routine monitoring compared with no monitoring - Very low certainty evidence Uncertain effect for all-cause mortality before hospital discharge, necrotising enterocolitis, duration of initial hospital stay Increases time to regain birthweight Benefits of effects for Māori No additional evidence available	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Minimal extra resources are required to measure aspirates. Resources required for Māori No additional evidence available	
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Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	A formal assessment of the certainty of evidence of the cost was not undertaken. Certainty of the evidence of resource requirements for Māori No additional evidence available	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	There are no studies that assess the specific cost-effectiveness of gastric aspiration compared with no gastric aspiration, particularly in the context of preterm infants. Cost-effectiveness for Māori No additional evidence available	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Preterm pēpi Māori may be impacted by systemic inequities in how feeding practices like gastric aspiration are applied. While there is limited ethnicity-specific data on gastric aspiration, broader evidence shows pēpi Māori often receive less consistent, evidence-based neonatal care. If clinical decisions around aspiration are influenced by variable protocols, clinician bias, or inconsistent communication with whānau, pēpi Māori may experience delayed feed progression or unnecessarily increased discomfort. Moreover, a lack of culturally safe communication may limit parental involvement in decisions about feeding procedures, contributing to inequitable care experiences and outcomes for whānau Māori in neonatal settings. Equity for Pacific families Pacific and other ethnic minority families may face similar inequities in the use of gastric aspiration before feeds for preterm infants. Differences in hospital protocols, coupled with language barriers and limited culturally tailored communication, may reduce family understanding or participation in decisions around feeding practices. Pacific infants, who are also more likely to be born preterm, may be exposed to unnecessary or inconsistent interventions if equity is not actively addressed. Refugee and migrant families may face additional barriers due to unfamiliarity with hospital systems. Equity for underrepresented groups Routine procedures like gastric aspirates may not be explained to families with language or health literacy barriers. Underrepresented groups may be less likely to question unfamiliar practices. Equity demands clear, compassionate communication and consistent protocols that ensure all families understand and feel confident in the care their baby receives.	

Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies	Current monitoring practice in Aotearoa New Zealand varies with some units only checking quality and some checking quality and volume. There may be reluctance to stop monitoring. Acceptability for Māori	

○ Don't know	No additional evidence available	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	A change in monitoring practice is probably feasible with clear guidance.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF	Very low	Low	Moderate	High			No included studies

	JUDGEMENT						
REQUIRED RESOURCES							
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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References

1. Abiramalatha, T.; Thanigainathan, S.; Ramaswamy, V.V.; Rajaiah, B.; Ramakrishnan, S. Re-feeding versus discarding gastric residuals to improve growth in preterm infants. *Cochrane Database Syst. Rev.* **2023**, *6*, Cd012940, doi:10.1002/14651858.CD012940.pub3.
2. Abiramalatha, T.; Thanigainathan, S.; Ramaswamy, V.V.; Rajaiah, B.; Ramakrishnan, S. Routine monitoring of gastric residual for prevention of necrotising enterocolitis in preterm infants. *Cochrane Database Syst. Rev.* **2023**, *6*, Cd012937, doi:10.1002/14651858.CD012937.pub3.

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EtD 23. Should continuous feeds or bolus feeds be used in preterm infants who require enteral feeding?

POPULATION:	Preterm infants who require enteral feeding
INTERVENTION:	Continuous feeds
COMPARISON:	Bolus feeds
MAIN OUTCOMES:	Critical outcomes Mortality Necrotising enterocolitis Time to full enteral feeds Duration of initial hospital stay Adverse effects Important but not critical Fully breastfed or breastmilk feeding at hospital discharge Faltering growth/body composition Sepsis: proven or suspected Neurodevelopmental impairment Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	Enteral feeding practices such as continuous feeding or bolus (or compressed/pump) feeding, are used to optimise nutrient delivery and support growth while minimising the risk of complications like necrotising enterocolitis and feed intolerance. Continuous feeding involves delivering milk at a constant rate over a 24-hour period, mimicking a more gradual nutrient delivery to the immature gut, such as the swallowing of amniotic fluid in <i>utero</i>. This approach is thought to reduce the stress on the gastrointestinal and respiratory systems and may improve feed tolerance. Continuous feeding is also hypothesised to lower the risk of necrotising enterocolitis by avoiding large volumes entering the stomach at one time, which could overstimulate the gut. In contrast, bolus or compressed feeding delivers milk at specific intervals, typically over a short duration, mimicking the natural intermittent feeding pattern seen in healthy term infants. Bolus feeding may promote cyclical gut motility and hormonal responses, supporting gastrointestinal maturation. However, it has been associated with a higher risk of feeding intolerance in some preterm infants due to the larger, intermittent volume. Compressed or pump feeding delivers milk or over

an extended period (e.g. a 2 hourly bolus feed over 60 minutes) using an electronic enteral feeding pump and can be used as a transition between continuous and bolus feeds. Evidence comparing these feeding methods is limited and inconsistent. Some studies suggest that continuous feeding may improve feed tolerance and reduce the time to achieve full enteral feeding, while others indicate no significant difference between continuous and bolus feeding in terms of necrotising enterocolitis incidence or overall clinical outcomes.

CONFLICT OF INTERESTS:

None

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence based on a Cochrane systematic review [1]. We also present evidence from 2 recent RCTs [2,3] and a cohort study [4]. Duration of initial hospital stay: RCT: No significant reduction in days to discharge compared to intermittent feeding (MD 1.55 days lower; 5.13 lower to 2.02 higher). Single RCT: No difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for median (IQR) length of hospital stay, respectively (44 (29.5-62.5); 50 (32.5-70); 43 (26-64.7) Days; n=146 infants) [Important]. Adverse effects - Feeding intolerance: RCT: No significant reduction in number of days of feeding interruptions for continuous feeding (MD 3.00 days lower, 9.50 lower to 3.50 higher). Single RCT: The number of occurrences in which gastric residual volume exceeded 50% was significantly lower in the slow infusion feeding group compared with intermittent bolus feeding (1.12 ± 1.56 vs. 2.15 ± 1.4, $p = 0.01$, n=106). Single RCT: The proportions of infants who developed feeding intolerance in continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups were similar (n [%]: 21 [51.2%], 20 [52.6%], and 22 [64.7%], respectively, n=146 infants) [Critical]. No faltering growth/body composition: RCT: Weight: Little or no effect in days to regain birthweight for continuous feeds (MD 0.38 days lower; 1.16 lower to 0.41 higher). The test for subgroup differences did not suggest variation in effect according to birthweight. Single RCT: The time to gain birthweight was significantly shorter in the slow infusion feeding group compared with intermittent bolus feeding (10.8 ± 3.2 versus 12.7 ± 4.17; $p = 0.01$, n=106). Single RCT: No difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for median time to regain birthweight (IQR), respectively (9 (6-12); 11 (6.5-13); 10 (7-12) Days; n=146 infants). Little or no effect on rate of gain in weight between groups (standardised mean difference (SMD) 0.09 Standard deviation (SD), 0.27 lower to 0.46 higher). The result of the test for subgroup differences suggests there may be a variation in effect between birthweight categories ($p=0.01$, $I^2 = 72.4\%$). However, since only one trial (93 infants) provided data stratified by birthweight	Population information for included evidence Population comprised infants <1500 g [1] Turkey [2]: RCT: Preterm infants with a gestational age between 24 + 0 and 31 + 6 India [2,3]: RCT: Preterm infants ≤ 32 weeks and $\leq 1,250$ g South Korea [4]: Cohort study: Birthweights <1,500 g or gestational ages <32 weeks' Premji 2021: Type(s) of milk feeds varied, including breastmilk (either mother's own milk or pasteurised donor breastmilk), preterm formula, or mixed feeding regimens. In some instances, preterm formula was initially diluted. Earlier studies also used water to initiate feedings. Kumar 2024 reported no differences in reported outcomes for infants $\leq 1,000$ g.

	category, the difference between subgroups may be due to chance. Single RCT: No difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for mean (SD) weight growth velocity (g/kg/day), respectively (13.6 (3.3); 13.2 (3.6); 14.1 (2.9); n=146 infants) [Important]. No faltering growth/body composition: RCT: Length: Little or no difference in rate of gain in length compared with intermittent feeding (MD 0.02 cm/week, 0.04 lower to 0.08 higher). The test for subgroup differences did not suggest variation in effect according to birthweight (P = 0.54, I² = 0%). Single RCT: No difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for mean (SD) length increment (cm/week), respectively (0.73 (0.17); 0.75 (0.17); 0.77 (0.17); n=146 infants) [Important]. No faltering growth/body composition: RCT: Head circumference. Little or no difference in rate of gain in head circumference compared with intermittent feeding (MD 0.01 cm/week, 0.03 lower to 0.05 higher). The test for subgroup differences did not suggest there may be variation in effect according to birthweight (P = 0.72, I² = 0%). Single RCT: No difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for mean (SD) head circumference, respectively (0.66 (0.12); 0.61 (0.14); 0.62 (0.14) cm; n=146 infants) [Important]. Sepsis: Suspected or proven: No difference in late-onset sepsis for continuous feeds versus intermittent feeds (28% vs. 28.3%) [Important]. Desirable effects for Māori No additional evidence available	
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Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with bolus feeds	Risk difference with and EG 2.1 continuous feeds
Mortality: RCT	146 (1 RCT)	⊕⊕⊕○ Moderate ^a	-	There was no difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for n (%) mortality respectively (4 (8.2%); 7 (14.3%); 5 (10.4%); n=146 infants).	
Necrotising enterocolitis: RCT	372 (5 RCTs)	⊕○○○ Very low ^{b,c,d}	RR 1.19 (0.67 to 2.11)	Study population	
				96 per 1,000	18 more per 1,000 (32 fewer to 107 more)
Necrotising enterocolitis: RCT	146 (1 RCT)	⊕⊕⊕○ Moderate ^e	-	There was no difference in necrotizing enterocolitis ≥ stage 2 n (%) between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups (1 (2%); 2 (4.1%); 2 (4.2%), n=146 infants).	
Time to full enteral feeds: RCT assessed with: Age at full enteral feedings days)	628 (7 RCTs)	⊕○○○ Very low ^{a,b,f}	-	The mean time to full enteral feeds: RCT was 27.65 days	MD 0.84 higher (0.13 lower to 1.81 higher)
Time to full enteral feeds: RCT	103	⊕○○○	-	The time to achieve full enteral feeding was similar between slow infusion feeding	

assessed with: Days to achieve full enteral feeding	(1 RCT)	Very low ^{a,b,ff,g}		and intermittent bolus feeding (13.6 ± 8.05 vs. 16.2 ± 12.3 $p = 0.20$, n=103 infants).	
Time to full enteral feeds: RCT	146 (1 RCT)	⊕⊕⊕○ Moderate ^f	-	In a trial of 146 infants, the time to reach full feeds in continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity were not significantly different (median [interquartile range]: 13 [10–16], 11.5 [9–17], and 13 [9.5–14.2] days, respectively, $p = 0.71$).	
Duration of initial hospital stay assessed with: Days to discharge	264 (4 RCTs)	⊕○○○ Very low ^{b,c,d}	-	The mean duration of initial hospital stay was 62 days	MD 1.55 lower (5.13 lower to 2.02 higher)
Duration of initial hospital stay: RCT	146 (1 RCT)	⊕⊕⊕○ Moderate ^f	-	There was no difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for median (IQR) length of hospital stay respectively (44 (29.5-62.5); 50 (32.5-70); 43 (26-64.7); n=146 infants).	
Adverse effects – feed intolerance: RCT assessed with: Number of days of feeding interruptions	171 (1 RCT)	⊕○○○ Very low ^{a,b,d}	-	The mean adverse effects – feed intolerance: RCT was 13 days	MD 3 lower (9.5 lower to 3.5 higher)
Adverse effects – feed intolerance: RCT	106 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The number of occurrences in which gastric residual volume exceeded 50% was significantly lower in the slow infusion feeding group compared with intermittent bolus feeding (1.12 ± 1.56 vs. 2.15 ± 1.4, $p = 0.01$, n=106).	
Adverse effects – feed intolerance: RCT	146 (1 RCT)	⊕⊕○○ Low ^{a,f}	-	The proportions of infants who developed feeding intolerance in continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups were similar (n [%]: 21 [51.2%], 20 [52.6%], and 22 [64.7%], respectively, n=146 infants).	
Fully breastfed or breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Faltering growth/body composition: RCT assessed with: Days to regain birthweight	610 (10 RCTs)	⊕○○○ Very low ^{b,c,d}	-	The mean faltering growth/body composition: RCT was 14.51 days	MD 0.38 lower (1.16 lower to 0.41 higher)
Faltering growth/body composition: RCT assessed with: Time to regain birthweight (Days)	106 (1 RCT)	⊕○○○ Very low ^{b,f,h}	-	The time to gain birthweight was significantly shorter in the slow infusion feeding group compared with intermittent bolus feeding (10.8 ± 3.2 versus 12.7 ± 4.17; $p = 0.01$, n=106).	
Faltering growth/body composition: RCT assessed with: Time to regain birthweight (Days)	146 (1 RCT)	⊕⊕⊕○ Moderate ^f	-	There was no difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for median time to regain birthweight (IQR) respectively (9 (6-12); 11 (6.5-13); 10 (7-12); n=146 infants).	
Faltering growth/body composition: RCT assessed with: End of intervention: rate of gain in weight	433 (8 RCTs)	⊕○○○ Very low ^{b,c,d}	-	The mean faltering growth/body composition: Not applicable	Standardised MD 0.09 Standard Deviation higher (0.27 lower to 0.46 higher)
Faltering growth/body composition: RCT assessed with: Weight growth velocity (g/kg/day)	146 (1 RCT)	⊕⊕⊕○ Moderate ^f	-	There was no difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for mean (SD) weight growth velocity (g/kg/day) respectively (13.6 (3.3); 13.2 (3.6); 14.1 (2.9); n=146 infants).	
Faltering growth/body composition: RCT assessed with: End of intervention: rate of gain in	433 (8 RCTs)	⊕○○○ Very low ^{b,c,d}	-	The mean faltering growth/body composition: RCT was 0.86 cm/week	MD 0.02 higher (0.04 lower to 0.08 higher)

length (cm/week)					
Faltering growth/body composition: RCT assessed with: Length increment (cm/week)	146 (1 RCT)	⊕⊕⊕○ Moderate ^f	-	There was no difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for mean (SD) length increment (cm/week) respectively (0.73 (0.17); 0.75 (0.17); 0.77 (0.17); n=146 infants).	
Faltering growth/body composition: RCT assessed with: End of intervention: rate of gain in head circumference (cm/week)	433 (8 RCTs)	⊕○○○ Very low ^{b,c,d}	-	The mean faltering growth/body composition: RCT was 0.75 cm/week	MD 0.01 higher (0.03 lower to 0.05 higher)
Faltering growth/body composition: RCT assessed with: Occipitofrontal circumference (cm/week)	146 (1 RCT)	⊕⊕⊕○ Moderate ^f	-	There was no difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for mean (SD) head circumference (cm/week) respectively (0.66 (0.12); 0.61 (0.14); 0.62 (0.14); n=146 infants).	
Neurodevelopmental impairment - not measured	-	-	-	-	-
Sepsis: proven or suspected: RCT assessed with: Late onset sepsis	103 (1 RCT)	⊕○○○ Very low ^{a,b}	not estimable	Study population	
				28.3 %	28%
Sepsis: proven or suspected: RCT assessed with: Late onset sepsis	146 (1 RCT)	⊕⊕⊕○ Moderate ^a	-	There was no difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for n (%) late-onset sepsis respectively (25 (51%); 23 (46.9%); 20 (41.7%); n=146 infants)	
Bronchopulmonary dysplasia	146 (1 RCT)	⊕⊕⊕○ Moderate ^a	-	There was no difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for n (%) bronchopulmonary dysplasia (8 (16.3%); 10 (20.4%); 8 (17.4%) n=146 infants).	
Retinopathy of prematurity assessed with: ROP requiring treatment	146 (1 RCT)	⊕⊕⊕○ Moderate ^a	-	There was no difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for n (%) ROP requiring treatment (3 (6.1%); 4 (8.2%); 1 (2.2%) n=146 infants).	
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds (<0.5 days) - not measured	-	-	-	-	-

- a. Downgraded one level for indirectness as the evidence is only reported in a single study
- b. Downgraded one level due to concerns about risk of bias
- c. Downgraded one level for indirectness as studies include a mixture of orogastric and/or nasogastric feeding regimes and infants of differing birthweights
- d. Downgraded one level for imprecision with confidence intervals crossing the line of no effect indicating both potential harm and benefit
- e. Downgraded one level as there are very small event rates
- f. Downgraded one level due to imprecision
- g. Downgraded two levels for imprecision with very wide confidence intervals crossing the line of no effect indicating both potential harm and benefit
- h. Downgraded one level for inconsistency
- i. Downgraded one level for heterogeneity between I2 = 60-80%

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence based on a Cochrane systematic review [1]. We also present evidence from 2 recent RCTs [2,3] and a cohort study [4]. Mortality Single RCT: No difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for n (%) mortality respectively (4 (8.2%); 7 (14.3%); 5 (10.4%); n=146 infants) [Critical]. Necrotising enterocolitis (NEC): RCT: No significant reduction on the risk of NEC (any stage) compared with intermittent feeding (18 per 1,000 more; 32 fewer to 107 more). Single RCT: No difference in necrotising enterocolitis ≥stage 2 n (%) between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups (1 (2%); 2 (4.1%); 2 (4.2%), n=146 infants) [Critical]. Time to full enteral feeding: RCT: No significant effect for increased time to reach full enteral feeding for infants receiving continuous feeding (MD 0.84 days; 0.13 lower to 1.81 higher). The test for subgroup differences did not suggest there may be variation in effect according to birthweight (P = 0.09, I² = 54.4%). Single RCT: The time to achieve full enteral feeding was similar between slow infusion feeding and intermittent bolus feeding (13.6 ± 8.05 vs. 16.2 ± 12.3 p = 0.20, n=103 infants). Single RCT: The time to reach full feeds in continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity were not significantly different (median [interquartile range]: 13 [10–16], 11.5 [9–17], and 13 [9.5–14.2] days, respectively, p = 0.71) [Critical]. Bronchopulmonary dysplasia: Single RCT: No difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for n (%) bronchopulmonary dysplasia (8 (16.3%); 10 (20.4%); 8 (17.4%) events n=146 infants) [Important]. Retinopathy of prematurity: Single RCT: No difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for n (%) retinopathy of prematurity requiring treatment (3 (6.1%); 4 (8.2%); 2 (2.2%) events; n=146 infants) [Important]. Sepsis: Suspected or proven: Single RCT: No effect of continuous feeds on risk of sepsis compared with intermittent feeds (14/50; 15/53 respectively). Single RCT: No difference between continuous infusion, intermittent bolus infusion, and intermittent bolus by gravity groups for n (%) late-onset sepsis, respectively (25 (51%); 23 (46.9%); 20 (41.7%) events; n=146 infants) [Important]. Undesirable effects for Māori No additional evidence available	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	The certainty of the evidence is moderate to very low. For some outcomes there are only a small number of events. Certainty of evidence for Māori No additional evidence available	

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis: RCT	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis: RCT	CRITICAL	⊕⊕⊕○ Moderate
Time to full enteral feeds: RCT assessed with: Age at full enteral feedings days)	CRITICAL	⊕○○○ Very low
Time to full enteral feeds: RCT assessed with: Days to achieve full enteral feeding	CRITICAL	⊕○○○ Very low
Time to full enteral feeds: RCT	CRITICAL	⊕⊕⊕○ Moderate
Duration of initial hospital stay assessed with: Days to discharge	CRITICAL	⊕○○○ Very low

Duration of initial hospital stay: RCT	CRITICAL	⊕⊕⊕○ Moderate
Adverse effects – feed intolerance: RCT assessed with: Number of days of feeding interruptions	CRITICAL	⊕○○○ Very low
Adverse effects – feed intolerance: RCT	CRITICAL	⊕○○○ Very low
Adverse effects – feed intolerance: RCT	CRITICAL	⊕⊕○○ Low
Fully breastfed or breastmilk feeding at hospital discharge - not measured	IMPORTANT	-
Faltering growth/body composition: RCT assessed with: Days to regain birthweight	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Time to regain birthweight	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Time to regain birthweight	IMPORTANT	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT assessed with: End of intervention: rate of gain in weight	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Weight growth velocity (g/kg/day)	IMPORTANT	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT assessed with: End of intervention: rate of gain in length (cm/week)	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Length increment (cm/week)	IMPORTANT	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT assessed with: End of intervention: rate of gain in head circumference (cm/week)	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Occipitofrontal circumference	IMPORTANT	⊕⊕⊕○ Moderate
Neurodevelopmental impairment - not measured	IMPORTANT	-
Sepsis: proven or suspected: RCT assessed with: Late onset sepsis	IMPORTANT	⊕○○○ Very low
Sepsis: proven or suspected: RCT assessed with: Late onset sepsis	IMPORTANT	⊕⊕⊕○

		Moderate
Bronchopulmonary dysplasia	IMPORTANT	⊕○○○ Very low
Retinopathy of prematurity assessed with: ROP requiring treatment	IMPORTANT	⊕○○○ Very low
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds (<0.5 days) - not measured	NOT IMPORTANT	-

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Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability. Values for Māori No additional evidence available	

Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	For continuous compared with intermittent feeding - Moderate certainty evidence Little or no effect on NEC, time to full enteral feeds, duration of hospital stay, faltering growth/body composition (weight, length, head circumference), sepsis For continuous compared with intermittent feeding - Low certainty evidence Probably little or no effect on feeding intolerance For continuous compared with intermittent feeding - Very low certainty evidence Little or no effect on NEC, time to full enteral feeds, duration of hospital stay, faltering growth/body composition (weight, length, head circumference), sepsis, bronchopulmonary dysplasia, retinopathy of prematurity Probably no difference in mortality Shorter time to regain birthweight Probably less feeding intolerance Balance of effects for Māori No available evidence	The Cochrane review concludes (Premji 2021): The clinical risks and benefits of continuous and intermittent nasogastric tube milk feeding cannot be reliably discerned from current available randomised trials. Further research is needed to determine if either feeding method is more appropriate for the initiation of feeds. A rigorous methodology should be adopted, defining feeding protocols and feeding intolerance consistently for all infants. Infants should be stratified according to birthweight and gestation, and possibly according to illness.
Resources required		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Continuous feeds require enteral feeding pumps. Most NICUs in Aotearoa New Zealand have access to loan enteral feeding pumps (\$1,000 to \$2,000 each) and feeding equipment. Intermittent and continuous feeds use tubing that is replaced 24 hourly, but continuous feeds require slightly more costly equipment than bolus feeding and result in more plastic waste. Continuous feeds require less nursing time to administer.	
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Very low ○ Low ● Moderate ○ High ○ No included studies	A formal assessment of the certainty of evidence of the cost was not undertaken. Certainty of evidence of required resources for Māori. No included studies on cost.	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	There are no studies that assess the specific cost-effectiveness of continuous versus bolus feeds, particularly in the context of preterm infants. Cost-effectiveness for Māori. No included studies on cost.	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori There is no evidence showing that pēpi Māori are systematically assigned to different feeding methods (e.g. continuous vs. bolus feeds) based on ethnicity. However, there is indirect evidence of systemic neonatal care inequities that may result in differential access or application of best-practice enteral feeding strategies, including those aimed at reducing NEC, accelerating time to full feeds and shortening NICU length of stay. Pēpi Māori receive fewer key interventions in NICU, which may impact on enteral feeding, such as antenatal corticosteroids, surfactant administration, and timely access to neonatal transport. This raises the possibility that pēpi Māori might have delayed progression to enteral feeds and receive less optimal feeding strategies, such as earlier transition to infant formula, which may be less well tolerated and delay full feeds. Equity for Pacific families	

	Variation in feeding methods across hospitals can lead to uncertainty for Pacific families, particularly if information is not communicated in culturally familiar ways. When families are not supported in understanding feeding methods, trust can be eroded. Equity means ensuring families are involved in discussions about feeding type and rationale. Equity for underrepresented groups Families with limited health literacy or English language proficiency may not be informed about the differences between feeding methods. Inconsistent explanations may affect their confidence in care. Equity requires inclusive communication and consistent feeding practices so that all families understand and support their infant's nutritional plan.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☐ Probably yes ☐ Yes ☒ Varies ☐ Don't know	Families are less involved/engaged with continuous feeds but otherwise continuous feeds are generally acceptable to staff and families. Acceptability for Māori No data available	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☐ Varies ☐ Don't know	The intervention is already in widespread use in Aotearoa New Zealand neonatal units, so is feasible. Feasibility for Māori No additional evidence available	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know

	JUDGEMENT						
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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References

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3. Kumar, V.; Thakur, A.; Garg, P.; Kler, N. Comparison of three modalities of feeding in preterm infants ≤ 32 weeks and $\leq 1,250$ g: A randomized controlled trial. *Am. J. Perinatol.* **2024**, 41, e1792-e1799, doi:10.1055/a-2074-1960.
4. Kim, M.J.; Kim, H.S.; Jung, Y.H.; Choi, C.W. The impact of slow infusion intermittent feeding on gavage feeding-associated cardiorespiratory deterioration in neonatal intensive care unit infants. *Neonatal Med* **2023**, 30, 49-54, doi:10.5385/nm.2023.30.2.49.

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EtD 24. In preterm infants does fortified EBM vs. unfortified EBM lead to improved growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?

POPULATION:	Preterm infants
INTERVENTION:	Fortified expressed breastmilk
COMPARISON:	Unfortified expressed breastmilk
MAIN OUTCOMES:	Critical outcomes Mortality Necrotising enterocolitis Adverse effects – milk curd obstruction, metabolic bone disease Neurodevelopmental impairment Fully breastfed or breastmilk feeding at hospital discharge Faltering growth/body composition Time to full enteral feeds Duration of initial hospital stay Sepsis: proven or suspected Important but not critical Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation - population perspective
BACKGROUND:	Expressed breastmilk is the preferred source of nutrition for preterm infants for who cannot yet breastfeed, due to its protective bioactive components, which support immune function, gastrointestinal maturation, and neurodevelopment. However, unfortified expressed breastmilk may not provide adequate amounts of protein, energy, and other key nutrients such as calcium, phosphorus and vitamins to meet the high nutritional demands of preterm infants. Fortifying expressed breastmilk with commercial multicomponent breastmilk fortifiers aims to address these deficits by providing most of the additional nutrients to support growth and development in one nutritional supplement. Fortified expressed breastmilk has been associated with improved growth compared to unfortified expressed breastmilk. This is particularly important for preterm infants, who are at high risk of faltering growth and neurodevelopmental impairment. Furthermore, fortified expressed breastmilk may help reduce the risk of metabolic bone disease/rickets of prematurity, a common complication caused by low body stores and inadequate vitamin D, calcium and phosphorus intake. The additional nutrients in fortified expressed breastmilk are also thought to support better clinical outcomes by improving overall nutritional status. Concerns about breastmilk fortifiers

CONFLICT OF INTERESTS:	include possible increased risk of necrotising enterocolitis or milk curd obstruction associated with cow's milk-based (bovine) fortifiers and some preterm infants struggle with feeding intolerance or gastrointestinal issues when using fortifiers. There are also concerns that the process of adding fortifier to breastmilk can alter the composition and benefits of breastmilk and concerns about the safety of storing fortified breastmilk in a fridge and for how long it can safely be stored.
	The following case-control study of milk curd obstruction (Reference 2) co-authors are on the Guideline Development Group: Barbara Cormack, Frank Bloomfield. Frank Bloomfield supervised the first author. \ The following 2020 Cochrane systematic review (Brown <i>et al</i>) co-author wrote this Evidence to Decision document: Julie Brown

Assessment

Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	In preterm infants, high serum alkaline phosphatase concentration, especially above 500 IU/L, is associated with an increased risk of metabolic bone disease and low bone mineralisation, potentially leading to metabolic bone disease (osteopenia or rickets of prematurity). Serum alkaline phosphatase evidence is based on a systematic review [1] and a case-control study [2] Necrotising enterocolitis (NEC): RCT: No significant reduction in NEC overall (9 more per 1,000; 7 fewer to 42 more) and for very preterm or VLBW infants (7 more per 1,000; 11 fewer to 47 more) [Critical]. Adverse effects: RCT: large increase in bone mineral density for fortified breastmilk MD 12 higher mg/cm; 6.28 higher to 17.72 higher). No difference in the prevalence of milk curd obstruction between fortified and unfortified breastmilk [Critical]. Adverse effects: Large reduction in ALP for fortified breastmilk (MD 141.93 lower; 203.93 lower to 79.92 lower) [Critical]. Neurodevelopmental impairment: RCT: No significant difference between fortified and unfortified feeds for Bayley II Psychomotor Development Index (MD 2.4 points higher; 1.9 lower to 6.7 higher) or Mental Bayley II Development Index (MD 2.2 points higher; 3.35 lower to 7.75 higher) at 18 months [Critical]. No faltering growth/body composition: RCT: Moderate increase in weight gain overall for fortified breastmilk (MD 1.76 g/kg/day higher; 1.3 higher to 2.22 higher); large increase in weight gain for very preterm or VLBW infants (MD 2.18 g/kg/day higher; 1.54 higher to 2.81 higher). Small increase in length overall for fortified breastmilk (MD 0.11 cm/week higher; 0.08 higher to 0.15 higher); small increase in length for very preterm or VLBW infants (MD 0.16 cm/week higher; 0.11 higher to 0.2 higher). Small increase in head circumference overall for	Population information for included evidence Cochrane review by Walsh 2019 [3] Median birthweight was 823 and 849 g for cases and controls, respectively, and median gestational age was 26 weeks for both groups. Brown <i>et al</i> Cochrane review [1]: 11 trials included only very preterm or VLBW infants. One trial included 'healthy preterm infants' but gave no birthweight criteria and the upper birthweight eligibility criteria for the remaining 6 studies ranged from 1600 - 2000 g. Studies included mother's own milk, donor milk or a mixture, or formula as a supplement.

	fortified breastmilk (MD 0.06 cm/week higher; 0.03 higher to 0.08 higher); small increase in head circumference for very preterm or VLBW infants (MD 0.07 cm/week higher; 0.03 higher to 0.11 higher). Little or no effect in weight (MD 0.03 kg lower; 0.31 lower to 0.25 higher); length (MD 0.19 cm lower; 0.98 lower to 0.6 higher) and head circumference (MD 0.1 cm lower; 0.37 lower to 0.18 higher) for fortified breastmilk at 12-18 months [Critical]. Duration of initial hospital stay: RCT: No significant effect on duration of hospital stay overall for fortified milk (MD 0.07 weeks lower; 0.35 lower to 0.21 higher). Small reduction on duration of hospital stay for very preterm of VLBW infants (MD 0.48 days lower; 0.89 lower to 0.08 lower) [Critical]. Desirable effects for Māori No additional evidence available	
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Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with unfortified expressed breastmilk	Risk difference with fortified expressed breastmilk
Mortality - not measured	-	-	-	-	-
Necrotising enterocolitis: RCT	1110 (6 RCTs)	⊕⊕○○ Low ^{a,b}	RR 1.37 (0.72 to 2.63)	Study population	
				26 per 1,000	9 more per 1,000 (7 fewer to 42 more)
Necrotising enterocolitis: RCT: Very preterm or VLBW	701 (8 RCTs)	⊕⊕○○ Low ^{a,b}	RR 1.28 (0.55 to 2.99)	Study population	
				23 per 1,000	7 more per 1,000 (11 fewer to 47 more)
Adverse effects: RCT assessed with: Serum alkaline phosphatase (IU/L)	363 (6 RCTs)	⊕○○○ Very low ^{a,c}	-	The mean adverse effects: RCT serum alkaline phosphatase was 812.3 IU/L	MD 141.93 lower (203.93 lower to 79.92 lower)
Adverse effects: RCT assessed with: Bone mineral content (mg/cm)	59 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean adverse effects: RCT was 47 mg/cm	MD 12 higher (6.28 higher to 17.72 higher)
Adverse effects: Retrospective case control study assessed with: Milk curd obstruction	20 cases 40 controls (1 non-randomised study)	⊕○○○ Very low ^{d,e}	-	8/20 (40%) of infants with milk curd obstruction had bovine derived multicomponent fortified human breastmilk and 27/40 (68%) of controls had bovine derived multicomponent fortified human breastmilk. p=0.08	
Neurodevelopmental impairment: RCT assessed with: Bayley II Psychomotor development index at 18 months [measurement scale not specified in review]	245 (1 RCT)	⊕○○○ Very low ^{a,c,d}	-	The mean neurodevelopmental impairment: RCT: Bayley II Psychomotor Development Index was 89.9 points	MD 2.4 higher (1.9 lower to 6.7 higher)
Neurodevelopmental impairment: RCT assessed with: Bayley II Mental development index	245 (1 RCT)	⊕○○○ Very low ^{a,c,d}	-	The mean neurodevelopmental impairment: RCT: Bayley II Mental Development Index was 103.8 points	MD 2.2 higher (3.35 lower to 7.75 higher)

at 18 months [measurement scale not specified in review]					
Fully breastfed or breastmilk feeding at hospital discharge: RCT - not measured	-	-	-	-	-
Faltering growth/body composition: RCT assessed with: Weight gain (g/kg/day)	951 (14 RCTs)	⊕⊕○○ Low ^{a,f}	-	The mean faltering growth/body composition: RCT was 15.12 g/kg/day	MD 1.76 higher (1.3 higher to 2.22 higher)
Faltering growth/body composition: RCT: Very preterm or VLBW assessed with: Weight gain (g/kg/day)	505 (8 RCTs)	⊕⊕○○ Low ^{a,f}	-	The mean faltering growth/body composition: RCT: Very preterm or VLBW was 15.93 g/kg/day	MD 2.18 higher (1.54 higher to 2.81 higher)
Faltering growth/body composition: RCT assessed with: Length (cm/week)	741 (10 RCTs)	⊕⊕○○ Low ^{a,f}	-	The mean faltering growth/body composition: RCT was 0.84 cm/week	MD 0.11 higher (0.08 higher to 0.15 higher)
Faltering growth/body composition: RCT: Very preterm or VLBW assessed with: Length (cm/week)	375 (5 RCTs)	⊕⊕○○ Low ^{a,f}	-	The mean faltering growth/body composition: RCT: Very preterm or VLBW was 0.85 cm/week	MD 0.16 higher (0.11 higher to 0.2 higher)
Faltering growth/body composition: RCT assessed with: Head growth (cm/week)	821 (11 RCTs)	⊕⊕⊕○ Moderate ^a	-	The mean faltering growth/body composition: RCT was 0.83 cm/week	MD 0.06 higher (0.03 higher to 0.08 higher)
Faltering growth/body composition: RCT: Very preterm or VLBW assessed with: Head growth (cm/week)	375 (5 RCTs)	⊕⊕○○ Low ^{a,f}	-	The mean faltering growth/body composition: RCT: Very preterm or VLBW was 0.88 cm/week	MD 0.07 higher (0.03 higher to 0.11 higher)
Faltering growth/body composition: RCT assessed with: Weight at 12-18 months (kg)	270 (2 RCTs)	⊕⊕○○ Low ^{a,b}	-	The mean faltering growth/body composition: RCT was 9.55 kg	MD 0.03 lower (0.31 lower to 0.25 higher)
Faltering growth/body composition: RCT assessed with: Length at 12-18 months (cm)	270 (2 RCTs)	⊕⊕○○ Low ^{a,b}	-	The mean faltering growth/body composition: RCT was 78 cm	MD 0.19 lower (0.98 lower to 0.6 higher)
Faltering growth/body composition: RCT assessed with: Head circumference at 12-18 months (cm)	270 (2 RCTs)	⊕⊕○○ Low ^{a,b}	-	The mean faltering growth/body composition: RCT was 47.5 cm	MD 0.1 lower (0.37 lower to 0.18 higher)
Time to full enteral feeds - not measured	-	-	-	-	-
Duration of initial hospital stay: RCT assessed with: Weeks	526 (6 RCTs)	⊕○○○ Very low ^{a,b,f}	-	The mean duration of initial hospital stay: RCT was 4.64 weeks	MD 0.07 lower (0.35 lower to 0.21 higher)
Duration of initial hospital stay: RCT: Very preterm or VLBW assessed with: Weeks	236 (3 RCTs)	⊕⊕⊕○ Moderate ^a	-	The mean duration of initial hospital stay: RCT: Very preterm or VLBW was 4.73 weeks	MD 0.48 lower (0.89 lower to 0.08 lower)
Sepsis: proven or suspected - not measured	-	-	-	-	-
Bronchopulmonary dysplasia - not measured	-	-	-	-	-

Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-

- a. Downgraded one level for risk of bias
- b. Downgraded one level for imprecision with confidence intervals crossing the line of no effect
- c. Downgraded two levels for imprecision with wide confidence intervals crossing the line of no effect
- d. Downgraded one level for indirectness as evidence based on a single trial
- e. Downgraded two levels for risk of bias as evidence is based on a single retrospective case-control study of a rare event
- f. Downgraded one level as heterogeneity was high between I2 =60-80%

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	If breastmilk fortifiers are not used, several nutrients need to be added to breastmilk individually at most feeds. The addition of these individual nutrients (energy, protein, fat, carbohydrate, vitamins, iron, calcium, phosphorus zinc and folic acid) adds to the risk of sepsis and feed intolerance. Undesirable effects for Māori No additional evidence available	A family may have a negative, or uncertain response to fortification as a concept and require time to engage with the approach and ask questions. Careful communication to the family re: the possible risks in accessible terminology e.g. rickets of prematurity etc. is advised.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Moderate to very low certainty of evidence overall Certainty of evidence for Māori No additional evidence available.	

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality - not measured	CRITICAL	-

Necrotising enterocolitis: RCT	CRITICAL	⊕⊕○○ Low
Necrotising enterocolitis: RCT: Very preterm or VLBW	CRITICAL	⊕⊕○○ Low
Adverse effects: RCT assessed with: Serum alkaline phosphatase (IU/L)	CRITICAL	⊕○○○ Very low
Adverse effects: RCT assessed with: Bone mineral content (mg/cm)	CRITICAL	⊕○○○ Very low
Adverse effects: Retrospective case control study assessed with: Milk curd obstruction	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: Psychomotor development index at 18 months [measurement scale not specified in review]	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: Mental development index at 18 months [measurement scale not specified in review]	CRITICAL	⊕○○○ Very low
Fully breastfed or breastmilk feeding at hospital discharge: RCT - not measured	CRITICAL	-
Faltering growth/body composition: RCT assessed with: Weight gain (g/kg/day)	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT: Very preterm or VLBW assessed with: Weight gain (g/kg/day)	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT assessed with: Length (cm/week)	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT: Very preterm or VLBW assessed with: Length (cm/week)	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT assessed with: Head growth (cm/week)	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT: Very preterm or VLBW assessed with: Head growth (cm/week)	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT assessed with: Weight at 12-18 months (kg)	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT assessed with: Length at 12-18 months (cm)	CRITICAL	⊕⊕○○ Low

Faltering growth/body composition: RCT assessed with: Head circumference at 12-18 months (cm)	CRITICAL	⊕⊕○○ Low
Time to full enteral feeds - not measured	CRITICAL	-
Duration of initial hospital stay: RCT assessed with: Weeks	CRITICAL	⊕○○○ Very low
Duration of initial hospital stay: RCT: Very preterm or VLBW assessed with: Weeks	CRITICAL	⊕⊕⊕○ Moderate
Sepsis: proven or suspected - not measured	CRITICAL	-
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Retinopathy of prematurity - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Duration of hospital stay is important to families (and has a wide impact on a range of factors for whānau depending upon overall duration, location(s) etc). From a parent's perspective weight gain can be seen as a cornerstone of their infant's progress as is full sucking feeds at discharge. Again, careful management is needed to ensure good information is communicated as to why these things may not be seen as crucial in the grand scheme of optimal nutritional management.	Sepsis is a huge concern for parents.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Fortified compared with unfortified breastmilk - Moderate certainty evidence No faltering growth/body composition (increase in head circumference) Shorter duration of hospital stay for very preterm or VLBW infants Fortified compared with unfortified breastmilk - Low certainty evidence No faltering growth/body composition (increase in weight gain, length, head circumference) Uncertain effect for NEC; faltering growth/body composition (weight gain, length, head circumference at 12-18 months) Fortified compared with unfortified breastmilk -Very low certainty evidence Increased bone mineral density Uncertain effect for neurodevelopmental impairment at 18 months, serum alkaline phosphatase, duration of initial hospital stay Balance of effects for Māori No additional evidence available.	
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Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Breastmilk fortifier \$3.75 per 100 mL Costs (for up to 100-120 days) Breastmilk fortifier \$3.75 per 100 mL at 180 mL/kg/day (\$5.80 to \$9 per day) Cost difference for fortified vs. unfortified breastmilk is approx. \$580 to \$900 per baby per admission of 100 days, (Large). Labour to add a fortifier to breastmilk by parent or nurse is minimal Labour to add a fortifier to breastmilk in a central milk preparation facility is higher However, if fortifier is not used, some or all of the following nutrients will need to be added to enteral feeds: Energy supplementation 3.6 to 6.8 mL/kg/day Calogen (long-chain triglyceride emulsion) Dose per baby per day 5 to 10 mL Calogen Cost per day Calogen \$0.40 to \$0.80 Cost per admission per infant (up to 100 days) Calogen \$40 to 80 Nutrient cost per day to replace nutrients in breastmilk fortifier	

	Vitamin A 2 drops/kg/d (2 to 3 drops Optimus Vitamin A) \$0.14 Vitamin D 1 drop/kg/d (2 to 3 drops Clinicians Vitamin D) \$0.30 Vitamin E 7 mg/kg/d (7 to 10 mg) \$0.12 Thiamine 200 µg/kg/d (200 to 300 µg) \$0.05 Folic acid 50 µg/kg/d (50 to 100 50 µg) \$0.06 Calcium 2.6 mmol/kg/d (2.6 to 3.9 mmol) \$2.60 Phosphorus 2.6 mmol/kg/d (2.6 to 3.9 mmol) \$0.82 Iron 3 mg/kg/d (3 to 4.5 mg) \$0.02 Zinc 2 mg/kg/d (2 to 3 mg) \$0.10 Sodium 3 mmol/kg/d (3 to 4.5 mmol) \$0.80 Potassium 2 mmol/kg/d (2 to 3 mmol) \$0.88 Iodine 50 µg/kg/d. (50 to 75 µg) \$0.07 Total \$5.95 per day Resources required for Māori Not different	
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Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	Costs are reasonably certain. Certainty of evidence of required costs for Māori No additional evidence available.	Aotearoa New Zealand Breastmilk fortifier \$3.75 per 100 mL

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the	There are no studies that assess the specific cost-effectiveness of fortified expressed breastmilk compared with unfortified expressed breastmilk, particularly in the context of preterm infants. Cost effectiveness for Māori	

comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No additional evidence available.	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Māori preterm pēpi are likely at increased risk of deficiencies of the vitamins and micronutrients supplied by breastmilk fortifier, due to the social determinants of health and nutrition (e.g. colonisation, racism, income, education, employment and housing) and therefore would benefit more from the use of breastmilk fortifiers. A study of the nutritional status of 413 Auckland children aged 6-23 months found the prevalence of vitamin D deficiency varied with ethnicity: Pacific 24%, Māori 11%, European 3% and other ethnic groups 16%. To date, no large Aotearoa New Zealand studies have measured vitamin D levels specifically in Māori preterm pēpi; however, based on adult and toddler data and considering skin tone and lack of sun exposure during NICU care, they are considered high-risk. Equity for Pacific families Pacific Island infants are overrepresented in the preterm infant population and also at higher nutrient deficiency risk. A study of vitamin D status of exclusively breastfed infants in Auckland aged 2-3 months found 24% were vitamin D deficient (25(OH)D <27.5nmol/L). Pacific infants may not consistently receive breastmilk fortification due to variable practice across hospitals and limited staff training in cultural engagement. Pacific families may not understand why fortifiers are needed if explanations are not provided in a culturally meaningful way. Equity requires clear guidance and inclusive conversations about infant nutrition. Equity for underrepresented groups Indian infants are overrepresented in the preterm infant population and also at higher nutrient deficiency risk. A study of vitamin D status of exclusively breastfed infants in Auckland aged 2-3 months found 24% were vitamin D deficient (25(OH)D <27.5nmol/L). A group at particular risk of symptomatic nutrient deficiency presenting to Starship Child Health are Indian children from vegan families. Migrant, refugee and rural families may not receive timely or adequate explanations about the role of fortifiers, especially when language or literacy barriers exist. This can lead to mistrust or passive consent. Equity means ensuring all families have access to understandable information and	

	consistent nutritional care regardless of setting.	
Acceptability Is the intervention acceptable to key interest-holders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☐ Varies ☐ Don't know	Breastmilk fortifier is widely used in Aotearoa New Zealand neonatal units so probably will be accepted. Acceptability for Māori No additional evidence available.	Bovine based fortifier may not be acceptable to vegans.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☐ Probably yes ☒ Yes ☐ Varies ☐ Don't know	Breastmilk fortifier is widely used in Aotearoa New Zealand neonatal units so will be feasible. Feasibility for Māori No additional evidence available.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			

	JUDGEMENT						
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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References

1. Brown, J.V.; Lin, L.; Embleton, N.D.; Harding, J.E.; McGuire, W. Multinutrient fortification of human milk for preterm infants. *Cochrane Database Syst. Rev.* **2020**, *6*, doi:10.1002/14651858.CD000343.pub4.
2. Walsh, O.; Anthony, R.; Wang, Z.; Cormack, B.E.; Bloomfield, F.H. Case-control study of milk curd obstruction in newborn infants in a tertiary surgical neonatal intensive care unit. *Arch Dis Child Fetal Neonatal Ed* **2024**, doi:10.1136/archdischild-2024-327565.
3. Walsh, V.; Brown, J.V.E.; Askie, L.M.; Embleton, N.D.; McGuire, W. Nutrient-enriched formula versus standard formula for preterm infants. *Cochrane Database Syst. Rev.* **2019**, *7*, Cd004204, doi:10.1002/14651858.CD004204.pub3.

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EtD 25. In preterm infants does commencing less than full strength fortified EBM compared with full fortified enteral feeds lead to shorter time to full enteral feeds improve growth, neurodevelopment, clinical outcomes, fewer nec cases, fewer gastrointestinal complications, less metabolic bone disease?

POPULATION:	Preterm infants receiving enteral feeds of expressed breastmilk
INTERVENTION:	Commencing less than full strength breastmilk fortifier
COMPARISON:	Commencing full strength breastmilk fortifier
MAIN OUTCOMES:	Critical for making a decision Mortality Neurodevelopmental impairment Time to full enteral feeds Faltering growth/body composition Necrotising enterocolitis (NEC) Important but not critical Adverse effects (other than mortality, BPD, NEC, sepsis anaemia of prematurity or ROP) Fully breastmilk feeding at hospital discharge Fully breastfeeding at hospital discharge Duration of initial hospital stay Sepsis: proven or suspected Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Of limited importance Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	There is evidence that multi nutrient fortification of breastmilk increases in-hospital growth of preterm infants, but fortification has not been shown to improve long-term growth and neurodevelopmental outcome. Breastmilk fortifiers are commonly used to help meet the increased energy, protein and micronutrient needs of preterm infants. Fortifiers are usually introduced once an infant is tolerating a certain volume of enteral feeds, but there is variation in whether they are started at full strength or half strength. The rationale for commencing at half strength is to reduce the risk of feeding intolerance or gastrointestinal complications. However, it remains unknown whether this approach leads to a shorter time to full enteral feeds, improved growth, better neurodevelopmental outcomes or fewer clinical complications such as NEC. Balancing the benefits of early optimal nutrition with the potential risks of fortifier intolerance is particularly important in preterm infants who are

transitioning from parenteral nutrition.

CONFLICT OF INTERESTS:

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	No studies were identified that addressed the question of whether commencing less than full-strength breastmilk fortifier compared with full-strength fortifier leads to a shorter time to full enteral feeds, improved growth, neurodevelopment, and clinical outcomes, or reduced NEC cases and gastrointestinal complications. Multicomponent breastmilk fortifiers were designed to be given at full strength to meet the nutritional requirements of preterm infants. Theoretical benefits of commencing less-than-full-strength fortifier are that it may improve feed tolerance or reduce the chances of developing NEC. Theoretical benefits of commencing full-strength fortifier are improved nutritional intake and better growth. The additional phosphate provided by fortifier may reduce hypophosphataemia and refeeding syndrome.	The addition of full-strength breastmilk fortifier increases the supply of phosphate from expressed breastmilk from 0.8 mmol/kg/day to 3.1 to 3.4 mmol/kg/day (at 180 mL/kg/day). This may be important for reducing the risk of refeeding syndrome due to inadequate early phosphate intake. Half fortifier (2.1 mmol/kg/day) does not meet the ESPGHAN recommended phosphate intake of 2.3 to 3.9 mmol/kg/day.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	Potential risks of commencing less-than-full-strength fortifier are: - Faltering growth, due to substantially lower nutrient intake - Increased risk of refeeding syndrome - Higher risk of contaminated feed or inaccurate measurement of the fortifier dose Theoretical risks of commencing full-strength fortifier are: - NEC - Reduced feed tolerance	180 mL/kg/day half fortified expressed breastmilk provides 133 kcal/kg/day and 3.6 g/kg/day protein 180 mL/kg/day fully fortified expressed breastmilk provides 158 kcal/kg/day and 4.9 g/kg/day protein

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No studies were identified which were applicable to this review question.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention	No studies were identified which were applicable to this review question.	

○ Favours the intervention ○ Varies ● Don't know		
Resources required		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	If the difference between half and full fortification of breastmilk fortifier is assumed to be 3 to 5 days, the additional cost of fortifier will be \$2 to \$4 per day, therefore a total of \$6 to \$20 depending on the size of the infant and volumes used (negligible). A new dose of fortifier needs to be prescribed again when changed to full strength. Resources required for Māori No additional evidence available.	
Certainty of evidence of required resources		
What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ● High ○ No included studies	Fairly certain	
Cost effectiveness		
Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention	No studies were identified	

○ Varies ● No included studies		
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Pēpi Māori are more likely to experience preterm birth and growth restriction yet may not consistently receive optimal fortification strategies due to variability in clinical practice. If less than full-strength fortification is used without clear reasoning or discussion, whānau Māori may be left uninformed about the impact on nutrition and development. In settings lacking culturally safe communication or equitable access to neonatal dietitian support, decisions around feed composition may disadvantage pēpi Māori. Equity requires standardised protocols, clear explanations and inclusive decision-making to ensure pēpi Māori receive appropriate and effective nutritional care from the beginning of enteral feeding. Equity for Pacific families Pacific families may not be informed about the reasoning behind starting with half-strength fortifier compared to full strength. Without culturally tailored explanations, families may feel excluded or unsure about feeding decisions. Equity requires clear, respectful communication that helps Pacific families understand and support the staged approach to fortification. Equity for underrepresented groups Families from underrepresented communities may be unaware of the benefits or risks associated with different fortifier strengths. Language barriers or low health literacy can limit their understanding. Equity-focused care must include consistent, accessible education to ensure all families are meaningfully involved in feeding plans and aware of their baby's needs.	
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know	Probably yes if there is evidence of benefit.	

Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know	Already in clinical practice in some NICUs At full strength, one packet of fortifier is added to 25 mL of expressed breastmilk. Using less than full-strength fortifier requires one packet to be added to 50 mL of breastmilk, and this takes twice as long to use, especially when the feed volume is low. Alternatively, the packet is cut in half or the powder is weighed, requiring very accurate scales for each area where the fortifier is added to breastmilk. Both these methods bring additional risk of contamination or inaccurate measurements.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF	Very low	Low	Moderate	High			No included studies

	JUDGEMENT						
REQUIRED RESOURCES							
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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EtD 26. In preterm infants does individualised fortification of EBM compared with standard fortified enteral feeds using commercially available fortifiers lead to shorter time to full enteral feeds improve growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?

POPULATION:	Preterm infants
INTERVENTION:	Individualised fortification
COMPARISON:	Standardised of expressed breastmilk fortification
MAIN OUTCOMES:	Critical outcomes Mortality Neurodevelopmental impairment Necrotising enterocolitis Fully breastfed or breastmilk feeding at hospital discharge Important but not critical Faltering growth/body composition Duration of initial hospital stay Time to full enteral feeds (<0.5 days) Bronchopulmonary dysplasia Feeding intolerance Sepsis: proven or suspected Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical guideline recommendation: patient perspective
BACKGROUND:	Optimal nutrition plays a key role in growth, neurodevelopment, metabolism and the overall survival of preterm infants. Due to their high nutritional requirements, breastmilk alone does not meet the nutritional needs of many preterm infants and fortification is required. Standard breastmilk fortification adds a fixed dose of commercial multicomponent breastmilk fortifier to breastmilk, based on a standard predefined estimated composition of human breastmilk. In contrast, individualised breastmilk fortification involves analysing a sample of breastmilk with a milk analyser to determine its nutrient composition or measuring the infant's blood urea nitrogen concentration and then adding one or more nutrients as modular additives to meet recommended nutritional intakes. Although standard fortification is common practice in most NICUs, standard commercial fortification may not satisfy the nutritional requirements of all preterm infants, given the variations in composition of expressed breastmilk. For this reason, individualised fortification may be needed to ensure that nutritional needs are being met. Concerns around individualised fortification, however, revolve around the

CONFLICT OF INTERESTS:	knowledge that blood urea nitrogen concentrations are dependent on kidney function and fluid turnover, and that preterm infants may have metabolic and absorptive variation. Therefore, individualised fortification may lead to insufficient or excessive actual nutrient intake. Ensuring that expressed breastmilk is being optimally fortified is critical to improving the care of preterm infants.
	None

Assessment

Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	The evidence is based on RCTs [1-13] Mortality: RCT: No significant reduction in mortality with individualised fortification (36 fewer per 1,000; 44 fewer to 29 more) [Critical] Necrotising enterocolitis (NEC): RCT: No significant reduction in NEC with individualised fortification (31 fewer per 1,000; 40 fewer to 53 more) [Critical]. No faltering growth/body composition: RCT: Increase in length (MD 0.52 mm/day higher; 0.41 higher to 0.64 higher) and head circumference (MD 0.21 mm/day higher; 0.12 higher to 0.30 higher) during the intervention for individualised fortification. Fat mass index was higher at the end of the intervention for individualised fortification (MD 0.5 kg/m² higher; 0.03 higher to 2.56 higher). Increased weight gain during the intervention for the individualised fortification (1.91 g/kg/day higher; 1.32 higher to 2.5 higher). No significant effect in weight z score at discharge (MD 0.10 points higher; 0.33 lower to 0.53 higher) and length z score at discharge (MD 0.27 points higher; 0.08 lower to 0.61 higher) and head circumference z-score at discharge (MD 0.23 points higher; 0.16 lower to 0.63 higher) or free mass index at end of the intervention (MD 0.2 kg/m² higher; 0.29 lower to 0.69 higher) for the individualised fortification [Important]. Bronchopulmonary dysplasia: RCT: No significant decrease in bronchopulmonary dysplasia for individualised fortification (87 fewer per 1,000; 185 fewer to 39 more) [Important]. Feeding intolerance: RCT: No significant decrease in feeding intolerance for individualised fortification (23 fewer per 1,000; 103 fewer to 111 more). [Important] Sepsis: RCT: No significant decrease in sepsis for individualised fortification (46 fewer per 1,000; 112 fewer to 66 more) [Important]. Retinopathy of prematurity: RCT: No significant effect on retinopathy of prematurity (0 fewer per 1,000; 100 fewer to 224 more) [Important]. Desirable effects for Māori No available evidence	Population information for included evidence Greece: RCT [1] : Preterm infants 24–32 weeks' gestation. India: RCT [2]: Infants ≤32 weeks' gestation or birthweight ≤1800 g. USA: RCT [3]: Preterm infants with birthweights of 600–1750 g and gestational ages between 26 and 34 weeks. USA: RCT [4]: Infants <31 completed weeks' gestation. USA [5]: RCT Infants with a birthweight 750-1250 g. Thailand: RCT [6]: Preterm infants of gestational age <32 weeks and weighing ≤1,800 g.

					USA: RCT [7]: Birthweight between 900 and 1,500 g. USA: RCT [8]: Very low birthweight infants. China: RCT [9]: Infants <34 weeks' gestation. Canada: RCT [10]: Infants <30 weeks' gestation. Poland: RCT [11]: Infants ≤32 weeks' gestation. Turkey: RCT [12]: <32 weeks' gestation and <1,500 g. Malaysia: RCT [13]: Infants <34 weeks' gestation and <1,500 g.
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Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with standardised expressed breastmilk fortification	Risk difference with E.G.2.3 individualised fortification
Mortality	181		RR 0.20	Study population	

	(2 RCTs)	⊕⊕○○ Low ^a	(0.02 to 1.66)	44 per 1,000	36 fewer per 1,000 (44 fewer to 29 more)
Neurodevelopmental Impairment - not measured	-	-	-	-	-
Necrotising Enterocolitis	142 (2 RCTs)	⊕⊕○○ Low ^a	RR 0.26 (0.03 to 2.27)	Study population	
				42 per 1,000	31 fewer per 1,000 (40 fewer to 53 more)
Full Breastmilk Feeding at Hospital Discharge - not measured	-	-	-	-	-
Full Breastfeeding at Hospital Discharge - not reported	-	-	-	-	-
Length gain (mm/day) during Intervention Period	261 (7 RCTs)	⊕○○○ Very low ^{b,c}	-	The mean length gain (mm/day) during Intervention Period was 1.17	MD 0.52 higher (0.41 higher to 0.64 higher)
Head Circumference Gain (mm/day) during Intervention Period	224 (6 RCTs)	⊕⊕⊕○ Moderate ^c	-	The mean head Circumference Gain (mm/day) during Intervention Period was 1.04	MD 0.21 higher (0.12 higher to 0.3 higher)
Fat Mass Index at End of Intervention (kg/m ²)	70 (1 RCT)	⊕⊕○○ Low ^a	-	The mean fat Mass Index at End of Intervention (kg/m ²) was 2.6	MD 0.5 higher (0.03 higher to 0.97 higher)
Weight Gain (g/kg/day) during Intervention	454 (10 RCTs)	⊕⊕○○ Low ^b	-	The mean weight Gain (g/kg/day) during Intervention was 16.47	MD 1.91 higher (1.32 higher to 2.5 higher)
Weight z-score at Discharge	51 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean weight z-score at Discharge was - 0.73	MD 0.1 higher (0.33 lower to 0.53 higher)
Length z-score at Discharge	51 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean length z-score at Discharge was - 0.73	MD 0.27 higher (0.08 lower to 0.61 higher)
Head Circumference z-score at Discharge	51 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean head Circumference z-score at Discharge was -0.63	MD 0.23 higher (0.16 lower to 0.63 higher)
Fat Free Mass Index (kg/m ²) at End of Intervention	70 (1 RCT)	⊕⊕○○ Low ^a	-	The mean fat Free Mass Index (kg/m ²) at End of Intervention was 9.7	MD 0.2 higher (0.29 lower to 0.69 higher)
Duration of Initial Hospital Stay (days)	99 (2 RCTs)	⊕⊕○○ Low ^a	-	The mean duration of Initial Hospital Stay (days) was 51.67	MD 0.28 higher (6.59 lower to 7.15 higher)
Time to Full Enteral Feeds (days)	30 (1 RCT)	⊕⊕○○ Low ^a	-	The mean time to Full Enteral Feeds (days) was 8.33	MD 0.67 higher (4.16 lower to 5.5 higher)
Bronchopulmonary dysplasia	215 (4 RCTs)	⊕⊕○○ Low ^a	RR 0.82 (0.62 to 1.08)	Study population	
				486 per 1,000	87 fewer per 1,000

					(185 fewer to 39 more)
Feeding Intolerance	204 (4 RCTs)	⊕⊕○○ Low ^a	RR 0.89 (0.52 to 1.52)	Study population	
				214 per 1,000	23 fewer per 1,000 (103 fewer to 111 more)
Sepsis	220 (3 RCTs)	⊕⊕○○ Low ^a	RR 0.78 (0.46 to 1.32)	Study population	
				207 per 1,000	46 fewer per 1,000 (112 fewer to 66 more)
Retinopathy of Prematurity	87 (2 RCTs)	⊕⊕○○ Low ^a	RR 1.00 (0.45 to 2.23)	Study population	
				182 per 1,000	0 fewer per 1,000 (100 fewer to 224 more)
Anemia of Prematurity - not reported	-	-	-	-	-
Cost - not reported	-	-	-	-	-
Time to Full Sucking Feeds - not reported	-	-	-	-	-

- a. Downgraded two levels for imprecision due to insufficient sample size and wide confidence interval
b. Downgraded two levels for inconsistency because $I^2 > 75\%$ and $P < 0.10$
c. Downgraded one level for imprecision due to insufficient sample size
d. Downgraded one level for risk of bias because allocation concealment and blinding were unclear for the one study

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Duration of hospital stay: RCT: No significant effect in hospital stay for individualised fortification (MD 0.28 days higher; 6.59 lower to 7.15 higher) [Important]. Time to full enteral feeds: RCT: No significant effect in the time to full enteral feeds for individualised fortification (MD 0.67 days higher; 4.16 lower to 5.5 higher) [Important]. Undesirable effects for Māori No available evidence	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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○ Very low ● Low ○ Moderate ○ High ○ No included studies	Moderate to very low certainty of evidence overall. Certainty of evidence for Māori No available evidence	
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Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality	CRITICAL	⊕⊕○○ Low ^a
Neurodevelopmental Impairment - not measured	CRITICAL	-
Necrotising Enterocolitis	CRITICAL	⊕⊕○○ Low ^a
Full Breastmilk Feeding at Hospital Discharge - not measured	CRITICAL	-
Full Breastfeeding at Hospital Discharge - not reported	CRITICAL	-
Length gain (mm/day) during Intervention Period	IMPORTANT	⊕○○○ Very low ^{b,c}
Head Circumference Gain (mm/day) during Intervention Period	IMPORTANT	⊕⊕⊕○ Moderate ^c
Fat Mass Index at End of Intervention (kg/m ²)	IMPORTANT	⊕⊕○○ Low ^a
Weight Gain (g/kg/day) during Intervention	IMPORTANT	⊕⊕○○ Low ^b
Weight z-score at Discharge	IMPORTANT	⊕○○○ Very low ^{a,d}
Length z-score at Discharge	IMPORTANT	⊕○○○ Very low ^{a,d}
Head Circumference z-score at Discharge	IMPORTANT	⊕○○○ Very low ^{a,d}
Fat Free Mass Index (kg/m ²) at End of Intervention	IMPORTANT	⊕⊕○○

		Low ^a
Duration of Initial Hospital Stay (days)	IMPORTANT	⊕⊕○○ Low ^a
Time to Full Enteral Feeds (days)	IMPORTANT	⊕⊕○○ Low ^a
Bronchopulmonary dysplasia / Chronic lung disease	IMPORTANT	⊕⊕○○ Low ^a
Feeding Intolerance	IMPORTANT	⊕⊕○○ Low ^a
Sepsis	IMPORTANT	⊕⊕○○ Low ^a
Retinopathy of Prematurity	IMPORTANT	⊕⊕○○ Low ^a
Anemia of Prematurity - not reported	IMPORTANT	-
Cost - not reported	IMPORTANT	-
Time to Full Sucking Feeds - not reported	NOT IMPORTANT	-

- a. Downgraded two levels for imprecision due to insufficient sample size and wide confidence interval
b. Downgraded two levels for inconsistency because $I^2 > 75\%$ and $P < 0.10$
c. Downgraded one level for imprecision due to insufficient sample size
d. Downgraded one level for risk of bias because allocation concealment and blinding were unclear for the one study

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ Important uncertainty or variability ☒ Possibly important uncertainty or variability ☐ Probably no important	Possibly important uncertainty or variability Values for Māori No data available	

uncertainty or variability ○ No important uncertainty or variability		
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Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Individualised fortification versus standardised EBM fortification: moderate certainty evidence Increase in head circumference during the intervention Individualised fortification versus standardised EBM fortification: low certainty evidence Increase in fat mass at the end of the intervention Increase in weight gain Uncertain effect on mortality, NEC, fat free mass at end of the intervention, duration of hospital stay, time to full enteral feeds, bronchopulmonary dysplasia, feeding intolerance, sepsis, retinopathy of prematurity Individualised fortification versus standardised EBM fortification: very low certainty evidence Increase in length during the intervention Uncertain effect on weight, length and head circumference z-score at discharge Balance of effects for Māori - No additional data	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	1. Clinical Equipment Human milk analyser (for macronutrient analysis of breastmilk) Blood sampling tools (for measuring blood urea nitrogen levels when using targeted fortification based on infant response) Modular nutrient supplements (individual components such as protein, carbohydrate and fat supplements to adjust milk composition) Sterile mixing and storage containers for handling fortified milk Calibrated scales and precision measuring tools for accurate preparation 2. Technology and Software	

	Data recording systems to track nutrient content, intake and infant response Clinical nutrition software for calculating individualised nutrient requirements and guiding fortification adjustments Electronic health record integration to support documentation and care planning 3. Human Resources Specialist neonatal dietitian with expertise in preterm infant nutrition Lactation consultants to support ongoing breastmilk supply and maternal education Neonatal nurses and doctors trained in administering individualised nutrition plans 4. Training and Protocol Development Training programmes for all relevant staff in: Use of milk analysers Safe preparation and storage of fortified milk Interpreting lab results for personalised nutrition planning Standard operating procedures to ensure consistent, safe and culturally appropriate practice Ongoing professional development to update staff on new evidence and best practice 5. Infrastructure and Support Systems Dedicated space for milk analysis and fortification preparation Robust infection control protocols to manage safe milk handling Clear communication channels between neonatal team members, dietitians and parents Equity-focused policies to ensure all families have equal access regardless of ethnicity, geography or hospital resources Resources required for Māori No additional data	
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Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	A formal assessment of the certainty of evidence of the cost was not undertaken. Certainty of evidence of required resources for Māori No additional data	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	There are no studies that assess the specific cost-effectiveness of individualised fortification compared with standardised EBM fortification, particularly in the context of preterm infants. Cost effectiveness for Māori No additional evidence available	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Pēpi Māori are more likely to be born preterm and face higher rates of growth restriction, neurodevelopmental impairment and mortality. Breastmilk fortification plays a critical role in supporting better outcomes, yet current standard fortification may not meet the specific needs of all preterm infants. If individualised fortification is introduced without equitable access to milk analysis technology, staff training or clinical oversight, Māori pēpi may be further disadvantaged. To reduce health inequities, any shift towards individualised nutrition must include a commitment to culturally safe care, resource equity and consistent application across all units serving whānau Māori and their preterm pēpi. Equity for Pacific families Pacific infants and those from other under-represented groups often face barriers to optimal neonatal nutrition due to inconsistent access to culturally appropriate care and specialised resources. Standard fortification may not provide enough flexibility to meet individual needs, yet individualised approaches risk widening inequities if not implemented fairly. These methods require specialist equipment, staff expertise and time, which may not be equally available in all hospitals or regions. Ensuring equity means addressing these gaps so that all preterm infants receive appropriately fortified breastmilk regardless of ethnicity or location. Equal opportunity for optimal nutrition is essential for reducing long-term disparities. Equity for underrepresented groups Migrant, rural and lower-income families may face reduced access to individualised fortification due to geography, transport challenges or language differences. Without clear	

	guidance and support, their preterm infants risk undernutrition. Equity means ensuring all units have the tools and systems to offer individualised care regardless of family background or location.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Individualised breastmilk fortification for preterm infants is likely to be acceptable to most stakeholders if implemented thoughtfully. Clinicians support its precision but would need training and resources. Parents may value tailored care but require culturally safe, clear explanations, especially whānau Māori and Pacific families. There may be concerns that this would widen inequities if only offered in well-resourced hospitals. Acceptability depends on ensuring consistent access, national guidance and respectful engagement with families. Without these, the approach risks being misunderstood or unevenly applied, limiting its impact on improving outcomes for preterm infants across Aotearoa New Zealand.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ● Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know	Individualised breastmilk fortification is feasible in Aotearoa New Zealand, particularly in tertiary hospitals where specialist staff, equipment and systems may already exist but would require substantial additional funding and resources. Wider implementation is limited by gaps in access to breastmilk analysers, neonatal dietitians and consistent training across regions. Smaller or rural units may lack the infrastructure and resources needed. Without a national strategy, implementation risks becoming inequitable, disadvantaging whānau Māori, Pacific families and others in under-resourced areas. Feasibility depends on targeted investment, standardised protocols, culturally safe care and equity-focused planning to ensure all preterm infants can benefit regardless of location or background.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know

	JUDGEMENT						
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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EtD 27. Should early fortification vs. later fortification of expressed breastmilk be used for preterm infants?

POPULATION:	Preterm infants
INTERVENTION:	Early fortification
COMPARISON:	Later fortification of expressed breastmilk
MAIN OUTCOMES:	Critical outcomes Mortality Necrotising enterocolitis Adverse effects – milk curd obstruction, metabolic bone disease Neurodevelopmental impairment Fully breastfed or breastmilk feeding at hospital discharge Faltering growth/body composition Time to full enteral feeds Duration of initial hospital stay Important but not critical Sepsis: proven or suspected Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation - population perspective
BACKGROUND:	Fortifying expressed breastmilk is a key nutritional intervention for preterm infants, designed to meet their elevated protein, energy, and micronutrient requirements. However, the optimal timing for introducing fortification—whether before or after full enteral feeds are achieved—remains an area of debate in clinical practice. Common practices are to start fortification when the infant's feed size reaches 5 mL or when daily enteral feed volume reaches 100 mL/kg/day. Another approach is to commence fortification earlier, in some cases as early as the first enteral feed. Commencing fortification early may provide earlier nutritional support, addressing deficits in protein, energy, calcium, and phosphorus that are critical for growth, avoiding refeeding syndrome, neurodevelopment and bone mineralisation. Early fortification could potentially lead to improved growth trajectories and earlier attainment of nutritional goals, reducing reliance on parenteral nutrition. On the other hand, concerns exist that introducing fortification before full enteral feeds are reached may increase the risk of gastrointestinal complications, including feed intolerance, milk curd obstruction and necrotising enterocolitis, due to the immature gastrointestinal system in preterm infants. Delaying fortification may mitigate these risks by delaying enhanced nutrition until the gastrointestinal system is more mature and better able to tolerate the added nutrients. However, this also leads to significant nutrient deficits as

CONFLICT OF INTERESTS:	parenteral nutrition is titrated down and delays the achievement of recommended nutrient intakes which may have ongoing implications for growth.
	None

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	The title of this question was changed from "<i>Should fortified expressed breastmilk be commenced before full enteral feeds are established vs. once enteral feeds have been established in preterm infants</i> " as no studies comparing the addition of fortifier before full enteral feeds were reached with after full enteral feeds were reached were found. Within the systematic reviews, the fortifier used in the Sullivan study was human breastmilk-based fortifier. The study has been included in the analysis as it was in the systematic review. Evidence from three systematic reviews [1-3] for the comparison of early (defined as ≤ 40 mL/kg/day) with later (≥ 75 mL/kg/day) fortification of breastmilk and two RCTs [4] [5]. No faltering growth/body composition: RCT: Little or no effect of early feeding on length (MD 0.1 higher cm/week; 0.03 lower to 0.22 higher); length z score at 4 weeks MD 0.03 points lower; 0.28 lower to 0.22 higher); length z score at 36 weeks' post-menstrual age (MD 0.03 points lower; 0.28 lower to 0.22 higher); time to regain birthweight (MD 0.06 days lower; 1.32 lower to 1.2 higher); weight z score at 4 weeks (MD 0.14 points higher; 0.02 lower to 0.3 higher); weight z score at 36 weeks' post-menstrual age (MD 0.13 points higher; 0.08 lower to 0.34 higher); or head circumference (MD 0.01 cm/week lower; 0.07 lower to 0.06 higher) [Critical]. No faltering growth/body composition: single RCT: Significant increase in median length, head circumference and weight velocity for early fortification. Significantly earlier time to regain birthweight in early fortification group [Critical]. No faltering growth/body composition: single RCT: No significant difference in weight, length or head circumference velocity at 28 days or 36 weeks [Critical]. Time to full enteral feeds: Single RCT: No difference between groups for time to full enteral feeds [Important]. Duration of initial hospital stay: Single RCT: No difference between groups for duration of hospital stay in both additional RCTs [Important]. Necrotising enterocolitis (NEC): RCT: No significant reduction in risk of NEC with	Population information for included evidence Systematic review [1]. Evidence compares commencing an enteral feed volume of ≤ 40 mL/kg/day versus delayed at ≥ 75 mL/kg/day. The gestational age of most included infants was 27–30 weeks, and all had a birthweight < 2000 g. Systematic review [2]. Two trials one of which included infants with birthweight < 1500 g. Early fortification started at 20 mL/kg/day and late fortification was 100 mL/kg/day. The second trial included infants with birthweight 500 to 1250 g. Early fortification started at 40 mL/kg/day and late fortification was 100 mL/kg/day. Systematic review [3] Included previously identified studies. USA: RCT [4]: Very low birthweight (VLBW) infants. India: RCT [5]: Infants ≤ 32 weeks' gestation. An additional Australian observational study [6] was found that looked at moderately preterm to late preterm, low birthweight infants at 80 mL/kg/day vs. 160 mL/kg/day. There was no significant different

	early feeding (6 fewer per 1,000; 43 fewer to 76 more) [Critical]. Necrotising enterocolitis (NEC): Single RCT: No difference in risk of NEC Early group 1/26 vs. late group 0/26[Important]. Sepsis: RCT: No significant reduction in risk of sepsis for early feeding (25 fewer per 1,000; 83 fewer to 69 more) [Important]. Sepsis: Single RCT: No event reported. No difference between groups in second additional RCT [Important]. Retinopathy of prematurity: Single RCT: No events reported in either group [Important]. Desirable effects for Māori No additional evidence available.	between groups for weight gain velocity or late onset sepsis. The early fortification group regained birthweight almost two days earlier than the later fortification group (7.5 vs. 9.4 days, $p < 0.01$). Feeding intolerance was decreased for early fortification group (24.4% vs. 47.6%, $p < 0.03$). There were no cases of NEC.
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Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with later fortification of expressed breastmilk	Risk difference with early fortification
Mortality: RCT	237 (2 RCTs)	⊕⊕⊕⊕ Very low ^{a,b}	RR 1.32 (0.30 to 5.77)	Study population 26 per 1,000	8 more per 1,000 (18 fewer to 122 more)
Necrotising enterocolitis	378 (3 RCTs)	⊕⊕⊕⊕ Very low ^{a,b}	RR 0.92 (0.41 to 2.05)	Study population 72 per 1,000	6 fewer per 1,000 (43 fewer to 76 more)
Necrotising enterocolitis	52 (1 RCT)	⊕⊕⊕⊕ Low ^c	-	Early group 1/26 vs. late group 0/26	
Adverse effects - not measured	-	-	-	-	-
Neurodevelopmental impairment - not reported	-	-	-	-	-
Fully breastfed or breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Faltering growth/body composition: RCT assessed with: Length (cm/week)	237 (2 RCTs)	⊕⊕⊕⊕ Moderate ^a	-	The mean faltering growth/body composition: RCT was 0.74 cm/week	MD 0.1 higher (0.03 lower to 0.22 higher)
Faltering growth/body composition: RCT assessed with: Length gain (cm/wk)	110 (1 RCT)	⊕⊕⊕⊕ High	-	Early fortification (n=55) median 1 (IQR 0.75-1.13) vs. late fortification (n=55) 0.88 (IQR 0.75-1.00) cm/week. P=0.031	
Faltering growth/body composition: RCT assessed with: Length velocity 28 days (cm/week)	52 (1 RCT)	⊕⊕⊕⊕ High	-	Early group (n=26) 1.0 +/-0.2 cm/week vs. late group (n=26) 1.0 +/- 0.2 cm/week (Not significant)	

Faltering growth/body composition: RCT assessed with: Length velocity 36 weeks (cm/week)	52 (1 RCT)	⊕⊕⊕⊕ High	-	Early group (n=26) 1.1 +/-0.2 cm/week vs. late group (n=26) 1.1 +/- 0.2 cm/week (Not significant)	
Faltering growth/body composition: RCT assessed with: Length z score at 4 weeks	99 (1 RCT)	⊕○○○ Very low ^{a,b,d}	-	The mean faltering growth/body composition: RCT was -0.97 points	MD 0.03 lower (0.28 lower to 0.22 higher)
Faltering growth/body composition: RCT assessed with: Length z score at 36 post-menstrual weeks	99 (1 RCT)	⊕○○○ Very low ^{a,b,d}	-	The mean faltering growth/body composition: RCT was 1.59 points	MD 0.01 higher (0.35 lower to 0.37 higher)
Faltering growth/body composition: RCT assessed with: Time to regain birthweight (days)	237 (2 RCTs)	⊕⊕○○ Low ^{a,e}	-	The mean faltering growth/body composition: RCT was 8.7 days	MD 0.06 lower (1.32 lower to 1.2 higher)
Faltering growth/body composition: RCT assessed with: Time to regain birthweight (days)	110 (1 RCT)	⊕⊕⊕○ Moderate ^f	-	Time to regain birthweight:Early fortification (n=55) mean 10.13 +/- 2.90 days vs. late fortification (n=55) 11.26 +/-3.06 days P=0.049.	
Faltering growth/body composition: RCT assessed with: Weight z score at 4 weeks	99 (1 RCT)	⊕○○○ Very low ^{a,d}	-	The mean faltering growth/body composition: RCT was -1.10 points	MD 0.14 higher (0.02 lower to 0.3 higher)
Faltering growth/body composition: RCT assessed with: Weight z score at 36 post-menstrual weeks	99 (1 RCT)	⊕○○○ Very low ^{a,d,e}	-	The mean faltering growth/body composition: RCT was -1.41 points	MD 0.13 higher (0.08 lower to 0.34 higher)
Faltering growth/body composition: RCT assessed with: Weight velocity 28 days (g/kg/day)	52 (1 RCT)	⊕⊕○○ Low ^d	-	Early group (n=26) 13.3 +/-2.8 g/kg/day vs. late group (n=26) 13.4 +/- 2.7 g/kg/day (Not significant)	
Faltering growth/body composition: RCT assessed with: Weight gain velocity (g/kg/d)	110 (1 RCT)	⊕⊕○○ Low ^g	-	Early fortification (n=55) median 11.6 (IQR 7.68-15.66) vs. late fortification (n=55) 8.99 (IQR 6.48 - 11.43) g/kg/day. P=0.012	
Faltering growth/body composition: RCT assessed with: Weight velocity 36 weeks (g/kg/day)	52 (1 RCT)	⊕⊕○○ Low ^d	-	Early group (n=26) 13.5 +/-2.6 g/kg/day vs. late group (n=26) 13.9 +/- 2.7 g/kg/day (Not significant)	
Faltering growth/body composition: RCT assessed with: Head circumference (cm/week)	237 (2 RCTs)	⊕⊕⊕○ Moderate ^a	-	The mean faltering growth/body composition: RCT was 0.66 cm/week	MD 0.01 lower (0.07 lower to 0.06 higher)
Faltering growth/body composition: RCT assessed with: Head circumference 28 days (cm/week)	52 (1 RCT)	⊕⊕⊕⊕ High	-	Early group (n=26) 0.8 +/-0.2 cm/week vs. late group (n=26) 0.8 +/- 0.2 cm/week (Not significant)	
Faltering growth/body composition: RCT assessed with: Head circumference gain (cm/wk)	110 (1 RCT)	⊕⊕⊕⊕ High	-	Early fortification (n=55) median 0.77 (IQR 0.65-0.90) vs. late fortification (n=55) 0.625 (IQR 0.5-0.875) cm/week. P=0.014	
Faltering growth/body composition: RCT assessed with: Head circumference 36 weeks (cm/week)	52 (1 RCT)	⊕⊕⊕⊕ High	-	Early group (n=26) 0.8 +/-0.2 cm/week vs. late group (n=26) 0.9 +/- 0.2 cm/week (Not significant)	
Time to full enteral feeds: RCT assessed with: feeding intolerance	168 (2 RCTs)	⊕○○○ Very low ^{a,b}	RR 1.13 (0.65 to 1.95)	Study population	
				209 per 1,000	27 more per 1,000

					(73 fewer to 199 more)
Time to full enteral feeds assessed with: ≥ 150 mL/kg/day	237 (2 RCTs)	⊕⊕○○ Low ^{a,e}	-	The mean time to full enteral feeds was 26.1 days	MD 0.27 higher (3.48 lower to 4.02 higher)
Time to full enteral feeds: RCT assessed with: Days	110 (1 RCT)	⊕⊕⊕⊕ High	-	Early fortification (n=55) mean 5.56 +/- 1.34 days vs. late fortification (n=55) 5.38 +/- 0.95 days; not significant.	
Duration of initial hospital stay: RCT assessed with: Days	237 (2 RCTs)	⊕○○○ Very low ^{a,b}	-	The mean duration of initial hospital stay: RCT was 72.9 days	MD 2.33 higher (6.44 lower to 11.11 higher)
Duration of initial hospital stay: RCT assessed with: Days	52 (1 RCT)	⊕⊕○○ Low ^e	-	Early group (n=26) 48 +/- 21 days vs. late group (n=26) 50 +/- 19 days (Not significant)	
Duration of hospital stay: RCT assessed with: Days	110 (1 RCT)	⊕⊕○○ Low ^e	-	Early fortification (n=55) median 25 (IQR 15-35) vs. late fortification (n=55) 18 (IQR 15-28) days. Not significant	
Sepsis: proven or suspected: RCT	378 (3 RCTs)	⊕○○○ Very low ^{a,b}	RR 0.86 (0.53 to 1.39)	Study population	
				176 per 1,000	25 fewer per 1,000 (83 fewer to 69 more)
Sepsis: proven or suspected: RCT assessed with: Late onset sepsis	52 (1 RCT)	⊕⊕○○ Low ^c	-	Early group 0/26 vs. late group 0/26	
Sepsis: RCT	110 (1 RCT)	⊕⊕⊕⊕ High	-	Early fortification 6/55 (11%) vs. late fortification 5/55 (9%); not significant.	
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Retinopathy of prematurity	52 (1 RCT)	⊕○○○ Very low ^{c,d}	not estimable	Study population	
				0 per 1,000	Not estimable no events
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-

- a. Downgraded one level for concerns around risk of bias, in particular blinding and selective outcome reporting
b. Downgraded two levels for imprecision with very wide confidence intervals that cross the line of no effect (signalling uncertainty about direction and magnitude of effect)
c. Downgraded two levels for imprecision due to small sample size and no or low events
d. Downgraded one level for indirectness as evidence is based on a single trial
e. Downgraded one level for imprecision
f. Downgraded one level for inconsistency due to variation in the data
g. Downgraded two levels for inconsistency due to wide variation in the data

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Mortality: RCT: No significant increase in mortality with early feeding (8 more per 1,000; 18 fewer to 122 more) [Critical]. Time to full enteral feeds: RCT: No significant increase in risk of feeding intolerance with early feeding (27 more per 1,000; 73 fewer to 199 more); or in feeds ≥ 150 mL/kg/day (MD 0.27 higher; 3.48 lower to 4.02 higher) [Critical]. Duration of initial hospital stay: RCT: No significant increase in duration of hospital stay for early feeding (MD 2.33 days higher; 6.44 lower to 11.11 higher) [Critical]. Undesirable effects for Māori No additional evidence available.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Moderate to very low certainty evidence overall Certainty of evidence for Māori No additional evidence available.	

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis	IMPORTANT	⊕⊕○○ Low
Adverse effects - not measured	CRITICAL	-
Neurodevelopmental impairment - not reported	CRITICAL	-
Fully breastfed or breastmilk feeding at hospital discharge - not measured	CRITICAL	-

Faltering growth/body composition: RCT assessed with: Length (cm/week)	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT assessed with: Length gain (cm/wk)	CRITICAL	⊕⊕⊕⊕ High
Faltering growth/body composition: RCT assessed with: Length velocity 28 days (cm/week)	CRITICAL	⊕⊕⊕⊕ High
Faltering growth/body composition: RCT assessed with: Length velocity 36 weeks (cm/week)	CRITICAL	⊕⊕⊕⊕ High
Faltering growth/body composition: RCT assessed with: Length z score at 4 weeks	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Length z score at 36 post-menstrual weeks	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Time to regain birthweight (days)	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT assessed with: Time to regain birthweight (days)	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT assessed with: Weight z score at 4 weeks	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Weight z score at 36 post-menstrual weeks	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Weight velocity 28 days (g/kg/day)	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT assessed with: Weight gain velocity (g/kg/d)	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT assessed with: Weight velocity 36 weeks (g/kg/day)	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT assessed with: Head circumference (cm/week)	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT assessed with: Head circumference 28 days (cm/week)	CRITICAL	⊕⊕⊕⊕ High
Faltering growth/body composition: RCT assessed with: Head circumference gain (cm/wk)	CRITICAL	⊕⊕⊕⊕ High

Faltering growth/body composition: RCT assessed with: Head circumference 36 weeks (cm/week)	CRITICAL	⊕⊕⊕⊕ High
Time to full enteral feeds: RCT assessed with: feeding intolerance	CRITICAL	⊕○○○ Very low
Time to full enteral feeds assessed with: ≥ 150 mL/kg/day	CRITICAL	⊕⊕○○ Low
Time to full enteral feeds: RCT assessed with: Days	CRITICAL	⊕⊕⊕⊕ High
Duration of initial hospital stay: RCT assessed with: Days	CRITICAL	⊕○○○ Very low
Duration of initial hospital stay: RCT assessed with: Days	IMPORTANT	⊕⊕○○ Low
Duration of hospital stay: RCT assessed with: Days	CRITICAL	⊕⊕○○ Low
Sepsis: proven or suspected: RCT	IMPORTANT	⊕○○○ Very low
Sepsis: proven or suspected: RCT assessed with: Late onset sepsis	IMPORTANT	⊕⊕○○ Low
Sepsis: RCT	CRITICAL	⊕⊕⊕⊕ High
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Retinopathy of prematurity	IMPORTANT	⊕○○○ Very low
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Some important uncertainty about or variability in how people value the main outcomes. Values for Māori No additional evidence available.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Early fortification vs. later fortification of EBM - high certainty evidence Probable increase in length and head circumference Uncertain effect on sepsis and time to full enteral feeds Early fortification vs. later fortification of EBM- moderate certainty evidence Uncertain effect on faltering growth/body composition (length; head circumference) Early fortification vs. later fortification of EBM- low certainty evidence Uncertain effect on NEC, time to regain birthweight, weight velocity at 28 days and 36 weeks, duration of initial hospital stay, time to full enteral feeds (≥ 150 mL/kg/day), sepsis Early fortification vs. later fortification of EBM- very low certainty evidence Uncertain effect on mortality, necrotising enterocolitis, faltering growth/body composition (length z score at 4 weeks; length z score at 36 weeks' post-menstrual age; weight z score at 4 weeks; weight z score at 36 weeks' post-menstrual age); time to full enteral feeds (feeding intolerance); duration of initial hospital stay; sepsis, retinopathy of prematurity. Balance of effects for Māori No additional evidence is available.	
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Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	If the difference between early and late addition of breastmilk fortifier is assumed to be 3 to 5 days, the additional cost of fortifier will be \$3 to \$6 per day, therefore a total of \$9 to \$30 depending on the size of the infant and volumes used (negligible). Resources required for Māori No additional evidence available.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ● High ○ No included studies	The cost is certain. Certainty of evidence of required costs for Māori No additional evidence available.	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	There are no studies that assess the specific cost-effectiveness of fortified expressed breastmilk commenced before full enteral feeds, particularly in the context of preterm infants. The cost difference in fortifier is trivial. Cost effectiveness for Māori No additional evidence is available.	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Pēpi Māori are more likely to be born preterm and experience higher rates of neonatal morbidity and mortality, yet face barriers to optimal nutrition, including limited access to culturally responsive lactation support and early fortification guidance. Delayed fortification could worsen hypophosphataemia, which is associated with higher morbidity and mortality and may worsen growth disparities and long-term health outcomes. Strengthening whānau-led education, integrating	

	tikanga Māori in neonatal care and ensuring equitable access to breastmilk fortification can improve outcomes. Equity for Pacific families Pacific preterm infants face disproportionate barriers to optimal nutrition, including financial constraints, language barriers and lower access to culturally safe neonatal care. Early fortification may prevent growth faltering, yet families may be unaware of its benefits. Providing multilingual education, supporting breastfeeding continuation alongside fortification and involving community leaders in neonatal nutrition strategies can bridge these inequities. Equity for underrepresented groups Families from underrepresented backgrounds may not receive adequate explanation about early versus later introduction of fortifiers. Without understanding the rationale, they may feel confused or marginalised in care. Equity requires accessible education and consistent clinical practice to ensure all families are informed and supported during early feeding decisions.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Acceptability for Māori No additional evidence available.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● No ○ Probably no ○ Probably yes ○ Yes ○ Varies	The intervention may not be feasible because the breastmilk fortifier powder used in Aotearoa New Zealand needs to be added to 25 mL of expressed breastmilk. If the feed volume is small, for instance, 2 mL every 2 hours for a 600 g infant = 40 mL/kg/day, if 25 mL of expressed breastmilk is available, it would take 12 hours to use 25 mL. The manufacturer's instructions say that fortified breastmilk should be	

○ Don't know	used immediately. In clinical practice, it may be stored in the fridge for 4 to 8 hours to avoid wasting breastmilk but not usually as long as for 12 hours. This will be an issue if fortifier is started before the feed volume reaches 5 mL. Feasibility for Māori No additional evidence available.	
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Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know

	JUDGEMENT						
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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EtD 28. Should human-based fortifier vs. bovine-based fortifier be used in preterm infants?

POPULATION:	Preterm infants
INTERVENTION:	Human milk-based fortifier
COMPARISON:	Bovine milk-based fortifier
MAIN OUTCOMES:	Critical for making a decision Mortality Neurodevelopmental impairment Necrotising enterocolitis (NEC) Adverse effects Fully breastmilk feeding at hospital discharge Faltering growth/body composition Important but not critical Duration of initial hospital stay Time to full enteral feeds Bronchopulmonary dysplasia Sepsis: proven or suspected Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Of limited importance Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical guideline recommendation - patient perspective
BACKGROUND:	For very preterm infants, mother's own breastmilk is the preferred feed, but multinutrient fortifiers are needed to meet their recommended nutritional requirements. Most fortifiers are bovine (cow's) milk-based, but with the increasing use of donor breastmilk, interest has grown in using multinutrient fortifiers derived from human milk. Research suggests a potential link between bovine-derived products and higher NEC risk, prompting the development of human milk-derived fortifiers, despite their high cost. These fortifiers are currently available in North America, the UK and Australia, but regulations, policies and ethical concerns regarding the commercialisation of human milk vary globally. The evidence supporting human milk-based fortifiers is limited, relying on a few randomised trials and observational studies. Given the importance of NEC as a cause of serious morbidity and mortality worldwide, the large costs associated with human-derived products to society along with the ethical issues raised, there is an urgent need to systematically review the evidence base for using human milk-derived fortifiers.
CONFLICT OF	None

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS			
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	We pooled data on 8 RCTs [1-8]. Necrotising enterocolitis (NEC): RCT: No significant reduction on NEC ≥ stage 2 (37 fewer per 1,000; 60 fewer to 3 more) or for surgical NEC (29 fewer per 1,000; 44 fewer to 8 more) [Critical]. No faltering growth/body composition: RCT: No significant effect on length increment (MD 0.16 cm/week lower; 0.33 lower to 0.01 higher); length on day 21 (MD 0.91 cm lower; 2.17 lower to 0.35 higher); rate of weight gain (MD 0.76 g/kg/day lower; 2.34 lower to 0.83 higher); weight on day 21 (MD 113.2 g lower; 276.33 lower to 49.93 higher); growth in head circumference (MD 0.04 cm/week higher; 0.11 lower to 0.2 higher); head circumference on day 21 (MD 0.15 cm higher; 1.2 lower to 1.5 higher) [Critical]. Time to reach full enteral feeds: RCT: Time to reach full enteral feeds (150 mL/kg/day) was a median of 10 days in both groups. Human milk fortification (n=115) median 10 days (IQR 8-15); Bovine milk fortification (n=113) median 10 days (IQR 7-15) [Important]. Bronchopulmonary dysplasia: RCT: No significant reduction in bronchopulmonary dysplasia (51 fewer per 1,000; 133 fewer to 57 more) [Important]. Retinopathy of prematurity: RCT: No significant reduction in retinopathy of prematurity (8 fewer per 1,000; 61 fewer to 56 more) [Important]. Desirable effects for Māori No additional evidence is available.	Population information for included evidence Italy: RCT [1]: Low birthweight infants. UK: RCT [2]: Infants <30 weeks' gestational age. UK: RCT [3]: <32 weeks' gestation or <1500 g who had reached full enteral feeds. Sweden: RCT [4]: Extremely preterm infants born between gestational week 22 + 0 and 27 + 6 fed exclusively human breastmilk. Brazil: RCT [5]: Very low birthweight infants. Canada: RCT [6]: Infants born <1250 g. Sweden/Italy: RCT [7]: Preterm infants with birthweights ranging from 940 g to 1750 g. USA: RCT [8]: Extremely premature infants birthweight 500 to 1250 g			
Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with bovine-based fortifier	Risk difference with E.G. 2.4 human-based fortifier
Mortality: RCT	714 (5 RCTs)	⊕⊕⊕○ Moderate ^a	RR 0.72 (0.42 to 1.23)	Study population	
				84 per 1,000	24 fewer per 1,000 (49 fewer to 19 more)
Neurodevelopmental impairment: RCT assessed with: Bayley III Cognitive score <85	116 (1 RCT)	⊕○○○ Very low ^{a,b,c}	RR 1.09 (0.56 to 2.12)	Study population	
				222 per 1,000	20 more per 1,000

					(98 fewer to 249 more)
Neurodevelopmental impairment: RCT assessed with: Bayley III language score <85	113 (1 RCT)	⊕○○○ Very low ^{a,b,c}	RR 0.89 (0.56 to 1.43)	Study population	
				404 per 1,000	44 fewer per 1,000 (178 fewer to 174 more)
Neurodevelopmental impairment: RCT: RCT assessed with: Bayley III Motor score < 85	115 (1 RCT)	⊕○○○ Very low ^{a,b,c}	RR 1.03 (0.52 to 2.04)	Study population	
				222 per 1,000	7 more per 1,000 (107 fewer to 231 more)
Neurodevelopmental impairment: RCT assessed with: Bayley III Cognitive score <70	116 (1 RCT)	⊕○○○ Very low ^{a,b,c}	RR 0.87 (0.37 to 2.04)	Study population	
				167 per 1,000	22 fewer per 1,000 (105 fewer to 173 more)
Neurodevelopmental impairment: RCT assessed with: Bayley III Language score <70	113 (1 RCT)	⊕○○○ Very low ^{a,b,c}	RR 0.93 (0.45 to 1.93)	Study population	
				212 per 1,000	15 fewer per 1,000 (116 fewer to 197 more)
Neurodevelopmental impairment: RCT assessed with: Bayley III Motor score <70	115 (1 RCT)	⊕○○○ Very low ^{a,b,c}	RR 0.71 (0.30 to 1.66)	Study population	
				185 per 1,000	54 fewer per 1,000 (130 fewer to 122 more)
Necrotising enterocolitis >= 2: RCT	600 (4 RCTs)	⊕⊕⊕○ Moderate ^a	RR 0.59 (0.34 to 1.03)	Study population	
				91 per 1,000	37 fewer per 1,000 (60 fewer to 3 more)
Necrotising enterocolitis surgical: RCT	463 (3 RCTs)	⊕⊕○○ Low ^{a,d}	RR 0.49 (0.21 to 1.14)	Study population	
				56 per 1,000	29 fewer per 1,000 (44 fewer to 8 more)
Adverse effect: RCT: Feeding interruption	353 (2 RCTs)	⊕○○○ Very low ^{a,c}	RR 0.99 (0.76 to 1.28)	Study population	
				391 per 1,000	4 fewer per 1,000 (94 fewer to 109 more)
Adverse effects: Metabolic bone disease of prematurity - not measured	-	-	-	-	-
Fully breastmilk feeding at hospital discharge: RCT assessed with: Mothers own milk at discharge	28 (1 RCT)	⊕○○○ Very low ^{a,b,c}	RR 0.64 (0.35 to 1.15)	Study population	
				786 per 1,000	283 fewer per 1,000 (511 fewer to 118 more)
Faltering growth / body composition: RCT: Length increment assessed with: (cm/week)	75 (2 RCTs)	⊕⊕○○ Low ^{a,e}	-	The mean faltering growth / body composition: RCT: Length increment was 1.18 cm/week	MD 0.16 lower (0.33 lower to 0.01 higher)

Faltering growth / body composition: RCT: Length Day 21 assessed with: (cm)	40 (1 RCT)	⊕○○○ Very low ^{a,b,e}	-	The mean faltering growth / body composition: RCT: Length Day 21 was 42.05 cm	MD 0.91 lower (2.17 lower to 0.35 higher)
Faltering growth / body composition: RCT: Weight Day 21 assessed with: (g)	40 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth / body composition: RCT: Weight Day 21 was 1,678.5 g	MD 113.2 lower (276.33 lower to 49.93 higher)
Faltering growth / body composition: RCT: Rate of weight gain assessed with: (g/kg/day)	282 (3 RCTs)	⊕○○○ Very low ^{a,c}	-	The mean faltering growth / body composition: RCT: Rate of weight gain was 17.06 g/kg/day	MD 0.76 lower (2.34 lower to 0.83 higher)
Faltering growth / body composition: RCT: Growth in head circumference assessed with: (cm/week)	75 (2 RCTs)	⊕⊕○○ Low ^{a,e}	-	The mean faltering growth / body composition: RCT: Growth in head circumference was 0.88 cm/week	MD 0.04 higher (0.11 lower to 0.2 higher)
Faltering growth / body composition: RCT: Head circumference Day 21 (cm) assessed with: (cm)	40 (1 RCT)	⊕⊕○○ Low ^{a,b}	-	The mean faltering growth / body composition: RCT: Head circumference Day 21 (cm) was 28.39 cm	MD 0.15 higher (1.2 lower to 1.5 higher)
Duration of hospital stay - not reported	-	-	-	-	-
Time to reach full enteral feeds: RCT	228 (1 RCT)	⊕⊕○○ Low ^{a,b}	-	Time to reach full enteral feeds, 150 mL/kg/day (days) - Human milk fortification (n=115) median 10 days (IQR 8-15) Bovine milk fortification (n=113) median 10 days (IQR 7-15)	
Bronchopulmonary dysplasia: RCT	543 (4 RCTs)	⊕○○○ Very low ^{a,c}	RR 0.92 (0.79 to 1.09)	Study population	
				632 per 1,000	51 fewer per 1,000 (133 fewer to 57 more)
Confirmed and suspected sepsis: RCT	754 (6 RCTs)	⊕○○○ Very low ^{a,c}	RR 1.03 (0.77 to 1.39)	Study population	
				188 per 1,000	6 more per 1,000 (43 fewer to 73 more)
Retinopathy of prematurity: RCT	705 (5 RCTs)	⊕○○○ Very low ^{a,b}	RR 0.97 (0.77 to 1.21)	Study population	
				267 per 1,000	8 fewer per 1,000 (61 fewer to 56 more)
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-

a. Downgraded one level for concerns for risk of bias

- b. Downgraded one level for indirectness as evidence is based on a single study
- c. Downgraded two levels for imprecision due to very wide confidence intervals that cross the line of no effect
- d. Downgraded one level for inconsistency as I² is 50-80%
- e. Downgraded one level for imprecision as confidence intervals cross the line of no effect
- f. Downgraded three levels for imprecision with extremely wide confidence intervals crossing the line of no effect

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Mortality: RCT: No significant reduction in mortality for human-based fortifier (24 fewer per 1,000; 49 fewer to 19 more) [Critical]. Neurodevelopmental impairment: RCT: No significant effect on Bayley III Cognitive score <85 (20 more per 1,000; 98 fewer to 249 more); Bayley III Language score <85 (44 fewer per 1,000; 178 fewer to 174 more); Bayley III Motor score < 85 (7 more per 1,000; 107 fewer to 231 more); Bayley III Cognitive score <70 (22 fewer per 1,000; 105 fewer to 173 more); Bayley III Language score <70 (15 fewer per 1,000; 116 fewer to 197 more) and Bayley III Motor score <70 (54 fewer per 1,000; 130 fewer to 122 more) [Critical]. Adverse effect: RCT: No significant effect on feeding interruptions (4 fewer per 1,000; 94 fewer to 109 more) [Critical]. Fully breastmilk feeding at hospital discharge: RCT: No significant reduction in fully breastmilk feeding at discharge (283 fewer per 1,000; 511 fewer to 118 more) [Critical]. Sepsis: RCT: No significant effect on sepsis (6 more per 1,000; 43 fewer to 73 more) [Important]. Undesirable effects for Māori No additional evidence available.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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● Very low ○ Low ○ Moderate ○ High ○ No included studies	Moderate to very low certainty of evidence overall. Certainty of evidence for Māori No additional evidence available.	
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Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT	CRITICAL	⊕⊕⊕○ Moderate
Neurodevelopmental impairment: RCT assessed with: Bayley III Cognitive score <85	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: Bayley III language score <85	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: RCT assessed with: Bayley III Motor score < 85	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: Bayley III Cognitive score <70	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: Bayley III Language score <70	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: Bayley III Motor score <70	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis >/= 2: RCT	CRITICAL	⊕⊕⊕○ Moderate
Necrotising enterocolitis surgical: RCT	CRITICAL	⊕⊕○○ Low
Adverse effect: RCT: Feeding interruption	CRITICAL	⊕○○○ Very low
Adverse effects: Metabolic bone disease of prematurity - not measured	CRITICAL	-
Fully breastmilk feeding at hospital discharge: RCT assessed with: Mothers own milk at discharge	CRITICAL	⊕○○○ Very low

Faltering growth / body composition: RCT: Length increment assessed with: (cm/week)	CRITICAL	⊕⊕○○ Low
Faltering growth / body composition: RCT: Length Day 21 assessed with: (cm)	CRITICAL	⊕○○○ Very low
Faltering growth / body composition: RCT: Weight Day 21 assessed with: (g)	CRITICAL	⊕○○○ Very low
Faltering growth / body composition: RCT: Rate of weight gain assessed with: (g/kg/day)	CRITICAL	⊕○○○ Very low
Faltering growth / body composition: RCT: Growth in head circumference assessed with: (cm/week)	CRITICAL	⊕⊕○○ Low
Faltering growth / body composition: RCT: Head circumference Day 21 (cm) assessed with: (cm)	CRITICAL	⊕⊕○○ Low
Duration of hospital stay - not reported	IMPORTANT	-
Time to reach full enteral feeds	IMPORTANT	⊕⊕○○ Low
Bronchopulmonary dysplasia	IMPORTANT	⊕○○○ Very low
Confirmed and suspected sepsis: RCT	IMPORTANT	⊕○○○ Very low
Retinopathy of prematurity: RCT	IMPORTANT	⊕○○○ Very low
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty about or variability in how much people value the main outcomes? Values for Māori No additional evidence available.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Human-based fortifier versus bovine-based fortifier for preterm infants - moderate certainty evidence Uncertain effect on mortality, NEC ($\geq$ stage 2) Human-based fortifier versus bovine-based fortifier for preterm infants - low certainty evidence Uncertain effect on surgical NEC, length increment, head circumference growth and head circumference at day 21, time to reach full enteral feeds Human-based fortifier versus bovine-based fortifier for preterm infants - very low certainty evidence Uncertain effect on neurodevelopmental impairment, feeding interruptions, fully breastmilk feeding at discharge, rate of weight gain, length and weight at day 21, bronchopulmonary dysplasia, sepsis and retinopathy of prematurity Balance of effect for Māori	

	No additional evidence available.	
Resources required		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Human-milk-derived breastmilk fortifier cost Cost for one day per infant at 180 mL/kg/day is approximately \$535 to \$803 per day. If used for ELBW infants (birthweight <1000 g) and continued until 34 weeks CGA (~10 weeks = 70 days), the cost would be \$37,450 to \$56,175 per baby per admission. Bovine-derived breastmilk fortifier cost Cost for one day per infant at 180 mL/kg/day is approximately \$5.80 to \$9 per day. If used for ELBW infants (birthweight <1000 g) and continued until 34 wks CGA (~10 weeks = 70 days), the cost would be \$406 to \$630 per baby (for 70 days) per admission Cost difference is approximately \$37,044 to \$55,545 per infant per admission. (Large). Resources required for Māori No additional evidence available.	Cost estimates were based on the cost of a human milk-derived fortifier that is available now in Australia and used in ELBW infants until they are 34 weeks corrected age. Moderately certain.
Certainty of evidence of required resources		
What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ● High ○ No included studies	The exact cost of using human milk-based fortifier in Aotearoa New Zealand is unknown but is unlikely to be less than what Australian hospitals pay. The exact cost of using bovine-based fortifier is certain.	
Cost effectiveness		
Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours	There are no studies that assess the specific cost-effectiveness of human-based fortifier compared with bovine-based fortifier, particularly in the context of preterm infants.	

the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	Cost-effectiveness would need to be assessed in the New Zealand setting, rather than relying solely on international data. This is because the background rate of breastmilk feeding and NEC are critical for a proper cost-benefit analysis. Cost effectiveness for Māori No additional evidence available.	
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Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Pēpi Māori experience higher rates of preterm birth and associated complications, including NEC, which disproportionately impacts whānau Māori due to systemic inequities in healthcare access and outcomes. The high cost of human-milk-derived fortifiers may create barriers to equitable access, exacerbating existing disparities in neonatal care. Furthermore, Māori perspectives on the use and commercialisation of human milk may differ from Western biomedical models, necessitating culturally appropriate consultation and decision-making. Ensuring Pēpi Māori receive optimal nutrition requires addressing affordability, accessibility and culturally safe healthcare policies that align with Te Tiriti o Waitangi obligations and Māori health aspirations. Equity for Pacific families Pacific infants also face a higher burden of preterm birth and associated complications, including NEC, which may be worsened by limited access to human milk-derived fortifiers due to financial and systemic barriers. Pacific communities often experience socioeconomic disadvantage, which can restrict access to expensive neonatal nutritional interventions, potentially leading to poorer health outcomes. Equity requires open discussion about the origin and purpose of fortifiers, respecting Pacific perspectives on shared nourishment and care. Equity for underrepresented groups Families from migrant or refugee backgrounds may be unfamiliar with human or animal-derived fortifiers and may have religious or cultural concerns. Without clear information in their preferred language, trust and consent may be affected. Equity demands culturally	

	appropriate education that supports informed decisions and aligns with families' values and beliefs.	
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☐ Varies ☐ Don't know	Already standard practice in some USA and Australian hospitals. May not be ethically justifiable for some, depending on the source of breastmilk used for human milk fortifier.	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☒ Probably no ☐ Probably yes ☐ Yes ☐ Varies ☐ Don't know	It is being used in more than one Australian NICU.	Probably not feasible due to the cost (especially in the current health environment)

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or	Probably no important uncertainty or	No important uncertainty or			

	JUDGEMENT						
		variability	variability	variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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EtD 29. In preterm infants does a preterm formula compared with a term formula lead to improved growth, neurodevelopment, clinical outcomes, fewer NEC cases, fewer gastrointestinal complications, less metabolic bone disease?

POPULATION:	Preterm infants
INTERVENTION:	Preterm infant formula
COMPARISON:	Term infant formula
MAIN OUTCOMES:	Critical outcomes Mortality Necrotising enterocolitis Neurodevelopmental impairment Adverse effects – metabolic bone disease Faltering growth/body composition Time to full enteral feeds Duration of initial hospital stay Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Important but not critical Sepsis: proven or suspected Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds Fully breastfed or breastmilk feeding at hospital discharge
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	Preterm formulas are specifically designed to meet the unique nutritional requirements of preterm infants, who have higher protein, energy, and micronutrient needs than term infants. These formulas are enriched with additional protein, energy and essential nutrients such as calcium, phosphorus, and vitamins to support optimal growth, bone mineralisation and neurodevelopment. In contrast, term formulas are formulated to meet the nutritional needs of full-term infants and provide lower levels of protein, energy, iron and other micronutrients. Feeding preterm infants with term formulas may not meet their increased nutritional demands, potentially leading to faltering growth, suboptimal neurodevelopment and a higher risk of metabolic bone disease due to inadequate vitamin, calcium and phosphorus intake. Feeding preterm infants with nutrient-enriched rather than standard formula might increase nutrient accretion and growth rates and might improve neurodevelopmental outcomes. Additionally, the enhanced nutrient content in preterm formulas may help reduce the risk of metabolic bone disease and support better overall clinical outcomes. However, preterm infants are at increased risk of gastrointestinal complications, including necrotising enterocolitis and altered body composition which may influence their long term cardiometabolic

CONFLICT OF INTERESTS:	health and these risks may be exacerbated by the use of enhanced nutrient formula. While both preterm and term formulas lack the protective bioactive components of breastmilk, the enhanced nutrient composition of preterm formulas may influence feeding tolerance, gastrointestinal outcomes and long-term health.
	The following 2019 Cochrane systematic review (Walsh <i>et al</i>) co-author wrote this Evidence to Decision document: Julie Brown

Assessment

Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence is based on one Cochrane review [1] and 1 RCT [2]. Necrotising enterocolitis: RCT: No significant reduction in necrotising enterocolitis (31 per 1,000 fewer; 66 fewer to 28 more) [Critical]. No faltering growth/body composition: RCT: No significant effect in days to regain birthweight for infants fed preterm formula (MD 1.48 days fewer; 4.73 lower to 1.77 higher). Moderate increase in weight gain (MD 2.4 g/kg/d higher; 1.6 higher to 3.3 higher). The effect indicated benefit whether the formula was the sole diet or supplemental to breastmilk). No significant effect in weight gain from enrollment to 120 days corrected age between nutrient-enriched formula and standard formula (MD 1.8 g/day, higher; 1.6 lower to 5.2 higher) [Critical]. No faltering growth/body composition: RCT: No evidence of a difference between nutrient enriched formula and standard formula for rate of length gain (MD 0.2 mm/week higher; 0.7 lower to 1.1 higher) or length gain from enrolment to 120 days corrected age between nutrient-enriched formula and standard formula (MD 0.004 mm/day higher; 0.003 lower to 0.012 higher) [Critical]. No faltering growth/body composition: RCT: Head circumference growth was faster among infants fed nutrient-enriched formula (MD 1.04 mm/week higher; 0.18 higher to 1.89 higher) but no evidence of a difference in head circumference gain from enrolment to 120 days corrected age between nutrient-enriched formula and standard formula (MD 0.000 mm/day; 0.001 lower to 0.001 higher) [Critical]. No faltering growth/body composition: Long-term growth: RCT: There was little or no effect for weight (kg) at 18 months post term between nutrient-enriched formula compared with standard formula (MD 0.06 kg, 0.21 lower to 0.33 higher); weight (kg) at 7.5 to 8 years post term (MD 0.30 kg, 0.55 lower to 1.15 higher); height (cm) at 18 months post term (MD 0.31 cm, 0.43 lower to 1.06 higher); height (cm) at 7.5 to 8	The Cochrane review identified seven trials in which a total of 590 preterm infants participated [1]. Most participants were clinically stable preterm infants of birthweight less than 1850 g. Few participants were extremely preterm, extremely low birthweight, or growth restricted at birth. Trials were conducted more than 30 years ago, were formula industry funded and were small with methodological weaknesses (including lack of masking) that might bias effect estimates. The additional RCT [2] included 40 late preterm infants randomised. The intervention was a nutrient-enriched formula with increased calories (73 kcal/100 mL) from protein, added bovine milk fat globule membrane, vitamin D and butyrate compared with a standard term formula 67 kcal/100 mL. The trial was terminated early due to recruitment challenges. Vitamin D status Best 2023 [2] In a trial of 40 late preterm infants, Vitamin D status, as measured by 25-hydroxyvitamin D3 derivatized with 4-

	years post term (MD 0.93 cm, 0.30 lower to 2.16 higher); head circumference (cm) at 18 months post term (MD 0.09 cm, 0.26 lower to 0.43 higher); or head circumference (cm) at 7.5 to 8 years post term (MD -0.12 cm, 0.45 lower to 0.21 higher) [Critical]. Neurodevelopmental impairment: RCT: No significant increase Bayley II Mental Development Index at 18 months post term for nutrient-enriched formula compared with standard formula (MD 2.81 points, 1.44 lower to 7.06 higher). Large increase for infants fed nutrient-rich formula on Bayley II Psychomotor Development Index score at 18 months post term compared with standard formula (MD 6.56 points, 2.87 more to 10.26 more). No significant effect on Weschler Performance Intelligence Quotient at 7.5 to 8 years post term (MD 0.06 points, 3.24 lower to 3.36 higher); or the Weschler Overall Intelligence Quotient at 7.5 to 8 years post term (MD 1.49 points, 1.61 lower to 4.59 higher) for nutrient-enriched formula compared with standard formula. No significant reduction in cerebral palsy at 18 months post term (10 per 1,000 fewer; 33 fewer to 51 more) [Critical]. Desirable effects for Māori No additional evidence available.	phenyl-1,2,4-triazoline-3,5-dione (PTAD), was higher in the nutrient enriched formula group 78.7 nmol/L compared to the standard formula group 68.9 nmol/L (P<0.0001).
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Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with a term formula	Risk difference with a preterm formula
Mortality: RCT assessed with: All-cause mortality	442 (2 RCTs)	 Low ^{a,b}	RR 1.12 (0.65 to 1.93)	Study population	
				90 per 1,000	11 more per 1,000 (32 fewer to 84 more)
Necrotising enterocolitis: RCT	489 (3 RCTs)	 Very low ^{a,b,c}	RR 0.72 (0.41 to 1.25)	Study population	
				112 per 1,000	31 fewer per 1,000 (66 fewer to 28 more)
Neurodevelopmental impairment: RCT assessed with: Cerebral palsy at 18 months post-term	377 (2 RCTs)	 Low ^{a,d}	RR 0.79 (0.3 to 2.07)	Study population	
				48 per 1,000	10 fewer per 1,000 (33 fewer to 51 more)
Neurodevelopmental impairment: RCT assessed with: Bayley (II) Mental development index - 18 months Scale from: 1 to 100	310 (2 RCTs)	 Very low ^{a,b,c}	-	The mean neurodevelopmental: RCT: Bayley II Mental Development Index was TBC	MD 2.81 higher (1.44 lower to 7.06 higher)
Neurodevelopmental impairment: RCT assessed with: Bayley II Psychomotor Development	310 (2 RCTs)	 Low ^{a,c}	-	The mean neurodevelopment: RCT: Bayley II Psychomotor Development Index was TBC	MD 6.56 higher (2.87 higher to 10.26)

Index at 18 months post term Scale from: 1 to 100					higher)
Neurodevelopmental impairment: RCT assessed with: Wechsler Overall Intelligence Quotient at 7.5 to 8 years post term	355 (2 RCTs)	⊕○○○ Very low ^{a,e}	-	The mean neurodevelopmental score: RCT: Wechsler Overall Intelligence Quotient was 99 points	MD 1.49 higher (1.61 lower to 4.59 higher)
Adverse effects- metabolic bone disease - not measured	-	-	-	-	-
Faltering growth/body composition: RCT assessed with: Time to regain birthweight (days)	74 (3 RCTs)	⊕○○○ Very low ^{a,d,e}	-	The mean faltering growth/body composition: RCT was 14.9 days	MD 1.48 lower (4.73 lower to 1.77 higher)
Faltering growth/body composition: RCT assessed with: Weight gain g/kg/day	440 (6 RCTs)	⊕⊕○○ Low ^{a,c}	-	The mean faltering growth/body composition: RCT was 12.12 g/kg/day	MD 2.43 higher (1.6 higher to 3.26 higher)
Faltering growth/body composition: RCT assessed with: Weight gain from enrolment to 120 days corrected age; g/day	40 (1 RCT)	⊕○○○ Very low ^{b,f,g}	-	The mean faltering growth/body composition: RCT was 28.0 g/day	MD 1.77 higher (1.63 lower to 5.18 higher)
Faltering growth/body composition: RCT assessed with: Weight (kg) at 18 months post term	334 (2 RCTs)	⊕⊕○○ Low ^{a,b}	-	The mean faltering growth/body composition: RCT was 10.25 kg	MD 0.06 higher (0.21 lower to 0.33 higher)
Faltering growth/body composition: RCT assessed with: Weight (kg) at 7.5 to 8 years post term	359 (2 RCTs)	⊕○○○ Very low ^{a,h}	-	The mean faltering growth/body composition: RCT was 23.25 kg	MD 0.3 higher (0.55 lower to 1.15 higher)
Faltering growth/body composition: RCT assessed with: Length gain mm/week	386 (5 RCTs)	⊕○○○ Very low ^{a,c,e}	-	The mean faltering growth/body composition: RCT was 9.58 mm/week	MD 0.22 higher (0.7 lower to 1.13 higher)
Faltering growth/body composition: RCT assessed with: Rate of length gain from enrolment to 120 days corrected age; mm/day)	40 (1 RCT)	⊕○○○ Very low ^{d,f,g}	-	The mean faltering growth/body composition: RCT was 0.11 mm/day	MD 0.004 higher (0.003 lower to 0.012 higher)
Faltering growth/body composition: RCT assessed with: Height (cm) at 18 months post term	334 (2 RCTs)	⊕○○○ Very low ^{a,h}	-	The mean faltering growth/body composition: RCT was 79.85 cm	MD 0.31 higher (0.43 lower to 1.06 higher)
Faltering growth/body composition: RCT assessed with: Height (cm) at 7.5 to 8 years post term	359 (2 RCTs)	⊕○○○ Very low ^{a,h}	-	The mean faltering growth/body composition: RCT was 122.05 cm	MD 0.93 higher (0.3 lower to 2.16 higher)
Faltering growth/body composition: RCT assessed with: Head circumference gain mm/week	399 (5 RCTs)	⊕⊕○○ Low ^{a,c}	-	The mean faltering growth/body composition: RCT was 8.22 mm/week	MD 1.04 higher (0.18 higher to 1.89 higher)
Faltering growth/body composition: RCT assessed with: Rate of head circumference gain from enrolment to 120 days corrected age; mm/day)	40 (1 RCT)	⊕○○○ Very low ^{d,f,g}	-	The mean faltering growth/body composition: RCT was 0.06 mm/day	MD 0 (0.001 lower to 0.001 higher)
Faltering growth/body composition: RCT assessed with: Head circumference (cm) at 18 months	334 (2 RCTs)	⊕○○○ Very low ^{a,h}	-	The mean faltering growth/body composition: RCT was 47.8 cm	MD 0.09 higher (0.26 lower to 0.43 higher)

post term					
Faltering growth/body composition: RCT assessed with: Head circumference (cm) at 7.5 to 8 years post term	359 (2 RCTs)	⊕○○○ Very low ^{a,h}	-	The mean faltering growth/body composition: RCT was 52.4 cm	MD 0.12 lower (0.45 lower to 0.21 higher)
Time to full enteral feeds - not measured	-	-	-	-	-
Duration of initial hospital stay: RCT assessed with: Duration of birth hospitalisation (Days)	31 (1 RCT)	⊕○○○ Very low ^{a,g,h}	-	The mean duration of initial hospital stay: RCT was 51 days	MD 1 higher (8.81 lower to 10.81 higher)
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Sepsis: proven or suspected - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-
Fully breastfed or breastmilk feeding at hospital discharge - not measured	-	-	-	-	-

- a. Downgraded one level for concerns around risk of bias
b. Downgraded one level for imprecision with wide confidence intervals crossing the line of no effect
c. Downgraded one level for indirectness as there were few infants who were VLBW or ELBW and so the evidence may not be fully representative
d. Downgraded one level for imprecision with confidence intervals crossing the line of no effect
e. Downgraded one level for inconsistency with of high heterogeneity >55%
f. Downgraded two levels for risk of bias as study was stopped early due to poor recruitment
g. Downgraded one level for indirectness as evidence is based on a single small study
h. Downgraded two levels for very wide confidence intervals crossing the line of no effect indicate both substantive benefit and harm

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Mortality: RCT: No significant increase in mortality for nutrient-enriched formula (11 per 1,000 higher; 32 fewer to 84 more). [Critical] Duration of initial hospitalisation: RCT: No significant difference for duration of birth hospitalisation (MD 1.00 day higher; 8.81 lower to 10.81 higher) [Critical]	Walsh 2019 identified seven trials in which a total of 590 preterm infants participated. Most participants were clinically stable preterm infants of birthweight less than 1850 g. Few participants were extremely preterm, extremely low birthweight, or growth restricted at birth. Trials were conducted more than 30 years ago, were

	Undesirable effects for Māori No additional evidence available.	formula industry funded, and were small with methodological weaknesses (including lack of masking) that might bias effect estimates.
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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Low to very low certainty evidence overall Certainty of evidence for Māori No additional evidence available.	The main body of evidence from the systematic review is based on studies that are over 30 years old. Preterm formulations are likely to be of different compositions now and generalisations of the findings are therefore limited.

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT assessed with: All-cause mortality	CRITICAL	⊕⊕○○ Low
Necrotising enterocolitis: RCT	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: Cerebral palsy at 18 months post term	CRITICAL	⊕⊕○○ Low
Neurodevelopmental assessed with: Bayley (1) Mental development index - 18 months	CRITICAL	⊕○○○ Very low
Neurodevelopment assessed with: Bayley (1) Psychomotor Development Index at 18 months post term	CRITICAL	⊕⊕○○ Low
Neurodevelopment assessed with: Weschler Overall Intelligence Quotient -7.5 to 8 years	CRITICAL	⊕○○○ Very low
Adverse effects- metabolic bone disease - not measured	CRITICAL	-
Faltering growth/body composition: RCT assessed with: Time to regain birthweight	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Weight gain g/kg/day	CRITICAL	⊕⊕○○

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	Probably no important uncertainty about or variability in how much people value the main outcomes. Values for Māori No additional evidence available.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Preterm compared with term formula for preterm infants - Low certainty of evidence Increase in head circumference mm/week, weight gain g/kg/day Reduced neurodevelopmental impairment Uncertain effect for mortality, neurodevelopmental impairment (cerebral palsy); faltering growth/body composition (weight (kg) at 18 months post term) Preterm compared with term formula for preterm infants - Very low certainty of evidence Faltering growth/body composition - longer time to regain birthweight Uncertain effect for necrotising enterocolitis, duration of initial hospitalisation, neurodevelopmental impairment Uncertain effect on faltering growth/body composition (weight gain and length gain from enrolment to 120 days corrected age; head circumference gain from enrolment to 120 days corrected age; length gain mm/week; weight (kg) at 7.5 to 8 years post term; height (cm) at 18 months post term; height (cm) at 7.5 to 8 years post term; head circumference (cm) at 18 months post term; head circumference (cm) at 7.5 to 8 years post term) Balance of effects for Māori No additional evidence available.	There is no evidence to suggest that a nutrient-enriched formula increased the mean rate of bodyweight gain in preterm infants. The body of evidence is however outdated. Nutrient formulations have changed over time since the evidence was published and the relevance of the evidence could be questioned.

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Aotearoa New Zealand Preterm infant formula (Liquid ready to feed) \$3.24 per 100 mL Aotearoa New Zealand Term infant formula (Liquid ready to feed) \$1.56 per 100 mL Costs (for up to 100-120 days) Preterm infant formula \$3.24 per 100 mL (\$5 to \$10 per day for a 1 kg baby, approx \$500 to \$1000 per baby per admission) Term infant formula \$1.16 to \$1.56 per 100 mL (\$2.08 to \$2.80 per day for a 1 kg baby, approx. \$2.50 to \$5 per day for a 1 kg baby, approx. \$250 to \$500 per baby per admission) Cost difference per baby per admission is approx. \$250 to \$500 Resources required for Māori No additional evidence available.	
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ● High ○ No included studies	Reasonable certainty about the resources required. Certainty of evidence of required costs for Māori No additional evidence available.	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the	There are no studies that assess the specific cost-effectiveness of preterm compared with term formula milk, particularly in the context of preterm infants. Cost effectiveness for Māori No additional evidence available.	

intervention ○ Favours the intervention ○ Varies ● No included studies		
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Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Preterm pēpi Māori may face inequities in access to appropriate formula feeding, including the use of preterm-specific formulas. Systemic inequities in neonatal care mean pēpi Māori are at greater risk of receiving inconsistent or non-guideline-based nutritional support. Whānau may not always be included in informed discussions about feeding choices, particularly in under-resourced or non-culturally responsive settings. Without standardised, equity-focused protocols and clear communication, pēpi Māori may be more likely to receive term formula, which could contribute to nutrient deficiencies, faltering growth and prolonged NICU stays. Equity for Pacific families Pacific preterm infants, like Māori, are at increased risk of nutritional disadvantage and systemic healthcare inequities. Access to preterm formula may be influenced by hospital location, funding, or staffing, leading to inconsistent care. Pacific families may face additional barriers, including language differences, limited culturally appropriate feeding education and reduced engagement in feeding decisions. Equity for underrepresented groups Other ethnic groups, including Asian and refugee communities, may encounter similar challenges if care is not culturally safe or inclusive. To ensure equitable outcomes, all preterm infants should have equal access to optimal nutrition, supported by clear guidelines and culturally responsive practice.	

Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No	Preterm formula is probably acceptable to health care providers in Aotearoa New Zealand	

○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	because there is already widespread use. Further research is needed with regard to the composition of our unique population. Acceptability for Māori No additional evidence available.	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Yes - already in widespread use. Feasibility for Māori No additional evidence available.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know

	JUDGEMENT						
REQUIRED							
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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EtD 30. In preterm infants for whom there is insufficient mother's own breastmilk, does screened pasteurised donor milk vs. screened unpasteurised donor milk improve outcomes (infection, NEC, neurodevelopment, time to full enteral feeds, time to discharge, breastmilk feeding at discharge, growth)?

POPULATION:	Preterm infants
INTERVENTION:	Unpasteurised (screened) donor milk
COMPARISON:	Pasteurised donor milk
MAIN OUTCOMES:	Critical for making a decision Mortality Neurodevelopmental impairment Adverse effects Fully breastmilk feeding at hospital discharge Important but not critical Fully breastfeeding at hospital discharge Faltering growth / body composition Duration of initial hospital stay Time to full enteral feeds Bronchopulmonary dysplasia Necrotising enterocolitis (NEC) Sepsis: proven or suspected Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Of limited importance Time to full sucking feeds
SETTING:	Any birth settings
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	Mothers' own breastmilk is the best source of nutrition for preterm infants, offering unmatched protective and developmental benefits. When mother's own breastmilk is unavailable or insufficient, donor breastmilk is the preferred alternative to infant formula because it is associated with better health outcomes, such as a lower risk of severe intestinal disease and infections. However, donor breastmilk is usually pasteurised to eliminate harmful pathogens. While pasteurisation ensures safety, it is costly, time-consuming and may damage some of the milk's important nutritional and protective components, raising concerns about its ability to meet the nutritional needs of preterm infants. Pasteurisation, typically performed through heating, destroys bacteria and viruses but also reduces beneficial components like proteins, immune-boosting factors, enzymes and growth factors. Pasteurisation reduces many of the normal commensal microbes, as well as significantly reducing or obliterating live immune cells, bioactive proteins and enzymes, collectively limiting some of the health benefits compared to a mother's own milk. This reduction may impair the growth and development of preterm

infants. On the other hand, unpasteurised donor milk retains these bioactive properties, potentially providing greater nutritional and immunological benefits. However, even with rigorous screening, there is a risk of transmitting bacterial or viral infections through unpasteurised donor milk. Important outcomes to consider include infection rates, severe intestinal disease, time to achieve full milk feeds, time to hospital discharge, growth, rates of breastmilk feeding at discharge, and developmental outcomes. Balancing the safety and nutritional benefits of donor milk is critical to improving the care of preterm infants.

CONFLICT OF INTERESTS:

None

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	We re-analysed and pooled the data from a systematic review conducted in 2023. Evidence is based on 2 RCTs [1,2] and 3 observational studies [3-5]. Unpasteurised donor milk compared to pasteurised donor milk resulted in: Mortality: RCT: No significant reduction in mortality (19 fewer per 1,000; 42 fewer to 46 more) [Critical]. Mortality: Cohort study: No significant effect on mortality (3 more per 1,000; 17 fewer to 37 more) [Critical] Duration of initial hospital stay: RCT: No effect on duration of initial hospital stay (MD 0.47 days higher; 1.64 lower to 2.58 higher) [Important]. Time to full enteral feeds: RCT: Moderate reduction in time to full enteral feeds (2 days lower; 3.35 lower to 0.65 lower) [Important]. Time to full enteral feeds: Cohort study: Moderate reduction in time to full enteral feeds MD 2.2 days lower; 4.06 lower to 0.34 lower) [Important]. Bronchopulmonary dysplasia: RCT: No significant reduction in bronchopulmonary dysplasia (71 fewer per 1,000; 131 fewer to 23 more) [Important]. Bronchopulmonary dysplasia: Cohort study: Large reduction in bronchopulmonary dysplasia (129 fewer per 1,000; 195 fewer to 12 fewer) [Important]. Necrotising enterocolitis: RCT: No significant reduction in necrotising enterocolitis (46 fewer per 1,000; 87 fewer to 36 more) [Important]. Necrotising enterocolitis: Cohort study: No significant effect on necrotising enterocolitis (6 fewer per 1,000; 29 fewer to 31 more) [important]. Sepsis: RCT: No significant reduction in sepsis (84 fewer per 1,000; 158 fewer to 23 more) [Important]. Sepsis: Cohort study: No significant reduction in sepsis (21 fewer per 1,000; 71 fewer to 34 more) [Important]. Retinopathy of prematurity: RCT: No significant effect on retinopathy of prematurity	Population information for included evidence Belgium, RCT [1]: Very low birthweight infants. India, RCT [2]: High-risk infants. France, observational study [3]: Very preterm infants China, cohort study [4]: Very preterm infants China, cohort study [5]: Very preterm infants

		(7 fewer per 1,000; 38 fewer to 75 more) [important]. Retinopathy of prematurity: Cohort study: Large reduction in retinopathy of prematurity (161 fewer per 1,000; 234 fewer to 65 fewer) [Important].			
		Desirable effects for Māori No additional evidence available			
Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with pasteurised donor milk	Risk difference with unpasteurised donor milk
Mortality- RCT	303 (1 RCT)	⊕⊕○○ Low ^{a,b}	RR 0.63 (0.21 to 1.88)	Study population	
				53 per 1,000	19 fewer per 1,000 (42 fewer to 46 more)
Mortality- Cohort	1290 (3 non-randomised studies)	⊕○○○ Very low ^{a,b}	OR 1.08 (0.61 to 1.90)	Study population	
				44 per 1,000	3 more per 1,000 (17 fewer to 37 more)
Neurodevelopmental impairment - not measured	-	-	-	-	-
Fully breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Fully breastfeeding at hospital discharge - not measured	-	-	-	-	-
Faltering growth / body composition - not measured	-	-	-	-	-
Duration of initial hospital stay- RCT assessed with: days	113 (1 RCT)	⊕○○○ Very low ^{a,b,c}	-	The mean duration of initial hospital stay- RCT was 7.96 days	MD 0.47 days higher (1.64 lower to 2.58 higher)
Time to full enteral feeds- RCT assessed with: days	303 (1 RCT)	⊕⊕⊕○ Moderate ^a	-	The mean time to full enteral feeds- RCT was 19 days	MD 2 days lower (3.35 lower to 0.65 lower)
Time to full enteral feeds- Cohort assessed with: days	157 (1 non-randomised study)	⊕○○○ Very low ^a	-	The mean time to full enteral feeds- Cohort was 27.7 days	MD 2.2 days lower (4.06 lower to 0.34 lower)
Bronchopulmonary dysplasia - RCT	303 (1 RCT)	⊕⊕○○ Low ^{a,b}	RR 0.69 (0.43 to 1.10)	Study population	
				230 per 1,000	71 fewer per 1,000 (131 fewer to 23 more)
Bronchopulmonary dysplasia	1290 (3 non-randomised studies)	⊕⊕○○ Low ^{a,d,e}	OR 0.43 (0.20 to 0.94)	Study population	
				262 per 1,000	129 fewer per 1,000

					(195 fewer to 12 fewer)
Necrotising enterocolitis- RCT	303 (1 RCT)	⊕⊕○○ Low ^{a,b}	RR 0.65 (0.34 to 1.27)	Study population	
				132 per 1,000	46 fewer per 1,000 (87 fewer to 36 more)
Necrotising enterocolitis- Cohort	1290 (3 non-randomised studies)	⊕○○○ Very low ^{a,b,d}	OR 0.91 (0.55 to 1.51)	Study population	
				68 per 1,000	6 fewer per 1,000 (29 fewer to 31 more)
Sepsis: proven or suspected- RCT	303 (1 RCT)	⊕⊕○○ Low ^{a,b}	RR 0.75 (0.53 to 1.07)	Study population	
				336 per 1,000	84 fewer per 1,000 (158 fewer to 23 more)
Sepsis: proven or suspected- Cohort	1290 (3 non-randomised studies)	⊕○○○ Very low ^{a,b,f}	OR 0.91 (0.71 to 1.16)	Study population	
				333 per 1,000	21 fewer per 1,000 (71 fewer to 34 more)
Retinopathy of prematurity- RCT	303 (1 RCT)	⊕○○○ Very low ^{a,g}	RR 0.89 (0.35 to 2.26)	Study population	
				59 per 1,000	7 fewer per 1,000 (38 fewer to 75 more)
Retinopathy of prematurity- Cohort	364 (2 non-randomised studies)	⊕⊕○○ Low ^{a,d,e}	OR 0.48 (0.31 to 0.76)	Study population	
				413 per 1,000	161 fewer per 1,000 (234 fewer to 65 fewer)

- a. Downgraded one level for indirectness because the included study (or studies) focused on very preterm infants, raising moderate concern about applicability to moderate and late preterm infants.
- b. Downgraded one level of imprecision due to the confidence interval values that suggest both benefit and harm (or no effect).
- c. Downgraded two levels of risk of bias due to the weak quality of the included study.
- d. Downgraded one level of inconsistency due to significant heterogeneity.
- e. Upgraded 2 levels for very large effect size
- f. Downgraded two levels of inconsistency due to substantial heterogeneity.
- g. Downgraded two levels of imprecision due to the wide confidence interval, small sample size, and low event rate

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies	A recent systematic review was conducted comparing diets for preterm infants containing unpasteurised mother's own milk and frozen or pasteurised mother's own milk, they found: None of the studies reported negative growth findings. Undesirable effects for Māori No additional evidence available	

○ Don't know		
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Moderate to very low certainty overall. Certainty of evidence for Māori No additional evidence available	
Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality- RCT	CRITICAL	⊕⊕○○ Low
Mortality- Cohort	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment - not measured	CRITICAL	-
Fully breastmilk feeding at hospital discharge - not measured	CRITICAL	-
Fully breastfeeding at hospital discharge - not measured	IMPORTANT	-
Faltering growth / body composition - not measured	IMPORTANT	-
Duration of initial hospital stay- RCT assessed with: days	IMPORTANT	⊕○○○ Very low
Time to full enteral feeds- RCT assessed with: days	IMPORTANT	⊕⊕⊕○ Moderate
Time to full enteral feeds- Cohort assessed with: days	IMPORTANT	⊕○○○ Very low
Bronchopulmonary dysplasia - RCT	IMPORTANT	⊕⊕○○ Low
Bronchopulmonary dysplasia	IMPORTANT	⊕⊕○○ Low

Necrotising enterocolitis- RCT	IMPORTANT	⊕⊕○○ Low
Necrotising enterocolitis- Cohort	IMPORTANT	⊕○○○ Very low
Sepsis: proven or suspected- RCT	IMPORTANT	⊕⊕○○ Low
Sepsis: proven or suspected- Cohort	IMPORTANT	⊕○○○ Very low
Retinopathy of prematurity- RCT	IMPORTANT	⊕○○○ Very low
Retinopathy of prematurity- Cohort	IMPORTANT	⊕⊕○○ Low

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ Important uncertainty or variability ☒ Possibly important uncertainty or variability ☐ Probably no important uncertainty or variability ☐ No important uncertainty or variability	Probably no important uncertainty or variability	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Unpasteurised donor milk compared to pasteurised donor milk - moderate low certainty evidence Reduction in time to full enteral feeds Unpasteurised donor milk compared to pasteurised donor milk - low certainty evidence Uncertain effect on mortality, bronchopulmonary dysplasia, necrotising enterocolitis, sepsis, retinopathy of prematurity Unpasteurised donor milk compared to pasteurised donor milk - very low certainty evidence Reduction in time to full enteral feeds Uncertain effect on mortality, duration of initial hospital stay, necrotising enterocolitis, sepsis, retinopathy of prematurity Balance of effects for Māori No additional evidence	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ● Moderate savings ○ Large savings ○ Varies ○ Don't know	Costs of screening donors \$40-\$300 per donor (region dependent Auckland based 2025 estimate) Lactation consultant time is approximately about 4 hours over the donor's journey (consultation, researching bloods, managing milk, and organising appropriate storage) \$223 to \$246 The cost of pasteurisation via a milk bank is ~\$16.00 per 100 mL (Christchurch Women's Hospital Milk Bank 2024) Aotearoa New Zealand Cost of unpasteurised screened donor breastmilk per infant per admission Screening donor \$40-\$300 per donor plus lactation consultant time \$223 to \$246 = \$263 to \$546 Aotearoa New Zealand Cost of pasteurised donor breastmilk per infant per admission \$16.00 per 100 mL at 180 mL/kg/day (\$28.80) for 50 days = \$1440 to \$2160	

	Cost: favours the intervention (unpasteurised screened donor milk) by \$1177 to \$1614 per infant per admission	
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	The cost are reasonably certain. Certainty of evidence of required resources for Māori No additional evidence available	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No studies assess the specific cost-effectiveness of unpasteurised versus pasteurised donor milk, particularly in the context of preterm infants. Based on these costings the intervention has a lower cost. Cost effectiveness for Māori No additional evidence available	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced	Equity for Māori	Māori parents made up approximately 7.6% of

○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	In Aotearoa New Zealand, milk banks are few and unevenly distributed, primarily serving tertiary hospitals. Whānau Māori, particularly those in rural areas, may not have access to pasteurised donor milk when it is needed. If hospital supply is limited or unavailable, some whānau may consider or rely on unpasteurised donor milk through informal networks, such as from friends, relatives or online milk-sharing communities. Cultural values around whakapapa, ukaipōtanga (nurturing), and tapu (sacredness) are also significant in shaping infant feeding decisions for many whānau Māori. These values may influence strong cultural views about: Who the milk comes from (for example, known vs. anonymous donors), The sacred nature of bodily fluids and infant food, and A preference for community-based trust over institutional systems. As a result, some whānau Māori may feel more comfortable using unpasteurised milk from known donors within their community, rather than anonymous pasteurised milk provided through the hospital system. Some hospital systems may not make space for these cultural preferences or fail to engage whānau Māori in meaningful kōrero (dialogue) about their options, beliefs and decision-making around donor milk. Equity for Pacific families Pacific families often live in areas where hospital-based donor milk is limited or not offered. Feeding decisions may be guided by collective values, relationships of trust and the preference for milk from familiar or culturally connected donors. Language barriers and limited culturally specific education can affect how Pacific parents understand and weigh the risks of unpasteurised milk. Inconsistent access and a lack of engagement from neonatal services may lead families to informal milk sharing by necessity rather than choice. To support equity, donor milk services must be expanded and adapted to include Pacific values and more culturally inclusive education. Equity for underrepresented groups Families from migrant, Asian, low-income or rural backgrounds may struggle to access pasteurised donor milk due to distance from tertiary hospitals, lack of transport or cost-related barriers. Health services may not always offer language support or inclusive education to guide informed decision-making. As a result, some families may turn to informal milk-sharing without fully understanding the safety risks. Others may avoid donor milk altogether due to lack of trust in the system. Ensuring equitable access includes expanding milk bank services, offering translated resources and engaging communities early in feeding discussions that reflect their realities and cultural values.	respondents in a 2024 Aotearoa New Zealand survey on this topic by Harris et al. While the survey did not report attitudes by ethnicity, it found strong support across all groups for the use of donated breastmilk when a mother's own milk was unavailable. In Aotearoa New Zealand, most donated breastmilk is accessed informally and is unpasteurised, due to limited access to hospital milk banks—particularly in the North Island, where many Māori families live. This suggests that Māori parents may be more likely to rely on unpasteurised donated milk out of necessity rather than informed choice. This carries increased risk, as unpasteurised milk is not screened or heat-treated to remove potential infections. The study highlighted inequities in access and the lack of national guidelines, which can disproportionately affect groups already facing unequal care. Because Māori were underrepresented in the survey, further research is needed to understand Māori perspectives and ensure culturally safe access to pasteurised donated milk.
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Acceptability

Is the intervention acceptable to key interest-holders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know	For unpasteurised breastmilk to be acceptable for use in neonatal care, the donor must be screened and tested for CMV, HIV 1 and 2, hepatitis B and C and HTLV 1 and 2.	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Pasteurisation requires access to donor milk from a Breastmilk Bank. There are six active human milk banks (all non-profit) in Aotearoa New Zealand, none of which are in Auckland (the largest, most populated city with two tertiary neonatal intensive care units). Women may also rely on informal (peer-to-peer) donation which relies on informal social networks. Donor EBM supplies (formal and informal) and milk banks are required. Other required resources include expressing and storage equipment, enteral feed warmers, lactation consultant time, bottles and nasogastric tubes. Evidence from a mixed-method national survey found that informal screening processes undertaken by parents and health professionals before informal human milk donation were lifestyle, including smoking status, medication, and drug and alcohol intake (44% and 36%, respectively) (Harris 2024). No cost data available. Evidence from a mixed-method national survey found that informal screening processes undertaken by parents and health professionals before informal EBM donation included serological screening such as CMV, HIV, and hepatitis C or B (30% and 39%, respectively) (Harris 2024). No cost data available. Pasteurisation of donor EBM obtained informally was not common. Feasibility for Māori No additional evidence available	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
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EtD 31. Should higher feed osmolality (>450 mOsm/kg) vs. lower feed osmolality in preterm infants to reduce feed intolerance and/or necrotising enterocolitis

POPULATION:	Preterm infants
INTERVENTION:	Higher feed osmolality (>450 mOsm/kg)
COMPARISON:	Lower feed osmolality
MAIN OUTCOMES:	Critical for making a decision Mortality Necrotising enterocolitis (NEC) Neurodevelopmental impairment Adverse effects (other than mortality, BPD, NEC, sepsis anaemia of prematurity or ROP) feed intolerance Fully breastmilk feeding at hospital discharge Important but not critical Faltering growth / body composition Duration of initial hospital stay Time to full enteral feeds Bronchopulmonary dysplasia Sepsis: proven or suspected Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Of limited importance Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical practice recommendation: patient perspective
BACKGROUND:	Preterm infants are particularly vulnerable to feeding intolerance and gastrointestinal complications due to the immaturity of their digestive system. Osmolality, a measure of the concentration of solutes in a solution, is an important factor in the safety and tolerance of enteral feeds. Feeds with higher osmolality (e.g. >450 mOsm/kg) have been associated with delayed gastric emptying, increased risk of feed intolerance and potential for mucosal injury, which may contribute to the development of NEC, a serious and often life-threatening condition. The American Academy of Paediatrics recommends feeds of <450 mOsm/kg H₂O. This recommendation remains without clear substantiation based on relevant trials, but the recommendation has led to high feed osmolality being considered to impact adverse events, particularly gastrointestinal dysfunctions and NEC. In preterm infants, feeds with an osmolality >600 (mOsm/kg H₂O) have been associated with NEC. Amniotic fluid has an osmolality of 275 mOsm/kg H₂O and EBM 296 mOsm/kg H₂O. Amylase from the breastmilk may induce hydrolysis of the dextrin content of both breastmilk fortifier and glucose polymers, leading to small osmotically active molecules of oligosaccharides. This, in turn, increases the osmolality of the feed, making it less

CONFLICT OF INTERESTS:	likely to be well tolerated. There is also evidence that additives can reduce the anti-infective properties of breastmilk when added too far in advance of a feed. The addition of breastmilk fortifier (especially 1¼ strength) or single nutrient additives (glucose polymers) to EBM substantially increases the osmolality.
	Clinical practice often involves the addition of oral medications to expressed breastmilk or other feeds prior to administration. Some medications (e.g. iron, multivitamins, some antibiotics) are hyperosmolar by nature and can significantly increase feed osmolality when added to small volumes of milk. Small volumes of 0.5–2 mL of breastmilk have been shown not to adequately dilute some medications to safe osmolality levels. For example, multivitamin preparations can raise osmolality to >800 mOsm/kg if added to <5 mL of expressed breastmilk. Determining whether higher feed osmolality increases the risk of feeding intolerance or NEC and establishing a minimum volume of breastmilk for safe medication dilution is essential to guide clinical decisions and protect this vulnerable population.
	None

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence is based on a systematic review including a human milk-based fortifier (8 RCTs, 2 observational studies) [1]. Adverse effects: Gastric emptying: RCT: Four of five studies reported no difference in gastric emptying for different osmolalities. One study reported delayed gastric emptying with feed osmolality of 539 mOsm/L compared with lower levels [Critical]. Adverse effects: Feeding intolerance: RCT + observational study: No differences reported for feeding intolerance [Critical]. Desirable effects for Māori No additional data	The osmolality of breastmilk is approximately 300 mOsm/kg, but is often increased to greater than 400 mOsm/kg by the addition of breastmilk fortifiers, nutritional supplements and medications. The American Academy of Pediatrics [2] advises that formulas for normal infants should have an osmolality no greater than approximately 450 mOsm/kg. Evidence to support this recommendation has not ever been presented. Sweden [3]: Retrospective cohort: Infants <28 weeks' gestation. NOTE: One of the observational studies included in the Ellis 2019 review included a study that used acidified liquid human milk fortifier. This product is not available in Aotearoa New Zealand. Several studies, including [4] have indicated that the osmolality of enteral feeds exceeds the American

				Academy of Pediatrics recommendation of 450 mOsm/kg. In some cases, osmolality was equal to or exceeded 2000 mOsm/kg. Osmolality was also increased when medications were added to expressed breastmilk with fortifier compared with expressed breastmilk.	
Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with lower feed osmolality be used	Risk difference with higher feed osmolality (>450 mOsm/kg)
Mortality - not measured	-	-	-	-	-
Necrotising enterocolitis: RCT and observational	460 (5 RCTs)	⊕○○○ Very low ^{a,b,c,d}	-	Five studies (n=460) reported the effects of dietary osmolality/osmolality on NEC and overall morbidity. An RCT reported a significantly higher NEC incidence in infants after receiving an elemental formula (650 mOsm/L) compared with a cow milk-based formula (359 mOsm/L) (87.5% vs. 25%, respectively; p<0.02). An observational study reported a significantly higher NEC incidence in infants receiving an acidified liquid fortifier (326 mOsm/kg) compared with those receiving a powdered fortifier (385 mOsm/kg) and a non-acidified liquid fortifier (385 mOsm/kg) (13%, 0% and 0%, respectively; p=0.0056). An RCT found no significant difference in NEC incidence comparing one fortifier (441 mOsm/kg) with a new fortifier with higher protein and micronutrient content (390 mOsm/kg). An observational study found no significant difference in NEC incidence with different feed osmolalities (451 mOsm/kg, 420 mOsm/kg and 378 mOsm/kg). An RCT reported no significant difference in overall morbidity (NEC and sepsis) in infants fed either a liquid fortifier (450 mOsm/kg) or a powder fortifier (385 mOsm/kg).	
Necrotising enterocolitis: Cohort study	253 (1 non-randomised study)	⊕○○○ Very low ^a	-	This study looked at the osmolality effects of commonly used medications which included paracetamol 24 mg/mL, Sodium chloride 4 mmol/mL and fluconazole 10 mg/mL. The maximum osmolality administered was 9,600 mOsm/kg (the osmolality of undiluted oral paracetamol). The odds ratio of developing NEC after receiving solutions with an osmolality exceeding 2,000 mOsm/kg was 0.92 (P = 0.83); >800 (OR 0.48; P = 0.71) and >450 (OR 0.31; P = 0.20). 95%CI were not provided.	
Neurodevelopmental impairment - not measured	-	-	-	-	-
Adverse effects: RCT assessed with: Gastric emptying	158 (5 RCTs)	⊕○○○ Very low ^{a,b,c}	-	Five studies (n=158) reported effects of feed osmolality/osmolality on gastric emptying. In one study, a mean gastric residual of 30% was found in infants 3 hours after feeding a casein hydrolysate formula (539 mOsm/L), whereas no gastric residual after feeding an 80% casein and 20% soy formula (204 mOsm/L) and 3.7% gastric residual with a casein formula (211 mOsm/L) were found. Another study found no change in gastric emptying	

				with a feed osmolality of 310 versus 155 mOsm/kg. However, gastric emptying was accelerated by decreasing osmolality from 310 to 155 mOsm/kg while increasing feed volume from 10 mL/kg to 20 mL/kg. Another study found no significant difference in gastric residuals after feeding different feeds with an osmolality ranging from 275 mOsm/L to 576 mOsm/L. Another study reported no significant difference in gastric emptying between feeding a soybean formula containing sucrose (279 mOsm/kg) or containing glucose (448 mOsm/kg). The fifth study reported no significant difference in gastric residuals after feedings with osmolalities ranging from 340 mOsm/L to 380 mOsm/L.	
Adverse effects: RCT and observational assessed with: Feeding intolerance	408 (4 RCTs)	⊕○○○ Very low ^{a,c,f}	-	Definitions of feeding intolerance varied among the studies but frequently included presence of abdominal distension, vomiting and delayed/with-held feedings. None of the four studies (n= 408) found significant differences in feeding tolerance with feed osmolalities up to 451 mOsm/kg.	
Fully breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Faltering growth / body composition - not measured	-	-	-	-	-
Duration of initial hospital stay - not measured	-	-	-	-	-
Time to full enteral feeds - not measured	-	-	-	-	-
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Sepsis: proven or suspected - not measured	-	-	-	-	-
Retinopathy of prematurity (ROP) - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-
a. Downgraded one level for unclear risk of bias b. Downgraded one level for inconsistency as studies reported different findings c. Downgraded one level for indirectness as not all studies included a comparison >450 mOsm/kg d. Downgraded one level for imprecision as event rates are low e. Downgraded two levels for imprecision as OR are provided but not the confidence intervals f. Downgraded one level for indirectness as definitions vary for feeding intolerance					
Undesirable Effects How substantial are the undesirable anticipated effects?					
JUDGEMENT	RESEARCH EVIDENCE			ADDITIONAL CONSIDERATIONS	

● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Necrotising enterocolitis (NEC): RCT + observational study: One study reported higher necrotising enterocolitis (NEC) incidence with feed osmolality of 650 mOsm/L compared with 359 mOsm/L; one found higher NEC incidence with the lowest feed osmolality (326 mOsm/kg compared with 385 mOsm/kg). The remaining three studies reported no difference for NEC between osmolarities. One cohort study reported no effect on NEC with increases in osmolality in excess of 2,000 mOsm/kg due to the addition of medications [Critical]. Undesirable effects for Māori No additional data	
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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Very low certainty of evidence overall.	

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality - not measured	CRITICAL	-
Necrotising enterocolitis: RCT and observational	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis: Cohort study	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment - not measured	CRITICAL	-
Adverse effects: RCT assessed with: Gastric emptying	CRITICAL	⊕○○○ Very low
Adverse effects: RCT and observational assessed with: Feeding intolerance	CRITICAL	⊕○○○ Very low
Fully breastmilk feeding at hospital discharge - not measured	CRITICAL	-
Faltering growth / body composition - not measured	IMPORTANT	-

Duration of initial hospital stay - not measured	IMPORTANT	-
Time to full enteral feeds - not measured	IMPORTANT	-
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Sepsis: proven or suspected - not measured	IMPORTANT	-
Retinopathy of prematurity - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-

Certainty of evidence for Māori - No additional data

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly some uncertainty Values for Māori No additional data	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison	Higher feed osmolality versus lower feed osmolality - very low certainty evidence Uncertain effect on gastric emptying, feeding intolerance and NEC	

● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Balance of effects for Māori No additional data	
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Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The cost differences between feeds or for nutritional supplements are minimal.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	The costs are certain. Certainty of evidence of required resources for Māori No additional data	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the	There are no studies that assess the specific cost-effectiveness of higher versus lower feed osmolarity in the context of preterm infants.	

comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	Cost effectiveness for Māori No additional data	
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Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Pēpi Māori are more likely to be born preterm and face higher rates of NEC and feeding complications due to systemic inequities in neonatal care. If feeds with high osmolality are used without appropriate dilution, the risk of harm may increase, particularly where resources or staff training are inconsistent. Whānau Māori may not be included in discussions about feed safety, medication administration or the role of breastmilk in reducing risk. Equity requires culturally safe care, standardised guidelines and transparent communication to ensure all pēpi Māori receive safe, well-tolerated feeds that support gut health and early development. Equity for Pacific families Pacific families may not be informed about how feed osmolality affects their baby's tolerance or risk of complications. If feeding plans are not clearly explained, families may feel excluded from important decisions. Equity requires culturally appropriate communication that builds understanding and trust in feeding strategies tailored to each infant. Equity for underrepresented groups Families from migrant or low-income backgrounds may not receive consistent explanations about the safety of higher or lower osmolality feeds. Without clear information, they may not understand changes in feeding tolerance. Equity means ensuring all families receive simple, accessible guidance to participate fully in decisions affecting their baby's nutrition.	

Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☐ Probably yes ☐ Yes ☒ Varies ☐ Don't know	Acceptability of the intervention may vary.	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☐ Probably yes ☒ Yes ☐ Varies ☐ Don't know	The intervention is feasible.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty	Possibly important	Probably no important	No important			

	JUDGEMENT						
	or variability	uncertainty or variability	uncertainty or variability	uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ●	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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EtD 32. Should withholding enteral feeds vs. not withholding enteral feeds be implemented for preterm infants requiring a blood transfusion, eye examination or for extubation?

POPULATION:	Preterm infants requiring a blood transfusion, eye examination or for extubation
INTERVENTION:	With-holding enteral feeds
COMPARISON:	not with-holding enteral feeds
MAIN OUTCOMES:	Critical outcomes Mortality Necrotising enterocolitis Adverse effects – aspiration Time to full enteral feeds Faltering growth/body composition Important but not critical Duration of initial hospital stay Neurodevelopmental impairment Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Sepsis: proven or suspected Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds Fully breastfed or breastmilk feeding at hospital discharge
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	Necrotising enterocolitis is a serious gut disease that affects very preterm infants; some will die of the disease and survivors are at high risk of long-term health and developmental problems. Preterm infants receive frequent feeds (every 1-3 hours) and they often need blood transfusions because they become anaemic (not enough red blood cells). There is concern that feeding infants during a blood transfusion may increase the risk of necrotising enterocolitis. The proposed mechanism is thought to involve reduced blood supply to the gut during transfusion, leading to ischaemia and inflammation, which may be made worse by ongoing enteral feeding. Withholding enteral feeds during transfusion is a strategy aimed at reducing gastrointestinal stress and the risk of necrotising enterocolitis. Withholding feeds may also help prevent aspiration during extubation by minimising the risk of gastric contents entering the airway. Others, however, think that it is more dangerous to stop feeds. Because of this, the way infants are cared for during a blood transfusion or extubation varies across the country; some infants have feeds stopped before, during and after a transfusion (around 12 hours in total), and others have feeds continued. However, withholding feeds may delay nutritional progression and prolong the time to full enteral feeding. Continuing feeds during transfusion avoids interruptions in nutrient delivery, potentially supporting more

CONFLICT OF INTERESTS:	consistent growth and development. The practice of stopping enteral feeds during extubation in preterm infants lacks robust evidence and remains a topic of debate. The primary concern is the potential risk of aspiration during the procedure. However, there is little evidence supporting the routine cessation of feeds for extubation. Balancing the potential benefits of feed interruption with the risks of delayed nutritional progression is essential to optimise outcomes for preterm infants undergoing eye examination, extubation and blood transfusions.
	None

Assessment

Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Withholding feeds for extubation - no randomised controlled trial evidence was found. Withholding feeds for eye examinations for retinopathy of prematurity We identified a Canadian RCT of 34 infants with mean gestational age of 28.6 weeks at birth undergoing a retinopathy of prematurity screening eye examination [1]. Infants were randomised to feeding 1 hour before eye examination or feeding schedule adjusted to ensure no feeding within 2 hours before eye examination. There was 19% less crying ($p=0.016$) in feeding versus no feeding group. Vomiting was 3-fold less in feeding versus no feeding group (4.2% vs. 12.5%, $p=0.38$). Gastric aspirates were less in feeding versus no feeding group ($p=0.18$). Diastolic blood pressure was lower and respiratory rate greater during the examination in feeding group ($p<0.05$), whereas pulse rate was greater at the start of the examination in feeding group ($p<0.05$). Withholding feeds for transfusion Evidence from Cochrane review [2]; 2 RCTs [3,4] and a systematic review of non-randomised studies [5]. Unpublished data were found for the WHEAT pilot trial [6] Time to full enteral feeds: RCT: Little or no difference for withholding feeds 8 ± 35 ($n=19$); full feeds 13 ± 46 ($n=18$); restricted feeds 8 ± 32 ($n=17$); ($P=0.88$) [Critical]. Necrotising enterocolitis (NEC): Non-randomised: Large decrease in risk of NEC for withholding feeds (13 fewer per 1,000; 17 fewer to 5 fewer) [Critical]. Retinopathy of prematurity: RCT: Lower incidence of ROP in withholding feeds group compared with continued feeding (8/52 vs. 13/58; $p=0.25$) [Important]. Duration of hospitalisation: RCT: Large effect for reduced duration of hospitalisation for the withholding feeding group compared with continued feeding (74 ± 24 days vs. 86 ± 39; $p=0.19$) [Important].	Randomised controlled trial evidence is insufficient to show whether stopping feeds has an effect on the incidence of subsequent NEC or death. Large, adequately powered RCTs are needed to address this issue. Population information for included evidence Retinopathy of prematurity screening eye examination [1]. Cochrane systematic review [2]: Infants born at 25 to 32 weeks' gestational age or at ≤ 38 weeks corrected gestational age. Turkey: RCT [3]: Preterm infants ≤ 32 weeks' gestation and/or ≤ 1500 g. Australia: RCT [4]: Preterm infants < 35 weeks' gestation. Systematic review [5]: Included studies involved very-low-birth-weight infants, except one study of low-birth-weight infants and one of ≤ 34 weeks' gestation. United Kingdom: Pilot RCT [6]: Preterm infants < 30 weeks' gestation

	Desirable effects for Māori No data available				
Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with not with-holding enteral feeds	Risk difference with EG 2.8 with-holding enteral feeds
Mortality: RCT: Transfusion assessed with: All-cause mortality	177 (1 RCT)	⊕○○○○ Very low ^{a,b,c}	not reported	Study population	
				8.2%	6.3%
Mortality: RCT: Transfusion assessed with: to 44 weeks' postmenstrual age	22 (1 RCT)	⊕○○○○ Very low ^{a,b,c}	not estimable as no events	Study population	
				0 per 1,000	0 fewer per 1,000 (0 fewer to 0 fewer)
Mortality: RCT: Transfusion	54 (1 RCT)	⊕○○○○ Very low ^{a,b,c}	-	No events reported for with-holding feeds; full feeds or restricted feeds	
Mortality: Transfusion	110 (1 RCT)	⊕○○○○ Very low ^{a,b,c}	not reported	Study population	
				6.8 %	No events
Necrotising enterocolitis: RCT: Transfusion	177 (1 RCT)	⊕○○○○ Very low ^{a,d,e}	not estimable	Study population	
				52 per 1,000	52 fewer per 1,000 (52 fewer to 52 fewer)
NEC within 48 hours of transfusion: RCT	22 (1 RCT)	⊕○○○○ Very low ^{a,d,f}	not estimable as no events	Study population	
				0 per 1,000	0 fewer per 1,000 (0 fewer to 0 fewer)
NEC at any time after transfusion: RCT	22 (1 RCT)	⊕○○○○ Very low ^{a,d,f}	not estimable as no events	Study population	
				0 per 1,000	0 fewer per 1,000 (0 fewer to 0 fewer)
Necrotising enterocolitis: RCT assessed with: Transfusion associated NEC	54 (1 RCT)	⊕○○○○ Very low ^{a,c,d}	-	No events reported for with-holding feeds; full feeds or restricted feeds	
Necrotising enterocolitis assessed with: within 72 hours of transfusion	110 (1 RCT)	⊕○○○○ Very low ^{a,b,d}	not reported	Study population	
				3.4%	No events
Necrotising enterocolitis: Non-randomised	7492		RR 0.47	Study population	

assessed with: Transfusion associated NEC	(7 non-randomised studies)	⊕○○○ Very low ^f	(0.28 to 0.80)	24 per 1,000	13 fewer per 1,000 (17 fewer to 5 fewer)
Adverse effects - not measured	-	-	-	-	-
Time to full enteral feeds: RCT: Transfusion assessed with: hours ± SD	54 (1 RCT)	⊕○○○ Very low ^{a,b,d}	-	With-holding feeds 8 ± 35 (n=19); full feeds 13 ± 46 (n=18); restricted feeds 8 ± 32 (n=17); (P=0.88)	
Faltering growth/body composition: RCT: Transfusion assessed with: Weight standard deviation scores	Not reported (1 RCT)	⊕○○○ Very low ^{a,d}	-	Mean change (SD) in weight standard deviation scores was -1.10 (0.93) in infants who had enteral feeds with-held compared with -0.96 (0.79) in infants who had continued feeds.	
Faltering growth/body composition: RCT: Transfusion assessed with: Head circumference standard deviation scores	Not reported (1 RCT)	⊕○○○ Very low ^{a,d}	-	Mean change (SD) in head circumference standard deviation scores was -0.79 (1.62) in infants who had enteral feeds with-held compared with -0.68 (1.63) in infants who had continued feeds.	
Duration of initial hospital stay: RCT: Transfusion assessed with: Days	110 (1 RCT)	⊕○○○ Very low ^{a,b,d}	-	Duration of hospitalisation (days, mean ± SD); with-holding feeds 74 ± 24 days (n=52); continued feeds 86 ± 39 (n=58); p=0.19	
Neurodevelopmental impairment - not measured	-	-	-	-	-
Bronchopulmonary dysplasia: RCT: Transfusion	110 (1 RCT)	⊕○○○ Very low ^{a,b,d}	not reported	Study population	
				60%	62%
Retinopathy of prematurity: RCT: Transfusion	110 (1 RCT)	⊕○○○ Very low ^{a,b,d}	not reported	Study population	
				22.4%	15.4%
Anaemia of prematurity - not measured	-	-	-	-	-
Sepsis: proven or suspected: RCT: Transfusion assessed with: Late onset sepsis	54 (1 RCT)	⊕○○○ Very low ^{a,b,d}	-	With-holding feeds 11/19; full feeds 10/18; restricted feeds 7/17 no statistical analysis as not appropriate to compare rates of long-term outcomes as feeding allocation was for one transfusion only	
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-
Fully breastfed or breastmilk feeding at hospital discharge - not measured	-	-	-	-	-

- a. Downgraded one level due to risk of bias concerns - no blinding of carers or health professionals: outcome assessors
b. Downgraded one level for imprecision
c. Downgraded one level for inconsistency
d. Downgraded one level for indirectness as evidence based on a single study
e. Downgraded two levels for imprecision due to small study of 22 infants with no events
f. Downgraded one level for risk of bias as these were non-randomised studies although they were mainly well conducted for their design

a)

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Transfusion Mortality: RCT: Uncertain effect due to no events or few events reported. Effect estimate not available [Critical]. Necrotising enterocolitis: RCT: Uncertain effect due to no events or few events reported. Effect estimate not available [Critical]. Faltering growth/body composition: RCT: Uncertain effect on weight z-scores in infants who had enteral feeds withheld, Mean-1.10 (SD 0.93) compared with infants who had continued feeds, Mean-0.96 (SD 0.79). Uncertain effect on head circumference standard deviation scores in infants who had enteral feeds withheld, mean -0.79 (SD 1.62) compared with infants who had continued feeds, mean -0.68 (SD 1.63) [Critical]. Bronchopulmonary dysplasia: RCT: Little or no difference between withholding and continued feeding for BPD (32/52 vs. 35/58; $p=0.73$) [Important]. Sepsis: RCT: High rates of late onset sepsis for withholding feeds 11/19; full feeds 10/18; restricted feeds 7/17 [Important]. Undesirable effects for Māori No additional data	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Very low certainty of evidence for transfusion evidence. Certainty of evidence for Māori No additional data	Evidence is based on a single RCT and unpublished data for a pilot RCT. Sample sizes are small and in one RCT no events were reported.

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT: Transfusion	CRITICAL	⊕○○○

assessed with: All-cause mortality		Very low
Mortality: RCT: Transfusion assessed with: to 44 weeks' postmenstrual age	CRITICAL	⊕○○○ Very low
Mortality: RCT: Transfusion	CRITICAL	⊕○○○ Very low
Mortality: Transfusion	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis: RCT: Transfusion	CRITICAL	⊕○○○ Very low
NEC within 48 hours of transfusion: RCT	CRITICAL	⊕○○○ Very low
NEC at any time after transfusion: RCT	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis: RCT assessed with: Transfusion associated NEC	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis assessed with: within 72 hours of transfusion	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis: Non-randomised assessed with: Transfusion associated NEC	CRITICAL	⊕○○○ Very low
Adverse effects - not measured	CRITICAL	-
Time to full enteral feeds: RCT: Transfusion assessed with: hours ± SD	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT: Transfusion assessed with: Weight standard deviation scores	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT: Transfusion assessed with: Head circumference standard deviation scores	CRITICAL	⊕○○○ Very low
Duration of initial hospital stay: RCT: Transfusion assessed with: Days	IMPORTANT	⊕○○○ Very low
Neurodevelopmental impairment - not measured	IMPORTANT	-
Bronchopulmonary dysplasia: RCT: Transfusion	IMPORTANT	⊕○○○ Very low

Retinopathy of prematurity: RCT: Transfusion	IMPORTANT	⊕○○○ Very low
Anaemia of prematurity - not measured	IMPORTANT	-
Sepsis: proven or suspected: RCT: Transfusion assessed with: Late onset sepsis	IMPORTANT	⊕○○○ Very low
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-
Fully breastfed or breastmilk feeding at hospital discharge - not measured	NOT IMPORTANT	-

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty about or variability in the value placed on the main outcomes Values for Māori No additional data	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention	Withholding enteral feeds compared with not withholding enteral feeds for preterm infants requiring a blood transfusion - very low certainty of evidence Uncertain effect on NEC from RCTs. Large reduction in NEC risk for non-randomised studies Uncertain effect for mortality, retinopathy of prematurity, mortality, bronchopulmonary dysplasia, faltering growth/body composition (weight and head	

or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	circumference), duration of hospitalisation, time to full enteral feeding, sepsis. Balance of effects for Māori No additional data	
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Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Minimal resources are required for this short-term intervention. Resources for Māori No additional data	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	A formal assessment of the certainty of evidence of the cost was not undertaken but is likely to be minimal. Certainty of evidence of required resources for Māori No additional data	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours	No studies assessed the specific cost-effectiveness of withholding enteral feeds compared with not withholding feeds for preterm infants requiring a blood transfusion.	

the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	Cost effectiveness for Māori No additional data	
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Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ● Don't know	Equity for Māori Pēpi Māori are more likely to be born preterm and face greater risks of NEC and feeding delays due to systemic inequities in neonatal care. Inconsistent practices around withholding feeds during blood transfusions, eye examinations or extubation may further disadvantage pēpi Māori if care decisions are not clearly explained or equitably applied. Delays in nutrition can impact growth and development, especially when whānau Māori are not involved in decision-making. Equity requires culturally safe care, transparent communication and national guidance that ensures all pēpi Māori receive safe, consistent and evidence-informed feeding practices during critical procedures. Equity for Pacific families Pacific families may not be informed about the rationale for withholding feeds during transfusion, leading to confusion or concern. Without culturally safe dialogue, trust in care can be affected. Equity requires clear, respectful explanations to ensure Pacific families understand and support temporary feeding changes during clinical procedures. Equity for underrepresented groups Migrant, rural and refugee families may struggle to understand the need to pause feeds during transfusion, especially without accessible information or interpreters. This can create fear or disengagement. Equity requires consistent communication and support that empowers all families to feel informed and confident in decisions about their baby's care.	

Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know	There is currently varied practice in Aotearoa New Zealand with some units withholding enteral feeds and other not doing so prior to blood transfusion. Acceptability for Māori No additional data	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	With clear guidance this could be feasible. Feasibility for Māori No additional data	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			

	JUDGEMENT						
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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EtD 33. What is the recommended enteral fluid intake?

POPULATION:	Preterm infants receiving full enteral feeds
INTERVENTION:	Higher (≥ 180 mL/kg/day)
COMPARISON:	Lower enteral fluid intake (< 180 mL/kg/day)
MAIN OUTCOMES:	Critical for making a decision Mortality Neurodevelopmental impairment Faltering growth / body composition Adverse effects (patent ductus arteriosus) Bronchopulmonary dysplasia Necrotising enterocolitis Important but not critical Fully breastmilk feeding at hospital discharge Fully breastfeeding at hospital discharge Duration of initial hospital stay Time to full enteral feeds Sepsis: proven or suspected Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Of limited importance Time to full sucking feeds
SETTING:	Any birth setting
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	Establishing optimal enteral fluid intake in preterm infants is critical for maintaining fluid balance, supporting growth and preventing complications such as dehydration, electrolyte imbalances and oedema. After achieving full enteral feeding, recommendations for fluid volumes vary widely across neonatal units, reflecting uncertainty in the evidence and differing clinical practices. It is essential to balance the need for sufficient volume for optimal growth with the risk of fluid overload, which may exacerbate conditions such as patent ductus arteriosus, bronchopulmonary dysplasia and NEC. In the first week after birth, the postnatal physiological diuresis, insensible water losses, gestational age and clinical status of the infant influence fluid requirements. However, there is limited high-quality evidence to define precise daily fluid intakes by postnatal age during this transitional period. Current practices typically involve cautious advancement of enteral feed volumes based on the volume of expressed breastmilk that is available and the tolerance of feeds. Standardised recommendations for enteral fluid management could reduce practice variation and improve outcomes by supporting consistent clinical decision-making. This question seeks to determine the recommended enteral fluid intake once preterm infants are on full enteral feeds but also to identify evidence of appropriate fluid intake targets by postnatal day during the first week after birth, without increasing the

	risk of adverse outcomes.
CONFLICT OF INTERESTS:	The following ProVIDe cohort study (Reference 3) co-authors for this topic are on the Guideline Development Group: Barbara Cormack, Frank Bloomfield are co-authors of the and are on the Guideline Development Group.

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	We identified one Cochrane review [1] and a report of a randomised trial within the review [2]. High versus standard volume of fortified human milk or preterm formula (High defined as >180 mL/kg/day and standard as ≤180 mL/kg/day) Mortality: RCT: No significant effect on all-cause mortality before discharge for higher versus lower enteral fluid volume (10 fewer per 1,000; 14 fewer to 51 more) [Critical]. Neurodevelopmental impairment: RCT: No significant effect on neurodevelopmental impairment for higher versus lower enteral fluid volume (120 fewer per 1,000; 213 fewer to 210 more) [Critical]. No faltering growth / body composition: RCT: Higher enteral fluid intake was associated with significantly higher weight gain during hospital stay (MD 2.58 g/kg/day higher; 1.41 higher to 3.76 higher). There was no significant difference in linear growth (MD 0.05 cm/week higher; 0.02 lower to 0.13 higher) or head circumference growth (MD 0.02 cm/week higher; 0.04 lower to 0.09 higher) during hospital stay. There was no significant difference in the number of infants with weight (75 fewer per 1,000; 193 fewer to 288 more), length (163 fewer per 1,000; 230 fewer to 138 more) or head circumference (27 fewer per 1,000; 41 fewer to 296 more) <10th percentile at 12 months' corrected age [Critical]. Adverse effects (patent ductus arteriosus): RCT: No significant effect on patent ductus arteriosus (11 fewer per 1,000; 36 fewer to 56 more) [Critical]. Bronchopulmonary dysplasia: RCT: No significant effect on bronchopulmonary dysplasia (1 more per 1,000; 49 fewer to 92 more) [Critical]. Necrotising enterocolitis (NEC): RCT: No significant effect on NEC (4 fewer per 1,000; 12 fewer to 48 more) [Critical]. Duration of initial hospital stay: RCT: No significant effect on duration of initial hospital stay (MD 1 days higher; 3.54 lower to 5.54 higher) [Important]. High versus standard volume of unfortified human milk or term formula (High	In a subgroup of 86 infants from a trial in the Cochrane review [2], there was no difference between high (180-200 mL/kg/day) versus standard (140-160 mL/kg/day) in fat mass, fat free mass or % body fat at 36 weeks postmenstrual age. The selection of these infants from the randomised sample was not clear. 160 mL/kg/day fortified expressed breastmilk 4 to 4.3 g/kg/day 160 mL/kg/day preterm formula 4.3 to 4.6 g/kg/day 160 mL/kg/day fortified expressed breastmilk 131 to 133 kcal/kg/day 160 mL/kg/day preterm formula 128 to 130 kcal/kg/day 180 mL/kg/day fortified expressed breastmilk provides 4.4 to 4.9 g/kg/day 180 mL/kg/day preterm formula provides 4.9 to 5.2 g/kg/day 180 mL/kg/day fortified expressed breastmilk provides 147 to 149 kcal/kg/day 180 mL/kg/day preterm formula provides 144 to 146 kcal/kg/day Additional supporting data Aotearoa New Zealand: Cohort analysis of ProVIDe RCT of 434 extremely low birthweight infants [3]. The study reported the relationship between higher

	defined as >200 mL/kg/day and standard as ≤200 mL/kg/day) No faltering growth / body composition: RCT: Higher enteral fluid intake was associated with significantly higher weight gain during hospital stay (MD 6.2 g/kg/day higher; 2.71 higher to 9.69 higher) [Critical]. Necrotising enterocolitis (NEC): RCT: No significant effect on NEC (1 more per 1,000; 30 fewer to 477 more) [Critical].	enteral/breastmilk volume intake in the first 4 weeks after birth and expected growth. Infants with mean week 4 total fluid intakes of 174-202 mL/kg/day were three times more likely (OR 3.0 [95% CI 1.3, 7.1, p=0.01]) to have <i>expected length growth</i> (defined as z-score change from birth to 36-week corrected age - 0.8 to 0.8) than those with mean week 4 fluid intake in the 166-173 mL/kg/day range. Mean expressed breastmilk intake of 157-173 mL/kg/day in week 3 increased the odds of achieving <i>expected length growth</i> by 3.4 (CI 1.5-7.3, p=0.002) times compared with 115 to 156 mL/kg/day. Mean expressed breastmilk intake of 174-202 mL/kg/day in week 3 increased the odds of achieving <i>target growth</i> (defined as change in z-score from birth to 36 weeks' CGA of between -0.8 and 0.8 in all three of weight, length and head circumference) by 3 times compared with mean expressed breastmilk intake of 157 to 173 mL/kg/day.
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Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with lower enteral fluid intake (< 180 mL/kg/day)	Risk difference with higher enteral fluid intake (>= 180 mL/kg/day)
Mortality: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: All-cause mortality before discharge	283 (2 RCTs)	⊕⊕○○ Low ^a	RR 0.24 (0.01 to 4.71)	Study population 14 per 1,000	10 fewer per 1,000 (14 fewer to 51 more)
Neurodevelopmental impairment: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: Neurodevelopmental impairment at 12 months' corrected age	47 (1 RCT)	⊕⊕○○ Low ^{b,c}	RR 0.52 (0.15 to 1.84)	Study population 250 per 1,000	120 fewer per 1,000 (213 fewer to 210 more)
Faltering growth / body composition: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: Weight gain during hospital stay (g/kg/day)	271 (2 RCTs)	⊕⊕○○ low ^a	-	The mean faltering growth / body composition: RCT: High versus standard volume of fortified human milk or preterm formula was 17.2 g/kg/day	MD 2.58 higher (1.41 higher to 3.76 higher)
Faltering growth / body composition: RCT: High versus standard volume of fortified human milk or preterm	271 (2 RCTs)	⊕⊕⊕○	-	The mean faltering growth / body composition: RCT: High versus standard	MD 0.05 higher (0.02 lower to 0.13 higher)

formula assessed with: Linear growth during hospital stay (cm/week)		Moderate ^c		volume of fortified human milk or preterm formula was 0.77 cm/week	
Faltering growth / body composition: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: Head growth during hospital stay (cm/week)	271 (2 RCTs)	⊕⊕⊕○ Moderate ^c	-	The mean faltering growth / body composition: RCT: High versus standard volume of fortified human milk or preterm formula was 0.71 cm/week	MD 0.02 higher (0.04 lower to 0.09 higher)
Faltering growth / body composition: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: Weight <10th percentile at 12 months' corrected age	47 (1 RCT)	⊕○○○ Very low ^{a,b}	RR 0.70 (0.23 to 2.15)	Study population	
				250 per 1,000	75 fewer per 1,000 (193 fewer to 288 more)
Faltering growth / body composition: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: Length < 10th percentile at 12 months' corrected age	47 (1 RCT)	⊕○○○ Very low ^{a,b}	RR 0.35 (0.08 to 1.55)	Study population	
				250 per 1,000	163 fewer per 1,000 (230 fewer to 138 more)
Faltering growth / body composition: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: Head circumference < 10th percentile at 12 months' corrected age	47 (1 RCT)	⊕○○○ Very low ^{b,d}	RR 0.35 (0.01 to 8.11)	Study population	
				42 per 1,000	27 fewer per 1,000 (41 fewer to 296 more)
Faltering growth / body composition: RCT: High versus standard volume of unfortified human milk or term formula assessed with: Weight gain during hospital stay (g/kg/day)	61 (1 RCT)	⊕⊕⊕○ Moderate ^b	-	The mean faltering growth / body composition: RCT: High versus standard volume of unfortified human milk or term formula was 18.7 g/kg/day	MD 6.2 higher (2.71 higher to 9.69 higher)
Adverse effects (patent ductus arteriosus): RCT: High versus standard volume of fortified human milk or preterm formula	271 (2 RCTs)	⊕⊕○○ Low ^a	RR 0.77 (0.28 to 2.12)	Study population	
				50 per 1,000	11 fewer per 1,000 (36 fewer to 56 more)
Bronchopulmonary dysplasia (BPD) / chronic lung disease: RCT: High versus standard volume of fortified human milk or preterm formula	271 (2 RCTs)	⊕⊕⊕○ Moderate ^c	RR 1.01 (0.57 to 1.81)	Study population	
				113 per 1,000	1 more per 1,000 (49 fewer to 92 more)
Necrotising enterocolitis (NEC): RCT: High versus standard volume of fortified human milk or preterm formula	283 (2 RCTs)	⊕⊕○○ Low ^a	RR 0.74 (0.12 to 4.51)	Study population	
				14 per 1,000	4 fewer per 1,000 (12 fewer to 48 more)
Necrotising enterocolitis: RCT: High versus standard volume of unfortified human milk or term formula	61 (1 RCT)	⊕○○○ Very low ^{b,e}	RR 1.03 (0.07 to 15.78)	Study population	
				32 per 1,000	1 more per 1,000

					(30 fewer to 477 more)
Fully breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Fully breastfeeding at hospital discharge - not measured	-	-	-	-	-
Duration of initial hospital stay: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: Days	271 (2 RCTs)	 Low ^a	-	The mean duration of initial hospital stay: RCT: High versus standard volume of fortified human milk or preterm formula was 64.05 days	MD 1 higher (3.54 lower to 5.54 higher)
Time to full enteral feeds - not measured	-	-	-	-	-
Sepsis: proven or suspected - not measured	-	-	-	-	-
Retinopathy of prematurity (ROP) - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-

- a. Downgraded two levels for imprecision due to wide confidence intervals crossing the line of no effect and low event rates
b. Downgraded one level for indirectness as evidence based on a single study
c. Downgraded one level for imprecision due to confidence intervals crossing the line of no effect
d. Downgraded three levels for imprecision due to extremely wide confidence intervals crossing the line of no effect and low event rates

Desirable effects for Māori

No additional evidence available

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	None identified. Undesirable effects for Māori No additional evidence available	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Very low to high certainty of evidence overall	

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: All-cause mortality before discharge	CRITICAL	⊕⊕○○ Low
Neurodevelopmental impairment: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: Neurodevelopmental impairment at 12 months' corrected age	CRITICAL	⊕⊕○○ Low
Faltering growth / body composition: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: Weight gain during hospital stay (g/kg/day)	CRITICAL	⊕⊕⊕⊕ High
Faltering growth / body composition: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: Linear growth during hospital stay (cm/week)	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth / body composition: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: Head growth during hospital stay (cm/week)	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth / body composition: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: Weight < 10th percentile at 12 months' corrected age	CRITICAL	⊕○○○ Very low
Faltering growth / body composition: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: Length < 10th percentile at 12 months' corrected age	CRITICAL	⊕○○○ Very low
Faltering growth / body composition: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: Head circumference < 10th percentile at 12 months' corrected age	CRITICAL	⊕○○○ Very low
Faltering growth / body composition: RCT: High versus standard volume of unfortified human milk or term formula assessed with: Weight gain during hospital stay (g/kg/day)	CRITICAL	⊕⊕⊕○ Moderate
Adverse effects (patent ductus arteriosus): RCT: High versus standard volume of fortified human milk or preterm formula	CRITICAL	⊕⊕○○ Low
Bronchopulmonary dysplasia: RCT: High versus standard volume of fortified human milk or preterm formula	CRITICAL	⊕⊕⊕○ Moderate

Necrotising enterocolitis (NEC): RCT: High versus standard volume of fortified human milk or preterm formula	CRITICAL	⊕⊕○○ Low
Necrotising enterocolitis: RCT: High versus standard volume of unfortified human milk or term formula	CRITICAL	⊕○○○ Very low
Fully breastmilk feeding at hospital discharge - not measured	IMPORTANT	-
Fully breastfeeding at hospital discharge - not measured	IMPORTANT	-
Duration of initial hospital stay: RCT: High versus standard volume of fortified human milk or preterm formula assessed with: Days	IMPORTANT	⊕⊕○○ Low
Time to full enteral feeds - not measured	IMPORTANT	-
Sepsis: proven or suspected - not measured	IMPORTANT	-
Retinopathy of prematurity (ROP) - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-

Certainty of evidence for Māori

No additional data

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability	Possibly important uncertainty or variability Values for Māori No additional research was identified.	

○ No important uncertainty or variability		
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Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	High versus standard volume of fortified human milk or preterm formula - High certainty evidence Increased weight gain during hospital stay High versus standard volume of fortified human milk or preterm formula - Moderate certainty evidence Uncertain effect on length and head circumference, bronchopulmonary dysplasia High versus standard volume of fortified human milk or preterm formula - Low certainty evidence Uncertain effect on mortality, neurodevelopmental impairment, patent ductus arteriosus, NEC, duration of hospitalisation High versus standard volume of fortified human milk or preterm formula - Very low certainty evidence Uncertain effect on weight, length or head circumference <10th percentile at 12 months' corrected age High versus standard volume of unfortified human milk or term formula- Moderate certainty evidence Increased weight gain during hospital stay High versus standard volume of unfortified human milk or term formula- Very low certainty evidence Uncertain effect on NEC Balance of effects for Māori No additional evidence	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The resources required are minimal, especially if using breastmilk.	
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Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Reasonably certain Certainty of evidence of required resources for Māori No additional evidence available	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No studies were found. Cost effectiveness for Māori No additional evidence available	Using lower enteral feed volumes may increase the need for individualised nutritional supplementation to achieve adequate growth. This requires additional resources such as referral to a dietitian.

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Pēpi Māori experience higher rates of preterm birth and neonatal morbidity. Ensuring recommended enteral fluid intakes are applied consistently for pēpi Māori is essential to address these disparities. Culturally safe care and equitable access to appropriately resourced neonatal services must be prioritised to support optimal growth and developmental outcomes. Equity for Pacific families Pacific infants are at increased risk of preterm birth and face barriers to accessing high-quality neonatal care. Clear recommendations for enteral fluid intake during the first week and at full feeds must be implemented equitably. Care should reflect Pacific values, respect family involvement and ensure access to appropriate support across all settings. Equity for underrepresented groups Infants from Asian, migrant, rural or lower socioeconomic backgrounds may experience inconsistent neonatal care practices. Standardising recommended enteral fluid intake during early neonatal care is vital to promote equitable outcomes.	A 2025 survey in Aotearoa New Zealand neonatal units showed access to a neonatal dietitian was inconsistent [4]. Rural hospitals and lower-resourced units are less likely to have access to specialist neonatal dietitians. This means that if faltering growth occurs, it may not be consistently managed, so feeding strategies that minimise the risk of faltering growth will increase equity.
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Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Probably acceptable as prescribing >180 mL/kg/day is common practice in some units. Acceptability for Māori No additional research available.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies	Already occurring in some units, so it is feasible. Feasibility for Māori No additional research available.	

o Don't know

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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References

1. Abiramalatha, T.; Thomas, N.; Thanigainathan, S. High versus standard volume enteral feeds to promote growth in preterm or low birth weight infants. *Cochrane Database Syst. Rev.* **2021**, 3, Cd012413, doi:10.1002/14651858.CD012413.pub3.
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3. Cormack, B.E.; Jiang, Y.; Harding, J.E.; Crowther, C.A.; Bloomfield, F.H. Relationships between neonatal nutrition and growth to 36 weeks' corrected age in ELBW babies-secondary cohort analysis from the Provide Trial. *Nutrients* **2020**, 12, 760, doi:10.3390/nu12030760.
4. Cormack, B.; Oliver, C.; Anscombe, Y.; Carson, G.; Allworth, S.; Gilroy, M.; Page D.; Little, H.; Alexander, T.; Australasian Neonatal Dietitians Network (ANDiN). Progress and Variation in Nutrition Care for Preterm Infants in Australasia: Results From the 2024 Australasian Neonatal Dietitians Network Survey. *J Paediatr Child Health.* **2026** Jan 8. doi: 10.1111/jpc.70281. Epub ahead of print. PMID: 41503953.

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EtD 35. In preterm infants receiving enteral feeds does enteral additional protein intake improve growth, clinical outcomes or neurodevelopment, or reduce NEC, gastrointestinal complications or less metabolic bone disease?

POPULATION:	Preterm infants receiving enteral feeds
INTERVENTION:	Additional enteral protein supplementation
COMPARISON:	No additional protein supplementation
MAIN OUTCOMES:	Critical outcomes Mortality Neurodevelopmental impairment Faltering growth/body composition Necrotising enterocolitis Important but not critical Adverse effects (gastrointestinal complications) Time to full enteral feeds Duration of initial hospital stay Fully breastfed or breastmilk feeding at hospital discharge Sepsis: proven or suspected Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation: population perspective
BACKGROUND:	Protein is a critical macronutrient for preterm infants, playing a central role in brain and other organ development, and tissue growth. Due to their rapid growth needs and limited body stores, preterm infants have higher protein requirements than term infants. These high protein requirements are not met by expressed breastmilk alone, even at very high volumes. Achieving adequate protein intake through enteral feeds is essential to support optimal growth, neurodevelopment, and overall health outcomes in this vulnerable population. Additional protein intake may promote better weight gain, lean body mass and enhance neurodevelopmental outcomes. However, the benefits of additional protein must be weighed against potential risks, including feeding intolerance, gastrointestinal complications, and neurotoxicity due to protein overload. Excessive protein intake may contribute to metabolic acidosis and elevated blood amino acids concentrations, particularly in infants with immature renal function. Additional protein may also increase the risk of necrotising enterocolitis and other gastrointestinal complications and may delay reaching full enteral feeds. Defining the optimal protein intake for preterm infants to ensure improved growth, neurodevelopment and clinical outcomes while minimising the

CONFLICT OF INTERESTS:	risk of adverse outcomes remains a key consideration in neonatal nutritional management. This question relates to protein supplementation that is in addition to, or instead of commercial breastmilk fortifier.
	The following Das <i>et al</i> systematic review co-authors are on the Guideline Development Group: Luling Lin and Frank Bloomfield and Barbara Cormack.
	The following Amissah <i>et al</i> systematic review co-author wrote this Evidence to Decision document: Julie Brown

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence based on two Cochrane reviews [1] and [2] and another systematic review [3]. NB This question relates to the optimal amount of enteral protein supplementation from or in addition to breastmilk fortifier or preterm formula Currently available fortifiers add either 1.3 or 1.4 g/kg/day of protein to breastmilk to make total protein intakes of: 160 mL/kg/day fortified expressed breastmilk provides 4.0 to 4.3 g/kg/day 180 mL/kg/day fortified expressed breastmilk provides 4.4 to 4.9 g/kg/day 160 mL/kg/day preterm formula provides 4.3 to 4.6 g/kg/day 180 mL/kg/day preterm formula provides 4.9 to 5.2 g/kg/day Studies reporting the optimal amount of protein supplementation from or in addition to breastmilk fortifier only No faltering growth/body composition: RCT: There was no significant difference between higher and lower protein for weight gain (SMD 0.27 SD higher; 0.1 lower to 0.64 higher). Meta-regression revealed a significant linear relationship between protein intake and weight gain (5.73 g/kg/day weight gain for each gram of protein/kg/day, $p = 0.001$). After adjusting for the energy intake in the included studies, this effect size increased to 8.78 g/kg/day for each additional gram per kg per day of protein intake [Critical]. No faltering growth/body composition: RCT: There was a significant increase for length gain for higher compared with lower protein (SMD 0.5 SD higher; 0.08 higher to 0.92 higher). The relationship between protein intake and length gain became significant once energy intake was adjusted for, with each gram per kg per day of protein intake associated with a 0.78 mm per week increase in length. ($p \leq 0.001$) [Critical]. No faltering growth/body composition: RCT: There was no significant difference between higher and lower protein for head circumference gain (SMD 0.06 SD higher; 0.46 lower to 0.59 higher) [Critical].	Population information for included evidence Systematic review of the effects of protein intake from fortified human milk in very preterm infants <32 weeks' gestation [4]. Higher protein was defined as 3.2 to 4.5 g/kg/day in four studies and 3.9–to 4.7 g/kg/day in six studies. Lower protein was defined as 2.9–to 4.0 g/kg/day and 3.2–4.2 g/kg/day. Cochrane systematic review [2]: preterm infants <37 completed weeks. The protein added from breastmilk fortifier was classified as: Low <1 g protein added to 100 mL EBM Moderate ≥ 1g to <1.4 g protein added to 100 mL EBM High ≥ 1.4 g protein added to 100 mL EBM Trials that compared two protein concentrations that fell within the same category as above were excluded. Systematic review [3]: preterm infants <37

	Studies reporting the optimal amount of protein supplementation from or in addition to breastmilk fortifier or preterm formula Mortality: RCT: High vs. moderate protein: No deaths in either the high or moderate protein groups [Critical]. Mortality: RCT: Moderate vs. low protein: No significant effect for reduced risk of mortality with moderate protein intake (19 fewer per 1,000; 35 fewer to 152 more) [Critical]. Neurodevelopmental impairment: RCT: No significant reduction in cerebral palsy for high vs. low protein (8 fewer per 1,000; 48 fewer to 212 more) [Critical]. No faltering growth/body composition: RCT: Very large increase in weight gain for protein supplementation (MD 3.8 g/kg/day higher; 2.9 higher to 4.7 higher). Small increase in length gain (MD 0.12 cm/week higher; 0.07 higher to 0.17 higher) and in head growth (MD 0.06 cm/week higher; 0.01 higher to 0.12 higher) [Critical]. No faltering growth/body composition: RCT: <i>High versus moderate protein supplementation:</i> Small increase in weight gain for high protein compared with moderate protein supplementation (MD 0.66 g/kg/day higher; 0.51 higher to 0.82 higher). No significant effect on length gain (MD 0.01 cm/week higher; 0.01 lower to 0.03 higher) or increase in head circumference (MD 0 cm/week; 0.01 lower to 0.02 higher). However, in the subgroup of trials that compared isocaloric fortifiers, there was a higher rate of length gain in infants fed a high versus moderate protein fortifier (MD 0.05 cm/week, 95% CI 0.01 to 0.09; studies = 4; N= 418), whereas there was no difference in length gain in the one trial that compared fortifiers that were non-isocaloric (MD 0.00 cm/week, 95% CI -0.02 to 0.02; N= 129). There were no subgroup differences by energy content for the outcomes of weight gain or head circumference gain [Critical]. No faltering growth/body composition: RCT: <i>Moderate versus low protein supplementation:</i> Very large increase in weight gain for moderate protein compared with low protein supplementation (MD 2.08 g/kg/day higher; 0.38 higher to 3.77 higher). Little or no increase in length gain (MD 0.09 cm/week higher; 0.05 higher to 0.14 higher) or increase in head circumference (MD 0.13 cm/week higher; 0 to 0.26 higher) [Critical]. No faltering growth/body composition: RCT: No significant effect on length in infancy for <i>high vs. low protein</i> (MD 0.18 cm higher; 0.61 lower to 0.97 higher) or length/height during the toddler period (MD 0.22 cm higher; 0.35 lower to 0.79 higher) [Critical]. Necrotising enterocolitis: RCT: No significant reduction in NEC with <i>high versus moderate</i> protein supplementation (9 fewer per 1,000; 30 fewer to 52 more). No significant effect on NEC with <i>low</i> protein supplementation compared with <i>moderate</i> supplementation (1 fewer per 1,000; 17 fewer to 255 more) [Critical]. Duration of initial hospital stay: RCT: <i>Moderate vs. low protein supplementation:</i> No significant reduction in duration of hospital stay for moderate protein supplementation (MD 3 days lower; 7.13 lower to 1.13 higher) [Important]. Sepsis: RCT: <i>Moderate versus low protein</i> concentration: No significant reduction in risk of	completed weeks. low <3.5 g/kg/d total protein intake High ≥3.5 g/kg/d total protein intake (2) Cochrane systematic review. included 4 studies of infants <32 weeks' gestation, one <33 weeks' and one up to and including 36 weeks' gestation.
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	sepsis for moderate protein supplementation (19 fewer per 1,000; 35 fewer to 152 more) [Important]. Desirable effects for Māori No additional evidence available.				
Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with no additional protein supplementation	Risk difference with additional protein supplementation
Mortality: RCT: High vs. moderate protein	101 (5 RCTs)	⊕⊕⊕○ Moderate ^a	-	None of the trials reported any deaths in either group	
Mortality: RCT: Moderate vs. low protein	112 (1 RCT)	⊕○○○ Very low ^{b,c}	RR 0.48 (0.05 to 5.17)	Study population	
				36 per 1,000	19 fewer per 1,000 (35 fewer to 152 more)
Neurodevelopmental impairment: RCT: High vs. low protein assessed with: Survival without neurodisability at or beyond 12 months' corrected age [measure not specified in review]	400 (1 RCT)	⊕○○○ Very low ^{c,d,h}	RR 0.94 (0.85 to 1.05)	Study population	
				927 per 1,000	56 fewer per 1,000 (139 fewer to 46 more)
Neurodevelopmental impairment: RCT: High vs. low protein assessed with: Cerebral palsy during toddler period [measure not specified in review]	926 (2 RCTs)	⊕○○○ Very low ^{c,e,f}	RR 0.85 (0.15 to 4.79)	Study population	
				56 per 1,000	8 fewer per 1,000 (48 fewer to 212 more)
Faltering growth/body composition: RCT: Protein source from human milk fortification only assessed with: Weight gain (g/kg/day)	530 (8 RCTs)	⊕○○○ Very low ^{c,g,h}	-	The mean faltering growth/body composition: RCT: Protein source from human milk fortification only was 17.65 g/kg/day	SMD 0.27 SD higher (0.1 lower to 0.64 higher)
Faltering growth/body composition: RCT assessed with: Weight gain (g/kg/day)	101 (5 RCTs)	⊕⊕○○ Low ^{c,g}	-	The mean faltering growth/body composition: RCT was 14.68 g/kg/day	MD 3.82 higher (2.94 higher to 4.7 higher)
Faltering growth/body composition: RCT: High vs. moderate protein assessed with: Weight gain (g/kg/day)	606 (6 RCTs)	⊕⊕⊕⊕ High	-	The mean faltering growth/body composition: RCT: High vs. moderate protein was 16.56 g/kg/day	MD 0.66 higher (0.51 higher to 0.82 higher)
Faltering growth/body composition: RCT: Moderate vs. low protein assessed with: Weight gain (g/kg/day)	176 (2 RCTs)	⊕○○○ Very low ^{c,i}	-	The mean faltering growth/body composition: RCT: Moderate vs. low protein was 13.79 g/kg/day	MD 2.08 higher (0.38 higher to 3.77 higher)
Faltering growth/body composition: RCT: Protein source from human milk fortification only assessed with: Length gain (mm/week)	174 (3 RCTs)	⊕⊕⊕⊕ High	-	The mean faltering growth/body composition: RCT: Protein source from human milk fortification only was 1.00 mm/week	SMD 0.5 SD higher (0.08 higher to 0.92 higher)

Faltering growth/body composition: RCT assessed with: Length gain (cm/week)	68 (4 RCTs)	⊕○○○ Very low ^{a,c,i}	-	The mean faltering growth/body composition: RCT was 0.75 cm/week	MD 0.12 higher (0.07 higher to 0.17 higher)
Faltering growth/body composition: RCT: High vs. moderate protein assessed with: Length gain (cm/week)	547 (5 RCTs)	⊕⊕⊕⊕ High	-	The mean faltering growth/body composition: RCT: High vs. moderate protein was 1.11 cm/week	MD 0.01 higher (0.01 lower to 0.03 higher)
Faltering growth/body composition: RCT: Moderate vs. low protein assessed with: Length gain (cm/week)	217 (3 RCTs)	⊕⊕○○ Low ^{c,f}	-	The mean faltering growth/body composition: RCT: Moderate vs. low protein was 0.8 cm/week	MD 0.09 higher (0.05 higher to 0.14 higher)
Faltering growth/body composition: RCT: High vs. low protein assessed with: Length in infancy (cm)	617 (2 RCTs)	⊕○○○ Very low ^{c,i}	-	The mean faltering growth/body composition: RCT: High vs. low protein was 69.31 cm	MD 0.18 higher (0.61 lower to 0.97 higher)
Faltering growth/body composition: RCT: High vs. low protein assessed with: Length/height during toddler period (cm)	1017 (3 RCTs)	⊕○○○ Very low ^{c,i}	-	The mean faltering growth/body composition: RCT: High vs. low protein was 79.73 cm	MD 0.22 higher (0.35 lower to 0.79 higher)
Faltering growth/body composition: RCT: Protein source from human milk fortification only assessed with: Head circumference (mm/week)	174 (3 RCTs)	⊕⊕○○ Low ^{h,i}	-	The mean faltering growth/body composition: RCT: Protein source from human milk fortification only was 0.93 mm/week SD	SMD 0.06 SD higher (0.46 lower to 0.59 higher)
Faltering growth/body composition: RCT assessed with: Head growth (cm/week)	68 (4 RCTs)	⊕○○○ Very low ^{a,c,g}	-	The mean faltering growth/body composition: RCT was 0.79 cm/week	MD 0.06 higher (0.01 higher to 0.12 higher)
Faltering growth/body composition: RCT: High vs. moderate protein assessed with: Head circumference gain (cm/week)	549 (5 RCTs)	⊕⊕⊕⊕ High	-	The mean faltering growth/body composition: RCT: High vs. moderate protein was 0.84 cm/week	MD 0 (0.01 lower to 0.02 higher)
Faltering growth/body composition: RCT: Moderate vs. low protein assessed with: Head circumference growth (cm/week)	217 (3 RCTs)	⊕○○○ Very low ^{c,i}	-	The mean faltering growth/body composition: RCT: Moderate vs. low protein was 0.76 cm/week	MD 0.13 higher (0 to 0.26 higher)
Necrotising enterocolitis: RCT	76 (1 RCT)	⊕○○○ Very low ^{a,b,d}	RR 1.11 (0.07 to 17.12)	Study population	
				25 per 1,000	3 more per 1,000 (23 fewer to 403 more)
Necrotising enterocolitis: RCT: High vs. moderate protein	326 (4 RCTs)	⊕⊕⊕○ Moderate ^h	RR 0.78 (0.27 to 2.27)	Study population	
				41 per 1,000	9 fewer per 1,000 (30 fewer to 52 more)
Necrotising enterocolitis: RCT: Moderate vs. low protein	112 (1 RCT)	⊕○○○ Very low ^{a,d,i}	RR 0.96 (0.06 to 15.05)	Study population	
				18 per 1,000	1 fewer per 1,000

					(17 fewer to 255 more)
Adverse effects (gastrointestinal complications) - not measured	-	-	-	-	-
Time to full enteral feeds: RCT assessed with: Feeding intolerance	17 (1 RCT)	⊕○○○ Very low ^{a,j}	RR 2.70 (0.13 to 58.24)	Study population	
				0 per 1,000	0 fewer per 1,000 (0 fewer to 0 fewer)
Time to full enteral feeds RCT: High vs. moderate protein assessed with: Days	162 (2 RCTs)	⊕⊕⊕○ Moderate ^h	-	The mean time to full enteral feeds RCT: High vs. moderate protein was 12.5 days	MD 0.26 higher (1.78 lower to 2.31 higher)
Duration of initial hospital stay: RCT assessed with: Days	20 (1 RCT)	⊕○○○ Very low ^{b,c,d}	-	The mean duration of initial hospital stay: RCT was 48.7 days	MD 18.5 higher (4.39 higher to 32.61 higher)
Duration of initial hospital stay: RCT: High vs. moderate protein assessed with: Days	92 (1 RCT)	⊕⊕○○ Low ^{b,d}	-	The mean duration of initial hospital stay: RCT: High vs. moderate protein was 73 days	MD 4 higher (3.71 lower to 11.71 higher)
Duration of initial hospital stay: RCT: Moderate vs. low protein assessed with: Days	41 (1 RCT)	⊕⊕○○ Low ^{d,h}	-	The mean duration of initial hospital stay: RCT: Moderate vs. low protein was 17 days	MD 3 lower (7.13 lower to 1.13 higher)
Sepsis: proven or suspected: RCT: Moderate vs. low protein	112 (1 RCT)	⊕○○○ Very low ^{b,d}	RR 0.48 (0.05 to 5.17)	Study population	
				36 per 1,000	19 fewer per 1,000 (35 fewer to 152 more)
Sepsis: proven or suspected: RCT: High vs. moderate protein	326 (4 RCTs)	⊕⊕⊕○ Moderate ^h	RR 1.18 (0.51 to 2.73)	Study population	
				53 per 1,000	9 more per 1,000 (26 fewer to 91 more)
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-

a. Downgraded one level for imprecision due to low event numbers or participant numbers

b. Downgraded two levels for very wide confidence intervals crossing the line of no effect suggesting imprecision with benefit and harm

a)

a. Downgraded one level for risk of bias concerns

b. Downgraded one level for indirectness as only reported in a single study

c. Downgraded one level for inconsistency following visual inspection of forest plot

- d. Downgraded one level for imprecision due to wide confidence intervals
- e. Downgraded one level for inconsistency as I² = 60-80%
- f. Downgraded one level for imprecision due to confidence intervals crossing the line of no effect
- g. Downgraded two levels for inconsistency as I² >80%
- h. Downgraded three levels for extremely wide confidence intervals crossing the line of no effect indicating significant benefit and harm

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Studies reporting the optimal amount of protein supplementation from or in addition to breastmilk fortifier or preterm formula Neurodevelopmental impairment: RCT: No significant effect on survival without neurodisability at or beyond 12 months' corrected age for high vs. low protein (56 fewer per 1,000; 139 fewer to 46 more) [Critical] Necrotising enterocolitis: RCT: No significant increase in NEC with protein supplementation (3 more per 1,000; 23 fewer to 403 more) [Critical]. Full enteral feeds: RCT: No effect on time to full enteral feeds (days) between protein and no protein supplementation (0 fewer per 1,000; 0 fewer to 0 fewer) [Important]. Full enteral feeds: RCT: High versus moderate protein supplementation: No significant effect on time to full enteral feeds (days) (MD 0.26 days higher; 1.78 lower to 2.31 higher) [Important]. Duration of initial hospital stay: RCT: Very large effect for increased duration of hospital stay for protein supplementation (MD 18.5 days higher; 4.39 higher to 32.61 higher) [Important]. Duration of initial hospital stay: RCT: High vs. moderate protein supplementation: No significant increase in duration of hospital stay for high protein supplementation (MD 4 days higher; 3.71 lower to 11.71 higher) [Important]. Sepsis: RCT: High versus moderate protein supplementation: No significant increase in risk of sepsis with high protein supplementation (9 more per 1,000; 26 fewer to 91 more) [Important] Undesirable effects for Māori No additional evidence available	Effects described are on weight gain, (not necessarily on avoiding faltering growth). The disproportionate effect on weight gain but much less effect on length or head circumference gain may be undesirable.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low	High to very low evidence overall	

○ Low ○ Moderate ○ High ○ No included studies	Certainty of evidence for Māori No additional evidence available.	
Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT: High vs. moderate protein	CRITICAL	⊕⊕○○ Low
Mortality: RCT: Moderate vs. low protein	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: High vs. low protein assessed with: Survival without neurodisability at or beyond 12 months' corrected age [measure not specified in review]	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT: High vs. low protein assessed with: Cerebral palsy during toddler period [measure not specified in review]	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT: Protein source from breastmilk fortification only assessed with: Weight gain (g/kg/day)	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Weight gain (g/kg/day)	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT: High vs. moderate protein assessed with: Weight gain (g/kg/day)	CRITICAL	⊕⊕⊕⊕ High
Faltering growth/body composition: RCT: Moderate vs. low protein assessed with: Weight gain (g/kg/day)	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT: Protein source from breastmilk fortification only assessed with: Length gain (cm/week)	CRITICAL	⊕⊕⊕⊕ High
Faltering growth/body composition: RCT assessed with: Length gain (cm/week)	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT: High vs. moderate protein assessed with: Length gain (cm/week)	CRITICAL	⊕⊕⊕⊕ High
Faltering growth/body composition: RCT: Moderate vs. low protein assessed with: Length gain (cm/week)	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT: High vs. low protein assessed with: Length in infancy (cm)	CRITICAL	⊕○○○ Very low

Faltering growth/body composition: RCT: High vs. low protein assessed with: Length/height during toddler period (cm)	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT: Protein source from breastmilk fortification only assessed with: Head circumference (cm/week)	CRITICAL	⊕⊕○○ Low
Faltering growth/body composition: RCT assessed with: Head growth (cm/week)	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT: High vs. moderate protein assessed with: Head circumference gain (cm/week)	CRITICAL	⊕⊕⊕⊕ High
Faltering growth/body composition: RCT: Moderate vs. low protein assessed with: Head circumference growth (cm/week)	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis: RCT	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis: RCT: High vs. moderate protein	CRITICAL	⊕⊕⊕○ Moderate
Necrotising enterocolitis: RCT: Moderate vs. low protein	CRITICAL	⊕○○○ Very low
Adverse effects (gastrointestinal complications) - not measured	IMPORTANT	-
Time to full enteral feeds: RCT assessed with: Feeding intolerance	IMPORTANT	⊕○○○ Very low
Time to full enteral feeds RCT: High vs. moderate protein assessed with: Days	IMPORTANT	⊕⊕⊕○ Moderate
Duration of initial hospital stay: RCT assessed with: Days	IMPORTANT	⊕○○○ Very low
Duration of initial hospital stay: RCT: High vs. moderate protein assessed with: Days	IMPORTANT	⊕⊕○○ Low ^{b,e}
Duration of initial hospital stay: RCT: Moderate vs. low protein assessed with: Days	IMPORTANT	⊕⊕○○ Low
Sepsis: proven or suspected: RCT: Moderate vs. low protein	IMPORTANT	⊕○○○ Very low
Sepsis: proven or suspected: RCT: High vs. moderate protein	IMPORTANT	⊕⊕⊕○ Moderate

Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Retinopathy of prematurity - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability Values for Māori No additional evidence available.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention	Studies reporting the optimal amount of protein supplementation from or in addition to breastmilk fortifier only Higher protein compared with lower protein - high certainty evidence Increase in length gain and increase in length gain when adjusted for energy intake Higher protein compared with lower protein - low certainty evidence Uncertain effect on head circumference Higher protein compared with lower protein - very low certainty evidence	Meta-regression [4] suggested most preterm infants may require 4.0–4.5 g/kg/day to achieve <i>in utero</i> growth rates, rather than 3.5–4.0 g/kg/day. There is a need to maintain appropriate energy: protein ratios.

○ Favours the intervention ○ Varies ○ Don't know	Increase in weight gain when adjusted for energy intake Studies reporting the optimal amount of protein supplementation from or in addition to breastmilk fortifier or preterm formula Protein supplementation compared with no protein supplementation- low certainty evidence Possible increase in <i>no faltering growth</i>/body composition (weight gain) Protein supplementation compared with no protein supplementation- very low certainty evidence Possible increase in <i>no faltering growth</i>/body composition (length gain; head circumference) Increase in duration of initial hospital stay Uncertain effect on necrotising enterocolitis No effect on time to full enteral feeds High protein compared with moderate protein supplementation- high certainty evidence Possible increase in <i>no faltering growth</i>/body composition (weight gain; length gain) No effect on faltering growth/body composition (head circumference) High protein compared with moderate protein supplementation- moderate certainty evidence Uncertain effect on necrotising enterocolitis, time to full enteral feeds, sepsis High protein compared with moderate protein supplementation- low certainty evidence No effect on mortality Increase in duration of initial hospital stay High protein compared with low protein supplementation - very low certainty evidence Uncertain effect on neurodevelopmental impairment, faltering growth/body composition (length) Moderate protein compared with low protein supplementation- low certainty evidence Possible increase in <i>no faltering growth</i>/body composition (length gain) Uncertain effect on duration of initial hospital stay Moderate protein compared with low protein supplementation- very low certainty evidence Uncertain effect on mortality, sepsis Possible increase in <i>no faltering growth</i>/body composition (weight gain) No effect on faltering growth/body composition (head circumference) Uncertain effect on necrotising enterocolitis Balance of effects for Māori No additional evidence available.	
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Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The cost of enteral protein supplementation is small (<\$0.20 per day) Requires additional dietetic resources which may limit its acceptability in some units Resources required for Māori No additional evidence available.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Costs are certain. Certainty of evidence of required costs for Māori No additional evidence available.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	There are no studies that assess the specific cost-effectiveness of additional enteral protein supplementation, particularly in the context of preterm infants. Cost effectiveness for Māori No additional evidence available.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Pēpi Māori are disproportionately affected by preterm birth and associated complications due to colonisation and ongoing inequities in health care. Without additional protein, breastmilk alone may not meet their nutritional needs, placing them at risk of poor growth and developmental delays. When protein supplementation is offered inconsistently or delayed due to systemic bias or resource gaps, these outcomes may worsen. Ensuring that whānau Māori have equitable access to supplementation, along with culturally safe information and support, is essential. This can help reduce health disparities and promote better lifelong outcomes for pēpi Māori and their whānau. Equity for Pacific families Pacific infants are also more likely to be born preterm and may encounter limited or inconsistent access to specialised nutrition support such as protein supplementation. Pacific families often value collective decision-making and may have unique feeding preferences but may not receive early or culturally responsive education about supplementation. Without adequate support, Pacific infants risk missing out on essential nutrients for brain and body development. Equity in this context means ensuring timely access to protein fortification and involving Pacific parents in feeding decisions through respectful, tailored communication that aligns with their cultural values. Equity for underrepresented groups Families from rural areas, migrant backgrounds or lower socioeconomic communities may face additional barriers to accessing consistent enteral protein supplementation. These include fewer neonatal resources, limited transport to tertiary hospitals and reduced access to culturally and linguistically appropriate support. Parents may not fully understand the purpose or benefits of supplementation, especially if they receive inconsistent messages from clinical staff. To ensure equity, guidelines must be applied consistently and education delivered in accessible ways. Standardising care while addressing structural barriers can help ensure all preterm infants receive the nutritional support needed for healthy development, regardless of where or to whom they are born.	

Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No	Already in widespread use.	

○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know	Requires additional dietetic resources which may limit its acceptability in some units. Some parents decline supplementation, due the protein source being cow's milk protein. Acceptability for Māori No additional evidence available.	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know	Already in widespread use. Feasibility for Māori No additional evidence available.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know

	JUDGEMENT						
REQUIRED							
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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References

1. Amissah, E.A.; Brown, J.; Harding, J.E. Protein supplementation of human milk for promoting growth in preterm infants. *Cochrane Database Syst. Rev.* **2020**, *9*, Cd000433, doi:10.1002/14651858.CD000433.pub3.
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EtD 36. Should routine glucose polymer supplementation vs. no supplementation be used in preterm infants receiving enteral feeds?

POPULATION:	Preterm infants receiving enteral feeds
INTERVENTION:	Routine glucose polymer supplementation
COMPARISON:	No glucose polymer supplementation
MAIN OUTCOMES:	Critical outcomes - Faltering growth/body composition - Necrotising enterocolitis - Adverse effects (long term cardiometabolic health) - Time to full enteral feeds Important but not critical - Neurodevelopmental impairment - Duration of initial hospital stay - Fully breastfed or breastmilk feeding at hospital discharge - Sepsis: proven or suspected - Mortality - Bronchopulmonary dysplasia - Retinopathy of prematurity - Anaemia of prematurity - Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making - Time to full sucking feeds - Growth/weight at day 30 - Feeding intolerance - Necrotising enterocolitis
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	Adequate nutrition is crucial for preterm infants to support growth, neurodevelopment, and overall clinical outcomes. Carbohydrate is an important energy source, contributing significantly to energy intake and supporting metabolic processes. In preterm infants, achieving sufficient energy intake for growth is often challenging due to their immature gastrointestinal systems and limited feeding tolerance. Carbohydrate supplementation in enteral feeds enhances energy provision and promotes weight gain. However, the balance between meeting energy needs and avoiding potential complications is critical. Excessive carbohydrate intake can lead to hyperglycaemia, increased insulin demand, and fat deposition, while inadequate carbohydrate and energy intake may impair growth and neurodevelopment. The impact of additional carbohydrate supplementation on clinical outcomes, including rates of necrotising enterocolitis and gastrointestinal tolerance, remains poorly understood. Potential benefits of supplementation include improved weight gain and growth velocity, while risks may include feeding intolerance, hyperglycaemia or osmotic diarrhoea.

CONFLICT OF INTERESTS:	Evidence regarding the long-term effects of carbohydrate supplementation on neurodevelopment and metabolic health in preterm infants is limited. Providing the optimal quantity of carbohydrates to supplement enteral feeds, ensuring that energy requirements are met without increasing the risk of adverse clinical and long-term metabolic outcomes is crucial.
	The following 2018 Cochrane systematic review (Amissah <i>et al</i>) co-author wrote this Evidence to Decision document: Julie Brown

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	No randomised controlled trial evidence was found to answer this clinical question. A 2018 Cochrane systematic review on this topic found no studies eligible for inclusion except an unblinded, quasi-RCT assessing the effects of carbohydrate in the form of a prebiotic added to breastmilk in (n=75) preterm infants. This search was updated by our team. One study [1] was found on glucose polymers added to the feeds of 14 VLBW infants (<1,500 g) who were supplemented with a glucose polymer (6 g/kg body weight/day). Seven-day periods of supplementation were alternated with seven-day periods of unsupplemented feeding. Adding the glucose polymer significantly increased the rate of weight gain in these infants from 105 g/week to 140 g/week; length and head circumference growth rates were not affected.	Despite a lack of evidence, carbohydrate in the form of glucose polymer powder has been added to feeds for preterm infants to improve their growth. Glucose polymer powder is a fine white powder derived from the controlled hydrolysis of corn starch. It is tasteless, low in electrolytes and low in osmolality, which lessens the potential for osmotic diarrhoea. It is generally well tolerated in small amounts, e.g. 3 g/100 mL. Glucose polymer powder contains 3.8 kcal per g.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	The Raffles <i>et al</i> study indicates that the addition of carbohydrate to feeds is likely to increase weight, but not length and head circumference growth, which may not be beneficial for long-term health.	Glucose polymers provide high energy densities without increasing the osmotic load and unlike lactose, they are better absorbed, as they do not require lactase for digestion but are dependent on glucoamylase, which is available in sufficient quantities. However, in preterm infants, it is recommended that lactose should account for 40% to 100% of the carbohydrate intake, as it is needed to aid mineral absorption and to foster prebiotic and lactase activities.
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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Very low	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability		

Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● Don't know	We found insufficient evidence on the short- and long-term effects of glucose polymer supplementation of breastmilk in preterm infants.	
Resources required		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The cost of glucose polymer powder is minimal.	
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ● High	Costs are certain.	

○ No included studies		
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No studies found.	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ● Don't know	Equity for Māori Pēpi Māori are more likely to experience growth restriction and suboptimal health outcomes due to systemic inequities in neonatal care. If carbohydrate supplementation is offered inconsistently or without a clear explanation, pēpi Māori may miss out on its potential benefits for growth and energy balance. Whānau Māori may not be included in discussions about the risks and benefits of supplementation, particularly where care is not culturally safe or communication is unclear. Equity requires standardised nutritional practices, equitable access to supplementation and respectful engagement with whānau Māori to ensure pēpi Māori receive the nutrition support needed for healthy development. Equity for Pacific families Pacific families may not receive clear explanations about carbohydrate supplementation or how it supports growth and energy needs in preterm infants. Without culturally appropriate information, its importance may be misunderstood. Equity requires accessible, respectful communication and	

	consistent access to supplementation to support optimal outcomes for Pacific infants. Equity for underrepresented groups Underrepresented families may face barriers in accessing carbohydrate supplements or understanding their purpose, particularly where language and resource gaps exist. Equity demands standardised nutritional practices and inclusive education that ensures all families are informed and empowered to support their infants' nutritional needs.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☐ Probably yes ☐ Yes ☒ Varies ☐ Don't know	May not be acceptable to all staff and parents.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☐ Varies ☐ Don't know	Has been in practice for many years.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE	Trivial	Small	Moderate	Large		Varies	Don't know

	JUDGEMENT						
EFFECTS							
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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References

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EtD 37. Should routine fat supplementation vs. no supplementation be used in preterm infants receiving enteral feeds?

POPULATION:	Preterm infants receiving enteral feeds
INTERVENTION:	Routine fat supplementation
COMPARISON:	No fat supplementation
MAIN OUTCOMES:	Critical outcomes Faltering growth/body composition Necrotising enterocolitis Adverse effects (long term cardiometabolic health Time to full enteral feeds Important but not critical Neurodevelopmental impairment Duration of initial hospital stay Fully breastfed or breastmilk feeding at hospital discharge Sepsis: proven or suspected Mortality Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds Growth/weight at day 30 Feeding intolerance Necrotising enterocolitis
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	Fat is a critical macronutrient for preterm infants, providing energy and essential fatty acids that are vital for growth, eye development and neurodevelopment. During fetal life, fat deposition accelerates in the third trimester, a process that is disrupted by preterm birth. As a result, preterm infants have limited fat and energy reserves and suboptimal levels of the essential fatty acids. Additional fat supplementation in enteral feeds is sometimes used to meet the high energy demands of preterm infants to promote weight gain and support neurodevelopmental outcomes. However, the benefits of fat supplementation must be balanced with potential risks, including feeding intolerance, gastrointestinal complications and altered body composition. Observational studies suggest associations between higher fat intake and improved growth outcomes, but excessive fat intake can reduce feeding tolerance or lead to fat malabsorption. Additionally, the type of fat used (e.g. medium-chain triglycerides vs. long chain fatty acids) may influence

	outcomes, with different formulations offering varying degrees of absorption and metabolic effects. It is important to determine whether the addition of fat supplements to breastmilk fed to preterm infants compared with no additional fat improves growth, brain development, body fat or obesity, without significant side effects especially for long term cardiometabolic health. This question relates to fat supplementation that is given in addition to, or instead of commercial breastmilk fortifier, to increase energy intake.
CONFLICT OF INTERESTS:	The following Amissah <i>et al</i> systematic review co-author wrote this Evidence to Decision document: Julie Brown

Assessment

Desirable Effects					
How substantial are the desirable anticipated effects?					
JUDGEMENT	RESEARCH EVIDENCE			ADDITIONAL CONSIDERATIONS	
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence from a systematic review [1] includes one small trial (n=14) and one RCT [2]. No faltering growth/body composition: RCT: No significant increase in weight at the end of the study (MD 40 g higher; 258.62 lower to 338.62 higher) [Critical]. No faltering growth/body composition: RCT: No significant effect on weight gain (MD 0.6 g /kg/day higher; 2.36 lower to 3.56 higher); length gain (MD 0.10 cm/week higher; 0.08 lower to 0.28 higher); head circumference (MD 0.15 cm/week higher; 0.07 lower to 0.37 higher) [Critical]. Time to full enteral feeds: RCT: No effect on feeding intolerance (unable to calculate absolute effect due to minimal or no events). Less time to achieve full enteral feeding in fat supplement group 12.12±6.26 days vs. control group 20.18±13.54 days ($p<0.001$) [Important]. Duration of hospital stay: RCT: Shorter duration of hospital stay in fat supplement group 52.00±21.32 vs. control (n=48) 73.22±22.79 days ($p<0.001$). [Important] Bronchopulmonary dysplasia: RCT: Reduced number of infants with bronchopulmonary dysplasia with fat supplementation 5/48 (10.4%) vs. Control 16/48 (33.3%) ($P=0.007$). [Important] Retinopathy of prematurity: RCT: No significant difference in retinopathy of prematurity with fat supplementation 23/48 (47.9%) vs. Control 17/48 (35.4 %). [Important] Desirable effects for Māori No available evidence			We do not envisage that further trials of fat supplementation will be conducted, as energy is currently added to expressed breastmilk as a component of multi-nutrient fortification. Population information for included evidence The Swedish trial included in the systematic review [1] examined preterm infants <32 gestational weeks and of birthweight <1,500 grams. Turkey: RCT [2]: Very low birthweight infants. 0.5 mL of olive oil /30 mL milk was added to each feed for infants in the intervention group.	
Outcomes		№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)
					Risk with no supplementation Risk difference with routine fat supplementation

Faltering growth/body composition: RCT assessed with: Weight gain (g/kg/day)	14 (1 RCT)	⊕○○○ Very low ^{a,b,c}	-	The mean faltering growth/body composition: RCT was 15.3 g/kg/day	MD 0.6 higher (2.36 lower to 3.56 higher)
Faltering growth/body composition: RCT assessed with: Weight at end of study (g)	14 (1 RCT)	⊕○○○ Very low ^{a,b,c}	-	The mean faltering growth/body composition: RCT was 2070 g	MD 40 higher (258.62 lower to 338.62 higher)
Faltering growth/body composition: RCT assessed with: Weight at discharge (g)	96 (1 RCT)	⊕○○○ Very low ^{a,b,e}	-	Weight at discharge intervention group (n=48) 1924.16±124.00 g vs. control group (n=48) 1949.68±163.16 g (Not significant)	
Faltering growth/body composition: RCT assessed with: Length (cm/week)	14 (1 RCT)	⊕○○○ Very low ^{a,b,c}	-	The mean faltering growth/body composition: RCT was 0.83 cm/week	MD 0.1 higher (0.08 lower to 0.28 higher)
Faltering growth/body composition: RCT assessed with: Head circumference (cm/week)	14 (1 RCT)	⊕○○○ Very low ^{a,b,c}	-	The mean faltering growth/body composition: RCT was 0.94 cm/week	MD 0.15 higher (0.07 lower to 0.37 higher)
Necrotising enterocolitis - not measured	-	-	-	-	-
Adverse effects (long term cardiometabolic health) - not reported	-	-	-	-	-
Time to full enteral feeds: RCT assessed with: Days	96 (1 RCT)	⊕○○○ Very low ^{a,b,e}	-	Transition time to full enteral nutrition (days) Intervention group (n=48) 12.12±6.26 days vs. control group (n=48) 20.18±13.54 days (P <0.001)	
Time to full enteral feeds: RCT assessed with: Feeding intolerance	16 (1 RCT)	⊕○○○ Very low ^{a,b,c}	RR 3.00 (0.14 to 64.26)	Study population	
				0 per 1,000	0 fewer per 1,000 (0 fewer to 0 fewer)
Neurodevelopmental impairment - not reported	-	-	-	-	-
Duration of initial hospital stay assessed with: Days	96 (1 RCT)	⊕○○○ Very low ^{a,b,e}	-	Length of hospital stay (days) Intervention (n=48) 52.00±21.32 vs. control (n=48) 73.22±22.79 days (p<0.001)	
Fully breastfed or breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Sepsis: proven or suspected	96 (1 RCT)	⊕○○○ Very low ^{a,b,e}	-	Intervention group 8/48 (16.7%) Control group 23/48 (47.9%) (P<0.001)	
Mortality - not measured	-	-	-	-	-
Bronchopulmonary dysplasia / chronic lung disease	96 (1 RCT)	⊕○○○ Very low ^{a,b,e}	-	Intervention 5/48 (10.4%) Control 16/48 (33.3%) P=0.007	
Retinopathy of prematurity	96 (1 RCT)	⊕○○○ Very low ^{a,b,e}	-	Intervention 23/48 (47.9%) Control 17/48 (35.4 %)	

				Not significant	
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-

- a. Downgraded one level risk of bias due to unclear reporting
- b. Downgraded one level for indirectness as evidence is based on a single study
- c. Downgraded one level for imprecision as there are wide confidence intervals that cross the line of no effect.
- d. Downgraded one level for imprecision due to small sample size
- e. Downgraded one level for indirectness as the population may not be generalisable as only included VLBW infants
- f. Downgraded one level for imprecision with wide variation around the mean

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	The single included study in the systematic review did not report on any of the other outcomes associated with this clinical question. Undesirable effects for Māori No available evidence	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	The evidence is based on a single, small study of 14 infants in a Swedish study published in 1989. Very low certainty evidence overall. Certainty of evidence for Māori No available evidence	

Outcomes	Importance	Certainty of the evidence (GRADE)
Faltering growth/body composition: RCT assessed with: Weight gain (g/kg/day)	CRITICAL	⊕○○○ Very low

Faltering growth/body composition: RCT assessed with: Weight at end of study (g)	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Length (cm/week)	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Head circumference (cm/week)	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis - not measured	CRITICAL	-
Adverse effects (long term cardiometabolic health) - not reported	CRITICAL	-
Time to full enteral feeds: RCT assessed with: Feeding intolerance	IMPORTANT	⊕○○○ Very low
Neurodevelopmental impairment - not reported	IMPORTANT	-
Duration of initial hospital stay assessed with: Days	IMPORTANT	⊕○○○ Very low
Fully breastfed or breastmilk feeding at hospital discharge - not measured	IMPORTANT	-
Sepsis: proven or suspected	IMPORTANT	⊕○○○ Very low
Mortality - not measured	IMPORTANT	-
Bronchopulmonary dysplasia / chronic lung disease	IMPORTANT	⊕○○○ Very low
Retinopathy of prematurity	IMPORTANT	⊕○○○ Very low
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ Important uncertainty or variability ☐ Possibly important	Unlikely to be uncertainty or variability in the value placed on the main outcomes.	

uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	Values for Māori No available evidence	
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Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Fat supplementation compared with unsupplemented breastmilk - very low certainty of evidence Reduction in time to full enteral feeds, duration of initial hospital stay, bronchopulmonary dysplasia Uncertain effect on feeding intolerance, weight, length and head circumference, retinopathy of prematurity Balance of effects for Māori No additional data	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Fat supplementation dose 3.6 to 6.8 mL/kg/day Calogen 4 to 7 mL/kg/day Liquigen Dose per baby per day 5 to 10 mL Calogen (long-chain triglyceride emulsion) 5 to 10 mL Liquigen (medium chain triglyceride emulsion) Cost per day Calogen \$0.40 to \$0.80 Liquigen \$2.15 to \$4.30 Cost per admission per infant (up to 100 days) Calogen \$40 to 80 Liquigen \$215 to \$430	Calogen is suitable for most infants (small cost).

	Resources required for Māori Similar - no additional data	
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ● High ○ No included studies	The cost of fat supplements in Aotearoa New Zealand is known. Certainty of evidence of required resources for Māori No additional data	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	There are no studies that assess the specific cost-effectiveness of fat supplementation compared with unsupplemented breastmilk, particularly in the context of preterm infants. Cost effectiveness for Māori No additional evidence available	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased	Equity for Māori Pēpi Māori, often born preterm or growth-restricted, may not consistently receive adequate nutrition due to variable hospital practices and limited regional resources. Culturally unsafe care and inadequate communication can prevent whānau Māori	

○ Increased ○ Varies ○ Don't know	from fully engaging in nutrition decisions. Equity requires national guidelines and culturally responsive care to ensure timely, appropriate supplementation if needed. Equity for Pacific families Pacific infants may experience inadequate nutrition due to systemic barriers, fragmented services and inconsistent clinician communication. Families may not be adequately supported to understand or advocate for nutritional needs. Equity demands standardised nutrition practices and culturally meaningful engagement to support optimal growth and reduce the length of hospital stay. Equity for underrepresented groups Infants from migrant, rural and lower-income families may experience barriers to adequate nutrition due to location, transport issues or lack of tailored health communication. These barriers can widen developmental disparities in preterm infants. Ensuring equitable nutrition requires clear national policies, accessible education and proactive outreach to support informed care across diverse communities.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Fat supplementation is easy to administer and is likely to be acceptable to most stakeholders. Acceptability for Māori No available evidence	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies	Fat supplementation is feasible in the Aotearoa New Zealand setting. Feasibility for Māori No available evidence	

o Don't know

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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References

1. Amissah, E.A.; Brown, J.; Harding, J.E. Fat supplementation of human milk for promoting growth in preterm infants. *Cochrane Database Syst. Rev.* **2020**, *8*, Cd000341, doi:10.1002/14651858.CD000341.pub3.

2. Aytemiz, S.; Sarı, M.; Yurttutan, S.; Çıkar, Y.; Topal, S.; Çaka, S.Y. Effects of enteral olive oil supplement on weight gain, length of hospital stay, and the development of some complications in preterm infants: A randomized controlled trial. *J Pediatr Res* **2024**, *11*, 95-102, doi:10.4274/jpr.galenos.2024.36937.

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EtD 39. In preterm infants who are enterally fed does routine zinc supplementation and monitoring compared with routine no supplementation and zinc monitoring reduce the incidence of zinc deficiency faltering growth, reduced immune function and impaired neurodevelopment?

POPULATION:	Preterm infants who are enterally fed
INTERVENTION:	Routine zinc supplementation or monitoring
COMPARISON:	no routine zinc supplementation or monitoring
MAIN OUTCOMES:	Critical outcomes Mortality Neurodevelopmental impairment Faltering growth/body composition – especially length growth Sepsis: proven or suspected Retinopathy of prematurity Important but not critical Adverse effects Time to full enteral feeds Duration of initial hospital stay Fully breastfed or breastmilk feeding at hospital discharge Bronchopulmonary dysplasia Necrotising enterocolitis Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	Zinc is a critical trace element for numerous physiological functions, including cell division, protein synthesis, and immune function. It plays a vital role in growth and neurodevelopment, making it particularly important for preterm infants, who have high nutritional demands and low body stores at birth. Zinc deficiency in preterm infants is associated with higher mortality, faltering growth, compromised immune responses, impaired neurodevelopment and skin rashes. Routine zinc supplementation for enterally fed preterm infants may help prevent deficiency by compensating for their limited stores. Additionally, zinc has immunomodulatory properties that could reduce the risk of infections, a common concern in preterm infants. If breastmilk fed, the preterm infant's mother's zinc status may also be important. Vegan and vegetarian mothers are at high risk of zinc deficiency, one of the causes of preterm birth. Zinc monitoring is one way to avoid zinc overload which may lead to zinc toxicity and adverse effects such as impaired copper absorption. Current practices for zinc monitoring and supplementation vary across neonatal units, reflecting uncertainty about the optimal approach. Zinc is being considered separately for this guideline, but in combination European

CONFLICT OF INTERESTS:	Consensus (ESPGHAN 2022) recommended nutrient intakes because Aotearoa New Zealand soil is zinc deficient. Preterm infants at higher risk of symptomatic zinc deficiency are those with faltering growth, and infants who have an enterostomy after gastrointestinal surgery. This question relates to zinc supplementation that is given in addition to, or instead of commercial breastmilk fortifier, to increase zinc intake.
	None

Assessment

Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	ESPGHAN 2022 recommended enteral nutrient intake for zinc is 2.0-3.0 mg/kg/day ESPGHAN 2022 also have a good practice point: Measurement of serum zinc should be considered in preterm infants with poor growth and low alkaline phosphatase level, especially if they have excessive GI fluid losses [1](2). Evidence is based on 3 systematic reviews of randomised/quasi-randomised trials [2-4]. Mortality: RCT: Large decrease in mortality for zinc supplementation (76 fewer per 1,000; 116 fewer to 5 fewer), the effect was greater in studies provided >3 mg/kg/day of zinc. No significant effect on all-cause mortality (8 fewer per 1,000; 15 fewer to 5 more) [Critical]. Neurodevelopmental impairment: RCT: Higher Bayley Scale of Infant Development version 1 (BSID I) mental development scores for zinc supplementation (MD 4.18 points higher; 6.51 higher to 1.85 higher); Moderate increase for BSID psychomotor development scores (MD 5.75 points higher; 4.83 higher to 16.33 higher). [Critical]. No significant effect for Griffith total neurodevelopmental score (MD 6.41 points higher; 2.35 lower to 15.17 higher) and large increase in Griffith motor developmental score (MD 9.54 points higher; 6.63 higher to 12.44 higher) [Critical]. No faltering growth/body composition: RCT: Large increase in weight gain (MD 378.6 g higher; 275.26 higher to 481.88 higher); (standardised mean difference (SMD) 0.46 standard deviation (SD) higher; 0.28 higher to 0.64 higher), (MD 0.5 z score points higher; 0.23 higher to 0.76 higher). [Critical]. The effect of zinc supplementation on weight was significantly higher in studies provided >3 mg/kg per day of zinc. Large increase in length (MD 2.92 cm higher; 1.53 higher to 4.31 higher), (SMD 0.75 SD higher; 0.36 higher to 1.14 higher), (MD 1.12 z score points higher; 0.63 higher to 1.61 higher). [Critical] No significant increase in head circumference (SMD 0.21 SD higher; 0.02 lower to 0.44 higher), moderate increase in head circumference (MD 0.56 cm higher; 0.23 higher to 0.9 higher) [Critical] Retinopathy of prematurity: RCT: Zinc supplementation did not significantly decrease the risk of retinopathy of prematurity (27 fewer per 1,000; 31 fewer to 53 more) [Critical].	There is some overlap in the included trials in the 3 included systematic reviews. Population information for included evidence Staub <i>et al</i> [3] included 5 RCTs (481 infants). Four included studies used doses of zinc <3 mg/kg/day. Supplementation was for more than four weeks in all studies. Sinha <i>et al</i> [4] included 14 trials (9940 infants) of low birthweight or preterm infants. 12 RCTs, 1 cluster randomised and 1 quasi-randomised. This review may include indirect evidence as term LBW infants were included. Two trials provided <3 mg per day, 10 trials provided 3 to 5 mg per day, and 4 trials provided >5 mg per day of elemental zinc to the infants. The time of start of intervention ranged from birth to 5.2 weeks and the median (interquartile range [IQR]) duration of supplementation was 140.7 days (98 to 182.7 days). Alshaikh [2] included 8 RCTs (742 infants) in preterm

	Adverse effects: RCT: Large reduction in diarrhoea with zinc supplementation (26 fewer per 1000; 43 fewer to 4 fewer) [Important]. Bronchopulmonary dysplasia: RCT: Zinc supplementation did not significantly decrease the risk of bronchopulmonary dysplasia (53 fewer per 1,000; 108 fewer to 62 more) [Important] Necrotising enterocolitis (NEC): RCT: Zinc supplementation did not significantly decrease the risk of NEC (58 fewer per 1,000; 63 fewer to 21 more) [Important]. Benefits for Māori No additional evidence	infants. Three of the eight studies included only very low birthweight (VLBW) infants while the remainder included mostly late-preterm infants. Five studies included preterm small-for-gestational-age infants in their studies while the remainder excluded those infants. Age of starting zinc supplementation varied between the studies from 1 day to 1 month of age. In 6 of the trials, infants in the zinc group received ~2–3 mg/kg/day. In two trials the dose was 10–11 mg/day. Serum zinc levels at end of intervention (<i>LabPlus Reference serum zinc range 9–17 µmol/L</i>) Staub (2021): significantly higher blood zinc level at the end of the intervention in the intervention group (MD 3.6 µmol/L higher, 95% CI 2.7 to 4.5; 3 RCTs, n=189 infants) Alshaikh (2022): significantly higher blood zinc level at 3 months corrected age (WMD 3.6 µmol/L, 95% CI 3.1 to 4.1, 4 trials, n = 276 infants). Very low birthweight infants (<1,500 g) - Two trials included VLBW infants and the pooled effects were consistent with the overall meta-analysis for mortality, bacterial sepsis, weight gain, linear growth and head growth. The data from the small number of studies and events as well as large confidence intervals may be insufficient to determine an effect in the subgroups. An additional RCT from Turkey was identified [5] that compared supplementation of 3 mg/day zinc with an additional 9 mg/day (total 12 mg/day) in 195 very low birthweight infants <32 weeks' gestational age. The trial found that 46 (47.4%) infants in the high dose group and 64 (65.3%) infants in the low dose group had feeding intolerance (p=0.01). NEC was observed in 11 infants (11.2%) in the low dose
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		group and only 1 infant (1%) in the high dose group ($p=0.003$). There was a negative correlation between high-dose zinc supplementation and number of culture-proven late onset sepsis episodes ($p=0.04$). No relationship between high-dose zinc supplementation and mortality, duration of hospital stay, bronchopulmonary dysplasia, and retinopathy of prematurity. Longer term neurodevelopmental outcome data are not available. An additional relevant implementation study by Seidu <i>et al</i> was identified after the search date for this question [6]. The study was conducted in the USA with very preterm (<33 weeks' gestation), very low birthweight (<1,500 g) infants. In the pre-implementation epoch zinc was provided at 450 $\mu\text{g/kg/day}$ (500 $\mu\text{g/kg/day}$ for infants <1,000g with zinc deficiency) in parenteral nutrition. Those with risk factors for zinc deficiency or a known deficiency received 3 to 3.5 mg/kg/day enteral supplementation. In the post-implementation epoch infants received 500 $\mu\text{g/kg/day}$ of zinc in parenteral nutrition (650 $\mu\text{g/kg/day}$ if zinc deficient). Once at 140 mL/kg/day of enteral feeds, infants received routine enteral zinc supplementation to achieve a total of 2.5 mg/kg/day until 36 weeks' post menstrual age or discharge; total intake was slightly increased by 0.3–0.5 mg/kg/day (to a total dose of 2.7 to 3 mg/kg/day). In Epoch-2 vs. Epoch-1 Adjusted mean length Z score increased by 0.27 points [95% CI 0.13 to 0.42, $P < 0.001$]. No significant difference in weight or head circumference z scores. There was no significant difference between epochs for bronchopulmonary dysplasia, late onset sepsis, NEC, severe retinopathy of prematurity, or mortality.
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				Retinopathy of prematurity was independently associated with the lowest serum zinc level [adjusted OR 0.042 (95% CI 0.006 to 0.306)].	
Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with no routine zinc monitoring or supplementation	Risk difference with routine zinc monitoring or supplementation
Mortality: RCT	345 (3 RCTs)	⊕⊕⊕○ Moderate ^a	RR 0.55 (0.31 to 0.97)	Study population 169 per 1,000	76 fewer per 1,000 (116 fewer to 5 fewer)
Mortality: RCT assessed with: All-cause mortality	8801 (6 RCTs)	⊕⊕○○○ Low ^b	RR 0.73 (0.46 to 1.16)	Study population 28 per 1,000	8 fewer per 1,000 (15 fewer to 5 more)
Neurodevelopmental impairment: RCT assessed with: Bayley Scale of Infant Development version 1 (BSID I) mental development scores	301 (2 RCTs)	⊕○○○○ Very low ^{b,c,d}	-	The mean neurodevelopmental impairment: RCT: Bayley I Mental Development score was 110.4 points	MD 4.18 higher (6.51 higher to 1.85 higher)
Neurodevelopmental impairment: RCT assessed with: Bayley Scale of Infant Development version 1 (BSID I) psychomotor development scores	301 (2 RCTs)	⊕○○○○ Very low ^{b,c,e}	-	The mean neurodevelopmental impairment: RCT: Bayley I Psychomotor Development score was 98.3 points	MD 5.75 higher (4.83 higher to 16.33 higher)
Neurodevelopmental impairment: RCT assessed with: Amiel- Tison scale	72 (1 RCT)	⊕○○○○ Very low ^{a,d,f}	-	In one trial of 72 infants the Amiel- Tison scale for measuring neurodevelopment was used and there was a reported RR of 0.09 for "hyperexcitability" (95% CI 0.01 to 0.7) and a RR of 0.22 for "brisk bicipital reflex" (95% CI 0.07 to 0.7), but alertness and attention was similar across groups (RR 0.47, 95% CI 0.05 to 4.99).	
Neurodevelopmental impairment: RCT assessed with: Griffith Scale Total neurodevelopmental score	114 (2 RCTs)	⊕○○○○ Very low ^{a,b,d,e}	-	The mean neurodevelopmental impairment: RCT: Griffith Scale Total Neurodevelopmental score was not reported	MD 6.41 higher (2.35 lower to 15.17 higher)
Neurodevelopmental impairment: RCT assessed with: Griffith Scale Motor developmental score	114 (2 RCTs)	⊕⊕⊕○ Moderate ^a	-	The mean neurodevelopmental impairment: RCT: Griffith Scale Motor Developmental score was not reported	MD 9.54 higher (6.63 higher to 12.44 higher)
Faltering growth/body composition: RCT assessed with: weight gain	481 (5 RCTs)	⊕⊕⊕○ Moderate ^a	-	The mean faltering growth/body composition: RCT not applicable	SMD 0.46 SD higher (0.28 higher to 0.64 higher)
Faltering growth/body composition: RCT assessed with: weight gain (g) at a follow-up median 22 weeks	798 (8 RCTs)	⊕⊕⊕○ Moderate ^a	-	The mean faltering growth/body composition: RCT was 5162.9 g	MD 378.57 higher (275.26 higher to 481.88 higher)

Faltering growth/body composition: RCT assessed with: weight z score 3-6 months	524 (7 RCTs)	⊕○○○ Very low ^{a,b}	-	The mean faltering growth/body composition: RCT was not reported	MD 0.5 higher (0.23 higher to 0.76 higher)
Faltering growth/body composition: RCT assessed with: Linear growth	289 (4 RCTs)	⊕○○○ Very low ^{a,g,h}	-	The mean faltering growth/body composition: RCT not applicable	SMD 0.75 SD higher (0.36 higher to 1.14 higher)
Faltering growth/body composition: RCT assessed with: length (cm) at a follow-up median 36 weeks	529 (6 RCTs)	⊕○○○ Very low ^{a,b}	-	The mean faltering growth/body composition: RCT was 60.4 cm	MD 2.92 higher (1.53 higher to 4.31 higher)
Faltering growth/body composition: RCT assessed with: length z-score	524 (7 RCTs)	⊕○○○ Very low ^{a,b}	-	The mean faltering growth/body composition: RCT was not reported	MD 1.12 higher (0.63 higher to 1.61 higher)
Faltering growth/body composition: RCT assessed with: head growth	289 (4 RCTs)	⊕○○○ Very low ^{a,e,h}	-	The mean faltering growth/body composition: RCT not applicable	SMD 0.21 SD higher (0.02 lower to 0.44 higher)
Faltering growth/body composition: RCT assessed with: head growth (cm) at a follow-up median 20 weeks	466 (5 RCTs)	⊕⊕○○ Low ^c	-	The mean faltering growth/body composition: RCT was 37.8 cm	MD 0.56 higher (0.23 higher to 0.9 higher)
Sepsis: proven or suspected: RCT	293 (2 RCTs)	⊕⊕○○ Low ^{a,e}	RR 1.11 (0.60 to 2.04)	Study population	
				116 per 1,000	13 more per 1,000 (47 fewer to 121 more)
Retinopathy of prematurity: RCT	193 (1 RCT)	⊕○○○ Very low ^{f,i}	RR 0.14 (0.01 to 2.70)	Study population	
				31 per 1,000	27 fewer per 1,000 (31 fewer to 53 more)
Adverse effects assessed with: Diarrhoea	Not reported (6 RCTs)	⊕⊕⊕○ Moderate ^a	RR 0.81 (0.68 to 0.97)	Study population	
				135 per 1,000	26 fewer per 1,000 (43 fewer to 4 fewer)
Time to full enteral feeds - not measured	-	-	-	-	-
Duration of initial hospital stay: RCT assessed with: days	398 (2 RCTs)	⊕○○○ Very low ^{a,i}	-	The mean duration of initial hospital stay: RCT was 28.35 days	MD 3.49 higher (7.11 lower to 14.08 higher)
Fully breastfed or breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Bronchopulmonary dysplasia / chronic lung disease: RCT	193 (1 RCT)	⊕○○○ Very low ^{e,f}	RR 0.66 (0.31 to 1.40)	Study population	
				156 per 1,000	53 fewer per 1,000 (108 fewer to 62 more)
Necrotising enterocolitis: RCT	193 (1 RCT)	⊕○○○ Very low ^{f,i}	RR 0.08 (0.00 to 1.33)	Study population	
				63 per 1,000	58 fewer per 1,000

					(63 fewer to 21 more)
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-

- a. Downgraded one level for concerns regarding risk of bias
- b. Downgraded two levels for serious inconsistency
- c. Downgraded two levels for serious concerns regarding risk of bias - all studies were low quality
- d. Downgraded one level for imprecision with wide confidence intervals
- e. Downgraded one level for imprecision with confidence intervals crossing the line of no effect
- f. Downgraded one level for indirectness as evidence is based on a single study
- g. Downgraded one level for serious inconsistency
- h. Downgraded one level for imprecision as n= <400
- i. Downgraded two levels for imprecision with wide confidence intervals crossing the line of no effect

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Sepsis: RCT: There was no significant increase in sepsis for zinc supplementation (13 more per 1,000; 47 fewer to 121 more) [Critical]. Duration of initial hospital stay: RCT: There was no significant increase in duration of hospitalisation with zinc supplementation (MD 3.5 days higher; 7.1 lower to 14.1 higher) [Important]. Undesirable effects for Māori No additional data	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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● Very low ○ Low ○ Moderate ○ High ○ No included studies	Moderate to very low certainty of evidence. Certainty of evidence for Māori No additional data	
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Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT	CRITICAL	⊕⊕⊕○ Moderate
Mortality: RCT assessed with: All-cause mortality	CRITICAL	⊕⊕○○ Low
Neurodevelopmental impairment: RCT assessed with: Bayley Scale of Infant Development version 1 (BSID I) mental development scores Scale from: 1 to 100	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: Bayley Scale of Infant Development version 1 (BSID I) psychomotor development scores Scale from: 1 to 100	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: Amiel- Tison scale (maximum score for the assessment is 36 points)	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: Griffith Scale Total neurodevelopmental score Scale from: 0 to 200	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: Griffith Scale Motor developmental score Scale from: 0 to 200	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT assessed with: weight gain	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT assessed with: weight gain (g) at a follow-up median 22 weeks	CRITICAL	⊕⊕⊕○ Moderate
Faltering growth/body composition: RCT assessed with: weight z score 3-6 months	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT	CRITICAL	⊕○○○

assessed with: Linear growth		Very low ^a
Faltering growth/body composition: RCT assessed with: length (cm) at a follow-up median 36 weeks	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: length z-score	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: head growth	CRITICAL	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: head growth (cm) at a follow-up median 20 weeks	CRITICAL	⊕⊕○○ Low
Sepsis: proven or suspected: RCT	CRITICAL	⊕⊕○○ Low
Retinopathy of prematurity: RCT	CRITICAL	⊕○○○ Very low
Adverse effects assessed with: Diarrhoea	IMPORTANT	⊕⊕⊕○ Moderate
Time to full enteral feeds - not measured	IMPORTANT	-
Duration of initial hospital stay: RCT assessed with: days	IMPORTANT	⊕○○○ Very low
Fully breastfed or breastmilk feeding at hospital discharge - not measured	IMPORTANT	-
Bronchopulmonary dysplasia / chronic lung disease: RCT	IMPORTANT	⊕○○○ Very low
Necrotising enterocolitis: RCT	IMPORTANT	⊕○○○ Very low
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability Values for Māori No additional data	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies	There is likely to be benefit for growth outcomes for zinc supplementation compared with no supplementation, but there is insufficient evidence for immune function and neurodevelopmental outcomes. There was no evidence for substantive harm with zinc supplementation. Serum zinc increased in infants who were supplemented, and this is important in Aotearoa New Zealand, where environmental zinc levels are known to be low. Zinc supplementation compared with no supplementation - moderate certainty of evidence Large decrease in mortality and adverse effects (diarrhoea) Large increase in weight Improvement in neurodevelopmental outcomes: Griffith motor developmental scale Zinc supplementation compared with no supplementation - low certainty of evidence Increase in head circumference	

○ Don't know	Uncertain effect on mortality, sepsis Zinc supplementation compared with no supplementation - very low certainty of evidence Increase in weight gain, length Improvement in neurodevelopmental outcomes (mental and psychomotor development) Uncertain effect on neurodevelopmental outcomes, head circumference, hospital stay, bronchopulmonary dysplasia, retinopathy of prematurity, necrotising enterocolitis Balance of effects for Māori No additional data	
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Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	At a dose of 10 mg per day Clinician's Zinc Liquid (1 mg elemental zinc per drop) is approx. 1 drop = 0.05 mL and \$11.62 for a 30 mL bottle. Therefore, 0.5 mL per day will cost \$0.19 per day. The cost of zinc supplementation is small to negligible. Resources required for Māori No additional data	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Costs are based on the only PHARMAC-funded liquid zinc supplement approved for use in New Zealand hospitals. Certainty of evidence of resource requirements for Māori No evidence available.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison	There are no studies that assess the specific cost-effectiveness of zinc supplementation vs. no supplementation, particularly in the context of preterm infants.	

○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ No included studies	Cost effectiveness for Māori No additional data	
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Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori While Aotearoa New Zealand is classified as a low-risk country for zinc deficiency at the population level, some studies suggest that certain groups may have low zinc intakes. Due to systemic inequities in food security and neonatal care, preterm pēpi Māori are at increased risk of zinc deficiency. This includes inconsistent monitoring and supplementation protocols, meaning pēpi Māori may not always receive timely or adequate zinc supplementation if not growing well. Whānau Māori may also experience limited access to culturally safe nutritional counselling, which can impact shared decision-making. Equity for Pacific families Aotearoa New Zealand research suggests that Pacific Island children may have low zinc intakes, and New Zealand soil is naturally low in zinc. Pacific Island infants are similarly at elevated risk of zinc deficiency, driven by higher rates of food insecurity and infection burden. Pacific families may face language barriers and reduced access to culturally appropriate nutrition support, which can limit engagement in supplementation decisions. Pacific families may not be routinely informed about zinc supplementation or the risks of deficiency in preterm infants. If screening and supplementation are inconsistently applied across services, Pacific infants may miss out. Equity requires standardised care, culturally appropriate communication and consistent monitoring to support growth and immune function. Equity for underrepresented groups Other at-risk groups include refugee, migrant, and some Asian communities, particularly where dietary zinc intake is low or disrupted. These populations often experience barriers in accessing healthcare, including neonatal nutritional care, and may not receive consistent or informed guidance on zinc needs. Equity requires equitable availability, regular screening and inclusive information to ensure all infants receive essential micronutrients.	

Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Based on the growth benefits and known low levels of zinc in Aotearoa New Zealand soil, this is probably an acceptable intervention. More evidence is needed to identify neurodevelopmental benefits or harms. Acceptability for Māori No additional data	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Zinc supplementation is feasible in Aotearoa New Zealand neonatal care. We are not aware of any Aotearoa New Zealand neonatal units that currently give routine supplementary enteral zinc, but some Australian hospitals do. There is testing for serum zinc if infants are not growing well or they have a stoma and if their serum zinc is low then supplements are given. Feasibility for Māori No additional data	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			

	JUDGEMENT						
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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EtD 40. Is switching from fortified EBM/preterm formula to unfortified EBM/term formula recommended in preterm infants before discharge or term?

POPULATION:	Preterm infants before discharge or term
INTERVENTION:	Switching from fortified EBM/preterm formula to unfortified EBM/term formula
COMPARISON:	Not switching from fortified EBM/preterm formula to unfortified EBM/term formula before discharge or term
MAIN OUTCOMES:	Consideration will be given to the evidence (or lack thereof) for Māori and non-Māori infants and their whānau Critical for making a decision Neurodevelopmental impairment Faltering growth/body composition Fully breastfeeding at hospital discharge Duration of initial hospital stay Time to full sucking feeds Adverse effects (metabolic bone disease) Important but not critical Mortality Fully breastmilk feeding at hospital discharge Necrotising enterocolitis (NEC) Sepsis: proven or suspected Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Of limited importance Time to full enteral feeds
SETTING:	Neonatal care
PERSPECTIVE:	
BACKGROUND:	Fortified expressed breastmilk or preterm formula is required by preterm infants during their hospital stay to meet their increased nutritional needs for growth and development. As they approach discharge or term-equivalent age, it is common practice to consider transitioning them to unfortified expressed breastmilk or standard term formula. In some NICUs, this may be considered at 36 weeks corrected gestational age or when the infant reaches 2,500 g or to induce hunger and encourage better breastfeeding. However, the timing of this switch remains controversial, and its impact on key outcomes such as time to discharge, breastfeeding success, growth and neurodevelopment is not known. Switching too early may compromise nutritional intake during a critical period of brain and body growth, while delaying the switch may prolong hospital stay or reduce breastfeeding confidence. Evidence is needed to determine whether making this transition at or before discharge affects length of stay, breastfeeding continuation,

CONFLICT OF INTERESTS:	or the infant's short- and long-term outcomes. Clear guidance would support consistent decision-making and help balance the benefits of continued nutritional support with the goal of promoting breastfeeding and timely discharge.
	None

Assessment

Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	No studies were identified which were applicable to this review question. The goal of fortification is to ensure that, at recommended feeding volumes (135–200 mL/kg/day), preterm infants receive nutrient intakes that support fetal-equivalent growth. These requirements are largely based on fetal nutrient accretion data and supported by empirical evidence. However, individual needs vary depending on clinical conditions such as fetal growth restriction or morbidity. These additional nutrient requirements decrease as an infant approaches 40 weeks but they do not suddenly change to the nutritional requirements of a term infant at 36 weeks or at 2,500 g. Theoretical benefits of continuing fortifier or preterm formula until discharge or term are: Avoidance of faltering growth due to substantially lower energy and nutrient intake of all nutrients as in Figure 1 below:	180 mL/kg/day expressed breastmilk or term formula provides ~119 kcal/kg/day and ~2.3 g/kg/day protein 180 mL/kg/day fortified expressed breastmilk provides 149 kcal/kg/day and 4.9 g/kg/day protein 180 mL/kg/day preterm formula provides 144 to 146 kcal/kg/day and 4.9 to 5.2 g/kg/day protein

Expressed breastmilk and fortified expressed breastmilk

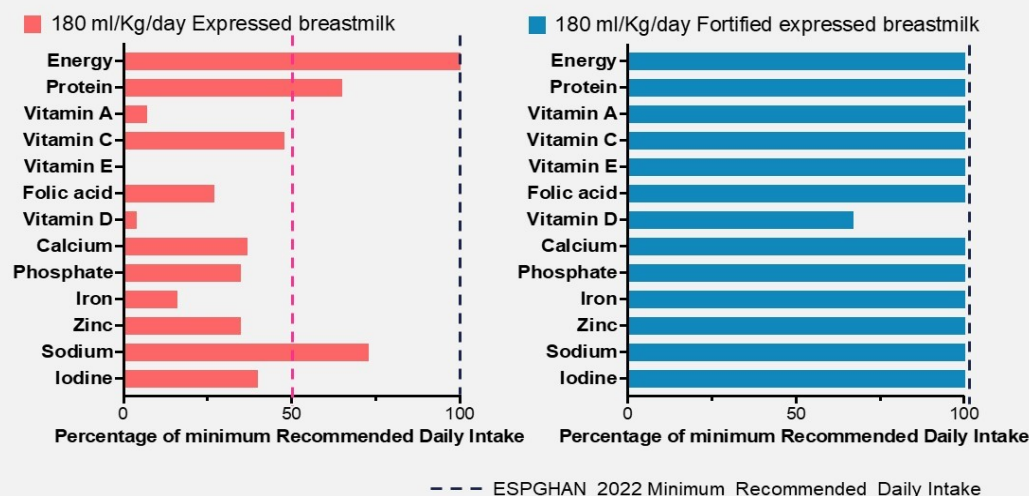


Figure 1 Difference in nutrient intakes between fortified and unfortified breastmilk at 180 mL/kg/day compared with minimum of ESPGHAN recommended nutrient intake ranges.

Inadequate protein intake in preterm infants is a key contributor to faltering growth, which is linked to impaired neurodevelopmental outcomes.

Better metabolic bone health

Deficiencies in specific nutrients such as calcium, phosphorus, zinc, iron, vitamins and iodine can lead to clinical problems like osteopenia or micronutrient deficiencies.

Fewer additives to feeds are needed

When fortifier or preterm formula ceases, additional iron, vitamins and other nutrients may need to be prescribed and added to feeds. This creates extra work for nurses and increases the risk of microbiological contamination.

Gradual transition to lower nutrient intake vs a large drop from one day to the next. In breastfed infants, the transition occurs gradually as the number of breastfeeds per day increases in the lead up to discharge.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	Theoretical risks are: Growth crossing centiles upwards As nutritional requirement decreases as the infant approaches 40 weeks, growth may start crossing centiles upwards. Lack of interest in breastfeeding due to enteral feeds meeting or exceeding nutritional requirements <i>Both these undesirable effects can be managed by reducing feeds to 120 to 150 mL/kg/day without stopping fortifier or preterm formula.</i> Prolonged length of hospital stay or reduced breastfeeding confidence There is no evidence to support this, and the reverse may be true. Better nutrition support may lead to earlier discharge and better ability to breastfeed.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No studies were identified which were applicable to this review question.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important	Possibly important uncertainty or variability	

uncertainty or variability ○ No important uncertainty or variability		
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Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● Don't know	There is no evidence that transitioning preterm infants from fortified expressed breastmilk/preterm formula to unfortified expressed breastmilk/term formula at discharge, rather than earlier, adversely affects time to discharge, breastfeeding continuation, growth or neurodevelopmental outcomes. Fortification or preterm formula provides the recommended nutritional intake for preterm infants. Discontinuing these before discharge means that nutritional requirements will not be met, which may have suboptimal consequences for some infants.	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Breastmilk fortifier \$3.75 per 100 mL Costs (for up to 100-120 days) Breastmilk fortifier \$3.75 per 100 mL at 180 mL/kg/day (\$5.80 to \$9 per day) Cost difference for fortified vs. unfortified breastmilk for 28 days is approx. \$162 to \$252 per infant. Labour to add a fortifier to breastmilk by parent or nurse is minimal Labour to add a fortifier to breastmilk in a central milk preparation facility is higher Aotearoa New Zealand Preterm infant formula (Liquid ready to feed) \$3.24 per 100 mL Aotearoa New Zealand Term infant formula (Liquid ready to feed) \$1.56 per 100 mL Costs (for 28 days) Preterm infant formula \$3.24 per 100 mL (\$5 to \$10 per day for a 1 kg infant, approx. \$140 to \$280 per baby per admission) Term infant formula \$1.16 to \$1.56 per 100 mL (\$2.08 to \$2.80 per day for a 1 kg infant, approx. \$2.50 to \$5 per day for a 1 kg baby, approx. \$70 to \$140 per baby per admission) Cost difference for preterm vs. term formula for 28 days is approx. \$70 to \$140 per infant.	

	Resources required for Māori No additional evidence available.	
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	The costs are certain.	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No studies were identified	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ● Don't know	Equity for Māori Pēpi Māori are more likely to be born preterm and face growth challenges linked to systemic inequities in care. If the transition from fortified to unfortified feeds before discharge occurs without standard guidance, pēpi Māori may be at risk of nutritional shortfalls. Inconsistent decision-making and lack of culturally safe communication may mean whānau Māori are not informed or involved in feeding plans. Equity requires clear national protocols and inclusive dialogue to ensure fortified feeds are continued where appropriate and that pēpi Māori receive sustained nutritional support during this critical transition to home and community care.	

	Equity for Pacific families Pacific infants may be switched to term formula too early if hospitals lack clear guidelines or resourcing, potentially impacting growth. Pacific families may not be informed about the reasons for continuing fortified feeds. Equity requires culturally safe discussions and standardised practices that support sustained nutrition through to discharge. Equity for underrepresented groups Underrepresented families may not receive guidance on when or why to switch from fortified to term feeds, especially where follow-up services are limited. Early switching may occur without parental awareness. Equity requires consistent discharge planning, inclusive education and support to ensure optimal nutrition is maintained across all communities.	
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☐ Probably yes ☐ Yes ☒ Varies ☐ Don't know	The intervention is acceptable to some but may not be acceptable to all staff and parents.	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☐ Varies ☐ Don't know	The intervention is feasible.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

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Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
☐	☒	☐	☐	☐

EtD 41. Should exposure to the smell or taste (or both) of breastmilk or formula administered with tube feeds vs. no exposure be used for preterm infants who are fed via an orogastric or nasogastric tube?

POPULATION:	Preterm infants who are fed via an orogastric or nasogastric tube
INTERVENTION:	Exposure to the smell or taste (or both) of breastmilk or formula administered with tube feeds
COMPARISON:	No exposure
MAIN OUTCOMES:	Critical outcomes Mortality Neurodevelopmental impairment Time to full enteral feeds Important but not critical Adverse effects Necrotising enterocolitis Sepsis: proven or suspected Faltering growth/body composition Fully breastfed or breastmilk feeding at hospital discharge Duration of initial hospital stay Time to full sucking feeds Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost
SETTING:	Neonatal care
PERSPECTIVE:	Clinical guideline recommendation - patient perspective
BACKGROUND:	Preterm infants, often struggle with oral feeding due to immature coordination of sucking, swallowing, and breathing. As a result, they rely on orogastric or nasogastric tube feeding for nutrition in the early weeks after birth. However, feeding intolerance is common in preterm infants, leading to delays in reaching full enteral and sucking feeds, which can prolong hospitalisation and increase healthcare costs. Smell and taste are key sensory stimuli that trigger physiological responses related to digestion and absorption. In term infants, exposure to the smell and taste of milk before feeding stimulates salivation, digestive enzyme secretion and gastric motility, potentially improving feeding efficiency. However, during tube feeding, milk bypasses the nasal and oral cavities, reducing sensory stimulation. Providing preterm infants with exposure to the smell or taste (or both) of breastmilk or formula during tube feeds has been proposed as a simple, non-invasive intervention to enhance feeding readiness and accelerate the transition to full sucking feeds. If effective, this intervention could lead to improved clinical outcomes, including faster attainment of full enteral feeds, reduced time to discharge and potentially improve neurodevelopmental outcomes. Evaluating the evidence on this practice is essential to determine its benefits and any potential adverse effects.

CONFLICT OF INTERESTS:

The following systematic review (Delgado-Paramo *et al*) co-authors are on the Guideline Development Group: Lilia Delgado-Paramo, Luling Lin and Frank Bloomfield.

The following DIAMOND study authors are on the Guideline Development Group: Tanith Alexander and Frank Bloomfield

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	Evidence based on Cochrane systematic review [1] and a 2-year follow-up of the DIAMOND trial [2]: Mortality: RCT: Little or no effect on mortality for exposure to the smell or taste (or both) of breastmilk or formula 0/260 and 1/272 [Critical]. Neurodevelopmental impairment: RCT: Decreased neurosensory impairment at 2 years for exposure to the smell or taste (or both) of breastmilk or formula (93 fewer per 1,000; 155 fewer to 31 fewer) [Critical]. Time to full enteral feeds: RCT: Little or no effect on time to full enteral feeds for exposure to the smell or taste (or both) of breastmilk or formula (MD 0.16 days lower; 0.45 lower to 0.12 higher) [Critical]. Necrotising enterocolitis (NEC): RCT: No significant reduction in NEC for exposure to the smell or taste (or both) of breastmilk or formula (5 fewer per 1,000; 38 fewer to 60 more) [Important]. Sepsis: RCT: Little or no effect on sepsis between groups 2/260 and 2/72 for both culture-proven and probable sepsis [Important]. No faltering growth/body composition: RCT: Little or no difference in fat-free mass z score at 4 months corrected age (Adj MD 0 points; 0.2 lower to 0.2 higher). No significant effect in weight z score 4 months' corrected age (Adj MD 0.12 points higher; 0.16 lower to 0.2 higher); length z score at day 14 (Adj MD 0.01 points higher; 0.11 lower to 0.12 higher); day 21 (Adj MD 0.13 points higher; 0.01 lower to 0.27 higher) and at discharge (Adj MD 0.03 points higher; 0.09 lower to 0.15 higher). No significant effect in head circumference z score for exposure to the smell or taste (or both) of breastmilk or formula at day 14 (Adj MD 0.08 points higher; 0.03 lower to 0.18 higher) and 4 months' corrected age (Adj MD 0.15 points higher; 0.04 lower to 0.34 higher) [Important]. Duration of initial hospital stay: RCT: Large reduction in duration of hospitalisation for exposure to the smell or taste (or both) of breastmilk or formula (MD 4.4 days lower; 5.65 lower to 3.15 lower) [Important]. Time to reach full sucking feeds: RCT: No significant reduction in time to reach full sucking feeds for exposure to the smell or taste (or both) of breastmilk or formula (MD 1.07 days lower; 2.63 lower to 0.5 higher) [Important]. Desirable effects for Māori	Cochrane systematic review [1]: Infants born <37 weeks' gestation. Aotearoa New Zealand: RCT [2]: 2-year follow-up DIAMOND trial, moderate-and-late preterm infants.

		In one of the studies in the Cochrane review, the DIAMOND trial, 84 of the 532 preterm pēpi enrolled (15.8%) were Māori. While the overall results found no significant differences in body composition or time to full enteral feeds for the smell and taste intervention, the data show that Māori pēpi were well represented.			
Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with no exposure	Risk difference with exposure to the smell or taste (or both) of breastmilk or formula administered with tube feeds
Mortality	532 (1 RCT)	⊕○○○ Very low ^{a,b,c}	not estimable	Study population	
				1/272	0/260
Neurodevelopmental impairment: RCT assessed with: 2-years	423 (1 RCT)	⊕○○○ Very low ^{a,b,c}	Adj RR 0.7 (0.5 to 0.9)	Study population	
				309 per 1,000	93 fewer per 1,000 (155 fewer to 31 fewer)
Time to full enteral feeds: RCT assessed with: Days	736 (4 RCTs)	⊕○○○ Very low ^{d,e,f}	-	The mean time to full enteral feeds: RCT was 14.09 days	MD 0.16 lower (0.45 lower to 0.12 higher)
Adverse effects: RCT	Not reported (2 RCTs)	-	-	No studies provided useable data on adverse effects. 1 study noted "no apparent adverse effects", and another stated that "No adverse events or side effects, no concerns with regard to acceptability to parents and no logistical implications for the delivery of smell and taste were observed in this study"	
Necrotising enterocolitis: RCT	435 (2 RCTs)	⊕○○○ Very low ^{a,g}	RR 0.93 (0.47 to 1.84)	Study population	
				71 per 1,000	5 fewer per 1,000 (38 fewer to 60 more)
Sepsis: proven or suspected: RCT assessed with: Culture proven	532 (1 RCT)	⊕○○○ Very low ^{a,b,c}	not estimable	Study population	
				2/272	2/260
Sepsis: proven or suspected: RCT assessed with: Probable	532 (1 RCT)	⊕○○○ Very low ^{a,b,c}	not estimable	Study population	
				2/272	2/260
Faltering growth/body composition: RCT assessed with: Fat free mass z score at 4 months corrected age	324 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was -0.7 points	Adj MD 0 (0.2 lower to 0.2 higher)
Faltering growth/body composition: RCT assessed with: Weight z score Day 7	493 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was -0.91 points	Adj MD 0.02 lower (0.06 lower to 0.02 higher)
Faltering growth/body composition: RCT assessed with: Weight z score Day 14	428 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was -0.94 points	Adj MD 0.05 lower (0.11 lower to 0)

Faltering growth/body composition: RCT assessed with: Weight z score Day 21	309 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was -0.90 points	Adj MD 0.05 lower (0.13 lower to 0.03 higher)
Faltering growth/body composition: RCT assessed with: Weight z score Day 28	182 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was -0.84 points	Adj MD 0.07 lower (0.19 lower to 0.05 higher)
Faltering growth/body composition: RCT assessed with: Weight z score Discharge	524 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was -0.81 points	Adj MD 0.03 lower (0.09 lower to 0.04 higher)
Faltering growth/body composition: RCT assessed with: Weight z score 4 months' corrected age	401 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was -0.08 points	Adj MD 0.12 higher (0.16 lower to 0.2 higher)
Faltering growth/body composition: RCT assessed with: Length z score Day 7	469 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was -0.20 points	Adj MD 0.06 lower (0.17 lower to 0.04 higher)
Faltering growth/body composition: RCT assessed with: Length z score Day 14	415 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was -0.36 points	Adj MD 0.01 higher (0.11 lower to 0.12 higher)
Faltering growth/body composition: RCT assessed with: Length z score Day 21	299 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was -0.45 points	Adj MD 0.13 higher (0.01 lower to 0.27 higher)
Faltering growth/body composition: RCT assessed with: Length z score Day 28	178 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was -0.47 points	Adj MD 0.07 lower (0.26 lower to 0.11 higher)
Faltering growth/body composition: RCT assessed with: Length z score Discharge	495 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was -0.25 points	Adj MD 0.03 higher (0.09 lower to 0.15 higher)
Faltering growth/body composition: RCT assessed with: Length z score 4 months' corrected age	401 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was 0.53 points	Adj MD 0.07 lower (0.27 lower to 0.13 higher)
Faltering growth/body composition: RCT assessed with: Head circumference z score Day 7	472 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was -0.27 points	Adj MD 0.07 lower (0.17 lower to 0.04 higher)
Faltering growth/body composition: RCT assessed with: Head circumference z score Day 14	420 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was -0.30 points	Adj MD 0.08 higher (0.03 lower to 0.18 higher)
Faltering growth/body composition: RCT assessed with: Head circumference z score Day 21	299 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was -0.15 points	Adj MD 0 (0.13 lower to 0.12 higher)
Faltering growth/body composition: RCT assessed with: Head circumference z score Day 28	178 (1 RCT)	⊕○○○ Very low ^{a,b,f}	-	The mean faltering growth/body composition: RCT was 0.04 points	Adj MD 0.06 lower (0.25 lower to 0.13 higher)
Faltering growth/body composition: RCT	500	⊕○○○	-	The mean faltering growth/body composition:	Adj MD 0.05 lower

assessed with: Head circumference z score Discharge	(1 RCT)	Very low ^{a,b,f}		RCT was 0.03 points	(0.15 lower to 0.05 higher)
Faltering growth/body composition: RCT assessed with: Head circumference z score 4 months' corrected age	401 (1 RCT)	⊕○○○ Very low ^{a,b,d,g}	-	The mean faltering growth/body composition: RCT was 0.58 points	Adj MD 0.15 higher (0.04 lower to 0.34 higher)
Fully breastfed or breastmilk feeding at hospital discharge: RCT	528 (1 RCT)	⊕○○○ Very low ^{a,b,c}	OR 0.89 (0.61 to 1.31)	Study population	
				719 per 1,000	24 fewer per 1,000 (110 fewer to 51 more)
Duration of initial hospital stay: RCT assessed with: Days	786 (5 RCTs)	⊕○○○ Very low ^{d,e}	-	The mean duration of initial hospital stay: RCT was 36.80 days	MD 4.4 lower (5.65 lower to 3.15 lower)
Time to reach full sucking feeds: RCT assessed with: Days	662 (3 RCTs)	⊕○○○ Very low ^{d,g}	-	The mean time to reach full sucking feeds: RCT was 37.2 days	MD 1.07 lower (2.63 lower to 0.5 higher)
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-

- a. Downgraded one level for risk of bias due to concerns about lack of blinding, including outcome assessors
b. Downgraded one level for indirectness as evidence is based on a single study
c. Downgraded one level for imprecision due to low/no events
d. Downgraded two levels for high risk of bias that may influence the outcome
e. Downgraded two levels for inconsistency as I² >80%
f. Downgraded one level for imprecision with confidence intervals crossing the line of no effect
g. Downgraded two levels for imprecision due to wide confidence intervals that cross the line of no effect

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Adverse effects: RCT: 1 study noted "no apparent adverse effects", and another stated that "No adverse events or side effects, no concerns with regard to acceptability to parents and no logistical implications for the delivery of smell and taste were observed in this study" [Important]. Faltering growth/body composition: RCT: No significant decrease in weight z scores for exposure to the smell or taste (or both) of breastmilk or formula at day 7 (Adj MD 0.02 points lower; 0.06 lower to 0.02 higher). Reduction in weight z score at Day 14 (Adj MD 0.05 points lower; 0.11 lower to 0). No significant effect on weight z score at day 21 (Adj MD 0.05 points lower; 0.13 lower to 0.03 higher);	

	day 28 (Adj MD 0.07 points lower; 0.19 lower to 0.05 higher) and at discharge (Adj MD 0.03 lower; 0.09 lower to 0.04 higher). No significant decrease in length z scores for exposure to the smell or taste (or both) of breastmilk or formula at day 7 (Adj MD 0.06 points lower; 0.17 lower to 0.04 higher); day 28 (Adj MD 0.07 points lower; 0.26 lower to 0.11 higher) and at 4 months' corrected age (Adj MD 0.07 points lower; 0.27 lower to 0.13 higher). No significant effect in head circumference z scores for exposure to the smell or taste (or both) of breastmilk or formula at day 7 (Adj MD 0.07 points lower; 0.17 lower to 0.04 higher); day 21 (Adj MD 0 points; 0.13 lower to 0.12 higher); day 28 (Adj MD 0.06 points lower; 0.25 lower to 0.13 higher) and at discharge (Adj MD 0.05 points lower; 0.15 lower to 0.05 higher) [Important]. Fully breastfed or breastmilk feeding at hospital discharge: RCT: No significant effect on infants exposed to smell or taste (or both) of breastmilk or formula who were fully breastfed or breastmilk feeding at hospital discharge (24 fewer per 1,000; 110 fewer to 51 more) [Important]. Undesirable effects for Māori None demonstrated	
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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Very low certainty of evidence overall	

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: 2-years	CRITICAL	⊕○○○ Very low
Time to full enteral feeds: RCT assessed with: Days	CRITICAL	⊕○○○ Very low
Adverse effects	IMPORTANT	-

Necrotising enterocolitis	IMPORTANT	⊕○○○ Very low
Sepsis: proven or suspected: RCT assessed with: Culture proven		⊕○○○ Very low
Sepsis: proven or suspected: RCT assessed with: Probable	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Weight z score Day 7	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Weight z score Day 14	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Fat free mass z score at 4 months corrected age	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Weight z score Day 21	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Weight z score Day 28	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Weight z score Discharge	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Weight z score 4 months' corrected age	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Length z score Day 7	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Length z score Day 14	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Length z score Day 21	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Length z score Day 28	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Length z score Discharge	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Length z score 4 months' corrected age	IMPORTANT	⊕○○○ Very low

Faltering growth/body composition: RCT assessed with: Head circumference z score Day 7	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Head circumference z score Day 14	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Head circumference z score Day 21	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Head circumference z score Day 28	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Head circumference z score Discharge	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Head circumference z score 4 months' corrected age	IMPORTANT	⊕○○○ Very low
Fully breastfed or breastmilk feeding at hospital discharge: RCT	IMPORTANT	⊕○○○ Very low
Duration of initial hospital stay: RCT assessed with: Days	IMPORTANT	⊕○○○ Very low
Time to reach full sucking feeds: RCT assessed with: Days	IMPORTANT	⊕○○○ Very low
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Retinopathy of prematurity - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-

Certainty of evidence for Māori

No additional evidence available

Values

Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability. Values for Māori No additional research available.	
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Exposure to smell or taste (or both) of breastmilk or formula versus no exposure - very low certainty evidence Decrease in neurodevelopmental impairment at 2 years, duration of initial hospital stay Uncertain effect on mortality, time to full enteral feeds, adverse effects, NEC, sepsis; weight, length, head circumference and fat free mass z scores, fully breastfeeding or breastmilk feeding at discharge, time to reach full sucking feeds Balance of effects for Māori No additional evidence	
Resources required		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Extra nursing time to administer smell and taste with every tube feed. Resourcing for Māori No additional evidence available	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	The costs are known. Certainty of evidence of required costs for Māori No additional evidence available.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	There are no studies that assess the specific cost-effectiveness of exposure to smell or taste (or both) of breastmilk or formula administered with tube feeds compared with no exposure, particularly in the context of preterm infants. Cost effectiveness for Māori No additional evidence available	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Pēpi Māori are more likely to be born preterm and experience poorer outcomes due to ongoing systemic inequities and the effects of colonisation. Interventions that support feeding tolerance and early transition to sucking feeds may reduce hospital stays and improve developmental outcomes, but only if applied equitably. Whānau Māori may face barriers to accessing culturally safe feeding support, consistent clinical practices and lactation guidance. Incorporating smell and taste exposure during tube feeds is a low-cost, non-invasive strategy that could be highly beneficial if introduced with equitable access, cultural understanding and whānau involvement in care planning from the earliest stages. Equity for Pacific families	

	Pacific infants are more likely to encounter delays in feeding progression due to inconsistent access to high-quality, culturally responsive care. Exposure to the smell or taste of milk during tube feeds may offer a simple and accessible method to enhance digestive readiness and shorten hospital stays. However, if this intervention is only adopted in select units or without adequate family education and support, existing disparities may persist or widen. Equity for underrepresented groups Migrant and rural families may not be offered or supported to provide smell or taste exposure due to staffing limitations or communication barriers. Without understanding its benefits, families may not advocate for it. Equity means ensuring all infants have access to low-cost, evidence-based interventions that promote feeding readiness and bonding.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☐ Varies ☐ Don't know	Was well-accepted in the DIAMOND trial Acceptability for Māori No additional evidence available.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☐ Varies ☐ Don't know	Relatively easy and quick intervention to apply in any unit Feasibility for Māori No additional evidence available.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
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References

1. Delgado Paramo, L.; Bronnert, A.; Lin, L.; Bloomfield, F.H.; Muelbert, M.; Harding, J.E. Exposure to the smell and taste of milk to accelerate feeding in preterm infants. *Cochrane Database Syst. Rev.* **2024**, *5*, Cd013038, doi:10.1002/14651858.CD013038.pub3.
2. Das, S.; Bloomfield, F.; Alexander, T.; Jiang, Y.; Gamble, G.; Lin, L.; Harding, J.E. Effect of different feeding strategies on neurosensory impairment at 2 years' corrected age in children born moderate-and-late preterm: Follow-up of the DIAMOND randomised trial. In Proceedings of PSANZ conference proceedings; pp. 6-40.

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Appendix H.3 – Evidence to Decision: Breastmilk and Breastfeeding

EtD 42a. Should sequential breastmilk expression vs. double breastmilk expression be used for mothers of preterm infants?

POPULATION:	Mothers of preterm infants
INTERVENTION:	Sequential breastmilk expression
COMPARISON:	Double breastmilk expression
MAIN OUTCOMES:	Critical outcomes Breastmilk supply/volume Fully breastfed or breastmilk feeding at hospital discharge Necrotising enterocolitis Mortality Neurodevelopmental impairment Sepsis: proven or suspected Time to full enteral feeds Important but not critical Adverse effects Faltering growth/body composition Duration of initial hospital stay Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation- patient perspective
BACKGROUND:	Breastmilk is the optimal source of nutrition for preterm infants, providing essential nutrients, immune protection and developmental benefits. However, many mothers of preterm infants face challenges in establishing and maintaining milk supply, particularly when direct breastfeeding is not immediately possible. Effective breastmilk expression strategies are critical for ensuring sufficient milk production and supporting breastfeeding or breastmilk feeding at discharge. The volume of breastmilk produced in the first 1 to 2 weeks may be a predictor of breastfeeding success. Insufficient expression frequency and volume may contribute to decreased milk production and early cessation of breastmilk feeding. The volume of breastmilk available for enteral feeding in the first two weeks after birth is an important determinant of how quickly parenteral nutrition can stop which reduces the risk of sepsis and whether the infant receives infant formula which increases the risk of necrotising enterocolitis. Additionally, double pumping (using an electric breast pump to express milk from both breasts simultaneously) may be more effective than single or sequential pumping. Understanding the evidence and whether it supports these practices and beliefs is essential to optimising milk production, minimising feeding related morbidity and mortality, and

CONFLICT OF INTERESTS:	supporting breastfeeding success for mothers of preterm infants.
	None

Assessment

Desirable Effects						
How substantial are the desirable anticipated effects?						
JUDGEMENT		RESEARCH EVIDENCE			ADDITIONAL CONSIDERATIONS	
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know		Double pumping [1-5] Breastmilk supply/volume: RCT: Milk yield higher with double pump vs. sequential expression [Critical]. Desirable effects for Māori No additional evidence available			Double pumping [1,2] Infants <1,500 gm and <32 weeks' gestation. [3] Overall mean infant birthweight was 1535 g (1610 g in the sequential group, and 1460 g in the simultaneous group); mean gestational age was 29.97 weeks (sequential 29.9, simultaneous 30.2). [4] Gestational ages of the infants varied between 25 to 38 weeks (31.9±3.8) and their birthweights were within 760 and 3200 grams (1554.8±663.6). [5] Cohort analysis within a RCT. Babies <34 weeks' admitted to Neonatal Intensive Care Unit (NICU).	
Outcomes		№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects' (95% CI)	
					Risk with breastmilk expression (double,)	Risk difference with breastmilk expression (sequential,)

Breastmilk supply/volume: RCT: Sequential vs. double pump assessed with: Milk weight (g)	36 (1 RCT)	⊕○○○ Very low ^{a,b,c}	-	Milk yield higher with double pump vs. sequential expression (88 g; 95%CI 79 - 97 vs. 51 g; 95%CI 46-56; P< 0.01).	
Breastmilk supply/volume: RCT: Sequential vs. double pump assessed with: Milk weight (g)	48 (2 RCTs)	⊕⊕○○ Low ^{a,f}	-	Pilot study n=9 Mean daily milk yield in the sequential single group ranged from a low of 158.4 gm on day 3 to a high of 505.8 g on day 20. The mean daily milk yield in the double pump group ranged from a low of 41.4 g on day 3 to a high of 741 g on day 41. The overall mean milk yield for the 40 days in the sequential single and double pump groups was 395.2 (SD 270.9) and 445.3 (SD 188.9) g, respectively. RCT n=39 Milk weight change was higher for double pump than sequential groups between weeks 2 and 5 (P=0.049).	
Breastmilk supply/volume: Cohort: Sequential vs. double pump assessed with: Total amount of milk expressed (mL)	62 (1 non-randomised study)	⊕○○○ Very low ^{d,e,f}	-	Although there was a tendency to obtain higher amounts of milk per day with simultaneous breast expression, no statistical difference was observed on any day between the two study groups. However, mothers in the simultaneous expression group achieved similar amounts of milk in shorter time periods. Time spent for each expression period was significantly lower in the simultaneous breast expression group.	
Breastmilk supply/volume: Cohort within RCT: Sequential vs. double pump assessed with: Milk weight (g/day) first 10 days	62 (1 non-randomised study)	⊕○○○ Very low ^{a,f}	-	Double pumping was a significant predictor of 10-day milk weight; (109 (31–186, p=0.007) g/day more for double pumping) Sequential: n=42 median 147 (25th/75th centile 78, 275) mL/day Double: n=20 median 288 (25th/75th centile 168, 386) mL/day	
Breastmilk supply/volume: Cohort within RCT: Sequential vs. double pump assessed with: Total milk weight (mL/day) during infant stay in NICU	47 (1 non-randomised study)	⊕○○○ Very low ^{a,f}	-	Double pumping was a significant predictor of milk volume expressed prior to infant discharge from neonatal intensive care. Sequential: n=35 median 220 (25th/75th centile 112, 349) mL/day Double: n=12 median 561 (25th/75th centile 202, 708) mL/day	
Necrotising enterocolitis - not measured	-	-	-	-	-
Mortality - not measured	-	-	-	-	-
Neurodevelopmental impairment - not measured	-	-	-	-	-
Sepsis: proven or suspected - not measured	-	-	-	-	-
Time to full enteral feeds - not measured	-	-	-	-	-
Adverse effects - not measured	-	-	-	-	-
Faltering growth/body composition - not measured	-	-	-	-	-
Duration of initial hospital stay - not measured	-	-	-	-	-
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-

Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-

- a. Downgraded one level for concerns for risk of bias
- b. Downgraded one level for indirectness as evidence is only reported in a single study
- c. Downgraded one level for indirectness as population was not generalisable, no very preterm infants were included
- d. Downgraded two levels for serious concerns for risk of bias including inadequate information on confounding factors
- e. Downgraded one level for indirectness as this study included critically ill neonates and included term infants
- f. Downgraded one level for imprecision due to small sample numbers

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	No undesirable effects were reported. Undesirable effects for Māori No additional evidence available	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Low to very low certainty of evidence overall. Certainty of evidence for Māori No additional evidence available	

Outcomes	Importance	Certainty of the evidence (GRADE)
Breastmilk supply/volume: RCT: Sequential vs. double pump assessed with: Milk weight (g)	CRITICAL	⊕○○○ Very low
Breastmilk supply/volume: RCT: Sequential vs. double pump assessed with: Milk weight (g)	CRITICAL	⊕⊕○○ Low

Breastmilk supply/volume: Cohort: Sequential vs. double pump assessed with: Total amount of milk expressed (mL)	CRITICAL	⊕○○○ Very low
Breastmilk supply/volume: Cohort within RCT: Sequential vs. double pump assessed with: Milk weight (g/day) first 10 days	CRITICAL	⊕○○○ Very low
Breastmilk supply/volume: Cohort within RCT: Sequential vs. double pump assessed with: Total milk weight (mL/day) during infant stay in NICU	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis - not measured	CRITICAL	-
Mortality - not measured	CRITICAL	-
Neurodevelopmental impairment - not measured	CRITICAL	-
Sepsis: proven or suspected - not measured	CRITICAL	-
Time to full enteral feeds - not measured	CRITICAL	-
Adverse effects - not measured	IMPORTANT	-
Faltering growth/body composition - not measured	IMPORTANT	-
Duration of initial hospital stay - not measured	IMPORTANT	-
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Retinopathy of prematurity - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-
a. Downgraded one level for concerns for risk of bias b. Downgraded one level for inconsistency as evidence is only reported in a single study c. Downgraded one level for indirectness as no very preterm infants were included d. Downgraded one level as evidence is based on a single study e. Downgraded one level as both RCTs are from the same research group with one being a pilot and one the full study. f. Downgraded two levels for serious concerns for risk of bias including inadequate information on confounding factors g. Downgraded one level as this study included critically ill neonates and included term infants h. Downgraded one level as standard deviations are wide suggesting imprecision i. Downgraded one level as there is substantive variation around the median value suggesting imprecision		
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty	Possibly important uncertainty or variability.	

or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Values for Māori No additional evidence available.	
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Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ● Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Double versus sequential pumping - low certainty evidence Increased milk yield Double versus sequential pumping - very low certainty evidence Increased milk yield Balance of effects for Māori No additional evidence	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies	Access to breast pumps Prenatal educational resources Access to breastfeeding support specialist and staff Resourcing for Māori No additional evidence available	

○ Don't know		
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	The costs are reasonably certain. Certainty of evidence of the required costs for Māori No additional evidence available.	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No studies reported on the cost-effectiveness of breastmilk expression for mothers of preterm infants. Cost effectiveness for Māori No additional evidence available	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced	Equity for Māori Māori mothers of preterm pēpi Māori face systemic barriers that affect their ability to establish and	

○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	maintain breastfeeding. Early and frequent breastmilk expression is vital to improving milk supply and long-term breastfeeding success, yet pēpi Māori are less likely to be exclusively breastfed at discharge. Delayed or infrequent expression may worsen these outcomes and reinforce existing inequities. Given the impact of colonisation on health systems and whānau support, structured support for early and consistent expression can empower wāhine Māori. Prioritising these practices in neonatal care may enhance breastfeeding rates and promote culturally responsive care for whānau Māori with preterm pēpi. Equity for Pacific families Pacific mothers may face barriers to early and frequent milk expression due to limited support, inconsistent staff engagement or lack of culturally aligned guidance. Although Pacific infants had high rates of transition to mother's own milk only, 22% still received alternative nutrition by day three, suggesting gaps in consistent breastfeeding support. Delayed or less frequent breastmilk expression may contribute to reduced supply and interrupted feeding progress. Equity requires respectful education and proactive lactation support that affirms Pacific values and promotes confidence in maintaining milk supply from birth. Equity for underrepresented groups Mothers from migrant, rural or low-income backgrounds may experience delays in accessing pumps, lactation advice or culturally appropriate care. These barriers can reduce early expression and long-term supply. Equity demands timely resources, interpreter services and individualised support to ensure all mothers can establish and maintain breastmilk feeding. Promoting early and frequent expression can improve outcomes by creating more equitable opportunities for breastfeeding success. Ensuring access to equipment, culturally appropriate education and staff support across all neonatal settings is essential to closing the gap in feeding disparities.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	While early, frequent breastmilk expression is clinically recommended to support milk supply for preterm infants, acceptability will vary across mothers and families depending on a range of personal, cultural and systemic factors. Emotional readiness: Parents of preterm infants are often under intense emotional stress. Some may feel overwhelmed by the expectation to express milk frequently and early, especially in the first hours after birth. Physical discomfort or health: Breastmilk expression—especially with a pump—can be physically uncomfortable. Some mothers recovering from a complicated birth or surgery may not feel able to express immediately. Time and capacity: Sequential expression is time intensive. Mothers caring for	

	other children, managing work or without consistent support may struggle to commit to a strict schedule. Acceptability for Māori No additional evidence was available	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Both pumping methods are probably feasible. Feasibility for Māori No additional evidence available.	Huang <i>et al</i> [6] reported on an implementation project to promote early, frequent and effective breastmilk expression. Breastmilk expression within 6 hours of birth of preterm infants (<37 weeks') increased from 23% to 87%. Compliance of expression for 8–12 times daily in the first 48 h after delivery also experienced dramatic improvement from 0 to 50%. The volume of breastmilk expression in the first 24 hours increased from 2.10 +/- 5.45 to 7.72 +/-17.19 mL on average. In the following 24 h, the volume improved from 7.08 +/-12.98 to 43.77 +/-80.86 mL.

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know

	JUDGEMENT						
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	●	○	○	○

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3. Jones, E.; Dimmock, P.W.; Spencer, A. A randomised controlled trial to compare methods of milk expression after preterm delivery. *Archives of Disease in Childhood - Fetal and Neonatal Edition* **2001**, *85*, F91-95, doi:10.1136/fn.85.2.f91.
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6. Huang, X.; Zhang, J.; Zhou, F.; Yang, Y.; Lizarondo, L.; McArthur, A. Promotion of early breast milk expression among mothers of preterm infants in the neonatal ICU in an obstetrics and gynaecology hospital: a best practice implementation project. *JBIM Evid Implement* **2020**, *18*, 278-287, doi:10.1097/xeb.0000000000000223.

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EtD 42b. Should early breastmilk expression vs. delayed breastmilk expression be used for mothers of preterm infants?

POPULATION:	Mothers of preterm infants
INTERVENTION:	Early breastmilk expression
COMPARISON:	Delayed breastmilk expression
MAIN OUTCOMES:	Critical outcomes Breastmilk supply/volume Fully breastfed or breastmilk feeding at hospital discharge Necrotising enterocolitis Mortality Neurodevelopmental impairment Sepsis: proven or suspected Time to full enteral feeds Important but not critical Adverse effects Faltering growth/body composition Duration of initial hospital stay Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation- patient perspective
BACKGROUND:	Breastmilk is the optimal source of nutrition for preterm infants, providing essential nutrients, immune protection and developmental benefits. However, many mothers of preterm infants face challenges in establishing and maintaining milk supply, particularly when direct breastfeeding is not immediately possible. Effective breastmilk expression strategies are critical for ensuring sufficient milk production and supporting breastfeeding or breastmilk feeding at discharge. Early initiation of breastmilk expression, within one to six hours of birth, is believed to stimulate milk production by mimicking the natural hormonal responses that occur with direct breastfeeding. Delayed initiation of breastmilk expression may result in lower milk volumes and reduced breastfeeding or breastmilk feeding rates at discharge. The volume of breastmilk available for enteral feeding in the first two weeks after birth is an important determinant of how quickly parenteral nutrition can stop which reduces the risk of sepsis and whether the infant receives infant formula which increases the risk of necrotising enterocolitis. Understanding the evidence and whether it supports these practices and beliefs is essential to optimising milk production, minimising feeding related morbidity and mortality, and supporting breastfeeding success for mothers of preterm infants.

CONFLICT OF INTERESTS:

None

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Breastmilk expression within 6 hours of birth [1-4] Breastmilk supply/volume: Cohort: Expressing within 6 hours of birth was associated with higher milk yield on day 4 (88.3 g, 95% CI 7.1 to 169.4) and day 14 (155.7 g, 95% CI 12.2 to 299.3) but not on day 21 (73.6 g, 95% CI -91.4 to 238.7). There was an interaction between expressing frequency and time to first expression ($p < 0.005$), with increased expressing frequency being associated with higher yield only in those who expressed within 6 hours. Cohort study: Women who expressed milk within 6 hours of delivery produced more milk than women who started expressing after 6 hours. The increased lactation was attributable to women who commenced expressing within one hour of delivery [Critical]. Fully breastfed or breastmilk feeding at hospital discharge: Retrospective case histories: Initiation of breastfeeding in the first 6 hours of life was associated with a relatively high probability of exclusive breastfeeding at hospital discharge (OR 2.38; 95% CI 1.19–4.75). Desirable effects for Māori No additional evidence available	Breastmilk expression within 6 hours of birth [1] Infants 23+0 to 31+6 weeks postmenstrual age [2] Infants' gestational age of 34–36 weeks [3] ≤ 1500 grams and ≤ 32 weeks' gestation [4] ≤ 1500 grams and ≤ 32 weeks' gestation

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with breastmilk expression (, delayed,)	Risk difference with breastmilk expression (early,)
Breastmilk supply/volume: RCT: 60 (early), 61–180 (intermediate) or 181–360 (late) minutes following delivery assessed with: Milk volume	180 (1 RCT)	⊕⊕○○ Low ^{a,c}	-	For mothers who initiated early mother's own milk production over time was significantly lower through the 42 days ($p = 0.045$) compared to the late group but did not differ between the intermediate and late groups when controlling for covariates (mode of delivery and prior lactation experience). While the late expression group produced more others own milk during the first three days, there were no differences for days 4 to 7 or weekly for six weeks.	
Breastmilk supply/volume: Cohort: (early <6 hours vs. later >6 hours from birth) assessed with: Milk yield (g)	120 (2 non-randomised studies)	⊕○○○ Very low ^{a,b,c}	-	One cohort study (UK) reported 51.7% expressed within 6 hours of birth (62/120) and 48.3% expressed more than 6 hours after birth (58/120). Expressing within 6 hours of birth was associated with higher milk yield on day 4 (88.3 g, 95% CI 7.1 to 169.4) and day 14 (155.7 g, 95% CI 12.2 to 299.3) but not on day 21 (73.6 g, 95%	

				CI –91.4 to 238.7). There was an interaction between expressing frequency and time to first expression (p<0.005), with increased expressing frequency being associated with higher yield only in those who expressed within 6 hours. Expressing within 2 hours of birth was not associated with further milk yield increase. One cohort study (USA) compared breastmilk volume in women who started expressing 6 hours or less after delivery versus more than 6 hours. Women who expressed within 6 hours after delivery produced more breastmilk during the initial expression session and on Days 6, 7, and 42. When mothers who began milk expression prior to 1 hour following delivery were removed from analysis, benefits of milk expression within 6 hours were no longer apparent. Initiation of milk expression within 6 hours following delivery may not improve lactation success in mothers of VLBW infants unless initiated within the first hour.	
Fully breastfed or breastmilk feeding at hospital discharge: Retrospective case histories: early <6 hours vs. later >6 hours from birth	84 (1 non-randomised study)	⊕○○○ Very low ^{a,d,e}	-	Initiation of breastfeeding in the first 6 hours of life was associated with a relatively high probability of exclusive breastfeeding at hospital discharge (OR 2.38; 95% CI 1.19–4.75).	
Necrotising enterocolitis - not measured	-	-	-	-	-
Mortality - not measured	-	-	-	-	-
Neurodevelopmental impairment - not measured	-	-	-	-	-
Sepsis: proven or suspected - not measured	-	-	-	-	-
Time to full enteral feeds - not measured	-	-	-	-	-
Adverse effects - not measured	-	-	-	-	-
Faltering growth/body composition - not measured	-	-	-	-	-
Duration of initial hospital stay - not measured	-	-	-	-	-
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-

- a. Downgraded one level for indirectness as evidence is only reported in a single study
- b. Downgraded one level for indirectness as studies were not generalisable as only in very preterm infants and Very low birthweight infants
- c. Downgraded two levels for imprecision due to extremely wide confidence intervals
- d. Downgraded two levels for concerns with risk of bias
- e. Downgraded one level for indirectness as study was in late preterm infants only

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Breastmilk expression within 6 hours of birth [1-3] Breastmilk supply/volume: RCT: For mothers who initiated early mother's own milk production over time was significantly lower through the 42 days ($p=0.045$). While the late expression group produced more others own milk during the first three days, there were no differences for days 4 to 7 or weekly for six weeks. Undesirable effects for Māori No additional evidence available	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Low to very low certainty of evidence overall. Certainty of evidence for Māori No additional evidence available	

Outcomes	Importance	Certainty of the evidence (GRADE)
Breastmilk supply/volume: RCT: 60 (early), 61–180 (intermediate) or 181–360 (late) minutes following delivery assessed with: Milk volume	CRITICAL	⊕⊕○○ Low
Breastmilk supply/volume: Cohort: (early <6 hours vs. later >6 hours from birth) assessed with: Milk yield (g)	CRITICAL	⊕○○○ Very low
Fully breastfed or breastmilk feeding at hospital discharge: Retrospective case histories: early <6 hours vs. later >6 hours from birth	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis - not measured	CRITICAL	-
Mortality - not measured	CRITICAL	-
Neurodevelopmental impairment - not measured	CRITICAL	-
Sepsis: proven or suspected - not measured	CRITICAL	-

Time to full enteral feeds - not measured	CRITICAL	-
Adverse effects - not measured	IMPORTANT	-
Faltering growth/body composition - not measured	IMPORTANT	-
Duration of initial hospital stay - not measured	IMPORTANT	-
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Retinopathy of prematurity - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability Values for Māori No additional evidence available.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Breastmilk expression within 6 hours of birth - low certainty evidence Lower milk volume Breastmilk expression within 6 hours of birth - very low certainty evidence Increased initial milk volume Increased exclusive breastfeeding at hospital discharge Balance of effects for Māori No additional evidence	
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Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Access to breast pumps Prenatal educational resources Access to breastfeeding support specialist and staff Resourcing for Māori No additional evidence available	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	The costs are moderately certain. Certainty of evidence of required costs for Māori No additional evidence available.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No studies reported on the cost effectiveness of breastmilk expression for mothers of preterm infants. Cost effectiveness for Māori No additional evidence available	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Māori mothers of preterm pēpi Māori face systemic barriers that affect their ability to establish and maintain breastfeeding. Early and frequent breastmilk expression is vital to improving milk supply and long-term breastfeeding success, yet pēpi Māori are less likely to be exclusively breastfed at discharge. Delayed or infrequent expression may worsen these outcomes and reinforce existing inequities. Given the impact of colonisation on health systems and whānau support, structured support for early and consistent expression can empower wāhine Māori. Prioritising these practices in neonatal care may enhance breastfeeding rates and promote culturally responsive care for whānau Māori with preterm pēpi. Equity for Pacific families Pacific mothers may face barriers to early and frequent milk expression due to limited support, inconsistent staff engagement or lack of culturally aligned guidance. Although Pacific infants had high rates of transition to mother's own milk only, 22% still received alternative nutrition by day three, suggesting gaps in consistent breastfeeding support. Delayed or less frequent breastmilk expression may contribute to reduced supply and interrupted feeding progress. Equity requires respectful education and proactive lactation support that affirms Pacific values and promotes confidence in maintaining milk supply from birth.	

	Equity for underrepresented groups Mothers from migrant, rural or low-income backgrounds may experience delays in accessing pumps, lactation advice or culturally appropriate care. These barriers can reduce early expression and long-term supply. Equity demands timely resources, interpreter services and individualised support to ensure all mothers can establish and maintain breastmilk feeding. Promoting early and frequent expression can improve outcomes by creating more equitable opportunities for breastfeeding success. Ensuring access to equipment, culturally appropriate education and staff support across all neonatal settings is essential to closing the gap in feeding disparities.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	While early breastmilk expression is clinically recommended to support milk supply for preterm infants, acceptability will vary across mothers and families depending on a range of personal, cultural and systemic factors. Emotional readiness: Parents of preterm infants are often under intense emotional stress. Some may feel overwhelmed by the expectation to express milk especially in the first hours after birth. Physical discomfort or health: Breastmilk expression—especially with a pump—can be physically uncomfortable. Some mothers recovering from a complicated birth or surgery may not feel able to express immediately. Time and capacity: Mothers caring for other children, managing work or without consistent support may struggle to commit to a strict schedule. Acceptability for Māori No studies available	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes	Probably feasible. Feasibility for Māori	Huang <i>et al</i> [5] reported on an implementation project to promote early, frequent and effective breastmilk expression. Breastmilk expression within 6 hours of birth of preterm infants (<37 weeks) increased from 23% to

○ Varies ○ Don't know	No additional evidence available.	87%. Compliance of expression for 8–12 times daily in the first 48 h after delivery also experienced dramatic improvement from 0 to 50%. The volume of breastmilk expression in the first 24 hours increased from 2.10 +/- 5.45 to 7.72 +/-17.19 mL on average. In the following 24 h, the volume improved from 7.08 +/-12.98 to 43.77 +/-80.86 mL.
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Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies

	JUDGEMENT						
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ●	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
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EtD 42c. Should frequent breastmilk expression vs. less frequent breastmilk expression be used for mothers of preterm infants?

POPULATION:	Mothers of preterm infants
INTERVENTION:	Frequent breastmilk expression
COMPARISON:	Less frequent breastmilk expression
MAIN OUTCOMES:	Critical outcomes Breastmilk supply/volume Fully breastfed or breastmilk feeding at hospital discharge Necrotising enterocolitis Mortality Neurodevelopmental impairment Sepsis: proven or suspected Time to full enteral feeds Important but not critical Adverse effects Faltering growth/body composition Duration of initial hospital stay Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation-patient perspective
BACKGROUND:	Breastmilk is the optimal source of nutrition for preterm infants, providing essential nutrients, immune protection and developmental benefits. However, many mothers of preterm infants face challenges in establishing and maintaining milk supply, particularly when direct breastfeeding is not immediately possible. Effective breastmilk expression strategies are critical for ensuring sufficient milk production and supporting breastfeeding or breastmilk feeding at discharge. Early initiation of breastmilk expression, within one to six hours of birth, is believed to stimulate milk production by mimicking the natural hormonal responses that occur with direct breastfeeding. Delayed initiation of breastmilk expression may result in lower milk volumes and reduced breastfeeding or breastmilk feeding rates at discharge. The frequency of breastmilk expression may also be a key factor in maintaining lactation because this follows the natural feeding patterns of newborns and may help prevent low milk supply. The volume of breastmilk produced in the first 1 to 2 weeks may be a predictor of breastfeeding success. Insufficient expression frequency and volume may contribute to decreased milk production and early cessation of breastmilk feeding. The volume of breastmilk available for enteral feeding in the first two weeks after birth is an important determinant of how quickly parenteral nutrition can stop which reduces the risk of sepsis and whether the infant receives infant

	formula which increases the risk of necrotising enterocolitis. Additionally, double pumping (using an electric breast pump to express milk from both breasts simultaneously) may be more effective than single or sequential pumping. Understanding the evidence and whether it supports these practices and beliefs is essential to optimising milk production, minimising feeding related morbidity and mortality, and supporting breastfeeding success for mothers of preterm infants.
CONFLICT OF INTERESTS:	None

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Breastmilk expression within 6 hours of birth [1-4] Breastmilk supply/volume: Cohort: Expressing within 6 hours of birth was associated with higher milk yield on day 4 (88.3 g, 95% CI 7.1 to 169.4) and day 14 (155.7 g, 95% CI 12.2 to 299.3) but not on day 21 (73.6 g, 95% CI -91.4 to 238.7). There was an interaction between expressing frequency and time to first expression ($p < 0.005$), with increased expressing frequency being associated with higher yield only in those who expressed within 6 hours. Cohort study: Women who expressed milk within 6 hours of delivery produced more milk than women who started expressing after 6 hours. The increased lactation was attributable to women who commenced expressing within one hour of delivery [Critical]. Fully breastfed or breastmilk feeding at hospital discharge: Retrospective case histories: Initiation of breastfeeding in the first 6 hours of life was associated with a relatively high probability of exclusive breastfeeding at hospital discharge (OR 2.38; 95% CI 1.19–4.75). Double pumping [5-9] Breastmilk supply/volume: RCT: Milk yield higher with double pump vs. sequential expression [Critical]. Frequent expression of breastmilk (≥ 8 times in 24 hours) after preterm birth [10] Breastmilk supply/volume: Cohort: Expressing frequency was positively associated with 24-hour milk yield. Expressing 8 or more times per day was associated with higher adjusted milk yield than expressing < 6 times (on day four, 146.8g, 95% CI 47.4 to 246.1), but not in comparison to expressing 6–7 times (on day four, 82.1g, 95% CI -25.9 to 190.1) Desirable effects for Māori No additional evidence available	Breastmilk expression within 6 hours of birth Levene 2024 [1] Infants 23+0 to 31+6 weeks postmenstrual age Prikhodko 2022 [2] Infants gestational age of 34–36 weeks Parker 2020 [3] ≤ 1500 g and ≤ 32 weeks' gestation Parker 2015 [4] ≤ 1500 g and ≤ 32 weeks' gestation Double pumping Jones 2001 [7] Overall mean infant birthweight was 1535 g (1610 g in the sequential group, and 1460 g in the simultaneous group); mean gestational age was 29.97 weeks (sequential 29.9, simultaneous 30.2). Hill 1996; Hill 1999 [5,6] < 1500 gm and < 32 weeks' gestation Köroğlu 2017 [8] Gestational ages of the infants varied between 25 to 38 weeks (31.9 ± 3.8) and their birthweights were within 760 and 3200 g (1554.8 ± 663.6). Fewtrell 2016 [9] Cohort analysis within a RCT. Babies < 34 weeks admitted to neonatal intensive care. Frequent expression of breastmilk (≥ 8 times in 24 hours) after preterm birth

		Levene 2024 [10] Infants were between 23+0- and 31+6-weeks' gestation. Some additional studies were identified that reported on frequency of expression but did not report on 8 or more sessions. Cohort study [11]. Preterm infants with gestational age 32 weeks or birthweight 1,500 g. Milk outputs on days 7, 14, and 42 of mothers with a pumping frequency of ≥ 6 times/d were greater than mothers with a pumping frequency of 6 times/day. On postpartum day 42, this difference was statistically significant ($t=-2.828$, $p=0.009$). Cohort study [12]. Babies <34 weeks' gestation. High intensity pumping (HIPG) resulted in significantly greater mean daily milk volume over the 14-day study compared with low intensity pumping (LIPG). Compared to mothers in the LIPG, HIPG mothers pumped more frequently per day (5 ± 2 times vs. 2 ± 2 times, $p < 0.001$), The 14-day cumulative mean pumped MOM volumes for the HIPG and LIPG were 4769 ± 3154 mL and 2582 ± 1492 mL, respectively ($p=0.02$). Cohort study [1] There was an interaction between expressing frequency and time to first expression ($p<0.005$), with increased expressing frequency being associated with higher yield only in those who expressed within 6 hours. Infants were 23+0- and 31+6-weeks' gestation. Australian cohort study [13]. Infants with median gestational age 29 weeks (24 to 32 weeks range). Comparing three expressions a day to four, five and six expressions/day there was no significant increase between three and four expressions or three and five expressions, but an increase between three and six expressions (228 g (95% CI: 43 to 414), $p=0.006$). Comparing four expressions a day to five and six, there
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		were increases for both (five: 170 g (95% CI: 42 to 298), $p=0.002$, six: 223 g (95% CI: 77 to 370), $p<0.001$). The daily milk production was not different between frequency of expressions of five, six, seven, eight and nine times. Mother should express 5+ times/day with a maximum interval of 7 hours. USA cohort study [14] of infants admitted to Neonatal Intensive Care Unit mean birthweight 1909 ± 902 g. Pumping frequencies stabilised by postnatal day 5, with mothers who achieved coming to volume (CTV; ≥ 500 mL/day for at least one 24-hour period during the first 14 days) pumping an average of 5 times per day, and those who did not achieve CTV pumping approximately 3 times per day on postnatal day 5. Of women who were pumping at least 5/day $\times$ Day 5, 66.7% achieved CTV compared with 29.4% of those who did not CTV.
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Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with breastmilk expression (double, delayed, less frequent)	Risk difference with breastmilk expression (sequential, early, frequent)
Breastmilk supply/volume: RCT: Sequential vs. double pump assessed with: Weight (g)	36 (1 RCT)	⊕○○○ Very low ^{a,b,c}	-	Milk yield is higher with double pump vs. sequential expression (88 g; 95%CI 79 - 97 vs. 51 g; 95%CI 46-56; $P< 0.01$).	
Breastmilk supply/volume: RCT: Sequential vs. double pump assessed with: Weight (g)	48 (2 RCTs)	⊕⊕○○ Low ^{a,d}	-	Pilot study $n=9$ Mean daily milk yield in the sequential single group ranged from a low of 158.4 gm on day 3 to a high of 505.8 g on day 20. The mean daily milk yield in the double pump group ranged from a low of 41.4 g on day 3 to a high of 741 g on day 41. The overall mean milk yield for the 40 days in the sequential single and double pump groups was 395.2 (SD 270.9) and 445.3 (SD 188.9) g, respectively. RCT $n=39$ Milk weight change was higher for double pump than sequential groups between weeks 2 and 5 ($P=0.049$).	
Breastmilk supply/volume: RCT: 60 (early), 61–180	180	⊕⊕○○	-	For mothers who initiated early mother's own milk production over time was	

(intermediate) or 181–360 (late) minutes following delivery assessed with: Milk volume	(1 RCT)	Low ^{b,e}		significantly lower through the 42 days (p=0.045) compared to the late group but did not differ between the intermediate and late groups when controlling for covariates (mode of delivery and prior lactation experience). While the late expression group produced more others own milk during the first three days, there were no differences for days 4 to 7 or weekly for six weeks.	
Breastmilk supply/volume: Cohort: (early <6 hours vs. later >6 hours from birth) assessed with: Milk yield (g)	120 (1 non-randomised study)	⊕○○○ Very low ^{b,e,f}	-	One cohort study (UK) reported 51.7% expressed within 6 hours of birth (62/120) and 48.3% expressed more than 6 hours after birth (58/120). Expressing within 6 hours of birth was associated with higher milk yield on day 4 (88.3 g, 95% CI 7.1 to 169.4) and day 14 (155.7 g, 95% CI 12.2 to 299.3) but not on day 21 (73.6 g, 95% CI -91.4 to 238.7). There was an interaction between expressing frequency and time to first expression (p<0.005), with increased expressing frequency being associated with higher yield only in those who expressed within 6 hours. Expressing within 2 hours of birth was not associated with further milk yield increase.	
Breastmilk supply/volume: Cohort: Frequent vs. less frequent expression	132 (1 non-randomised study)	⊕○○○ Very low ^{b,f}	-	Expressing frequency was positively associated with 24-hour milk yield, with an adjusted 30.5g increase per expressing session on day four (95% CI 15.7 to 45.3) and 94.4g on day 21 (95% CI 62.7 to 126.2). Expressing 8 or more times per day was associated with higher adjusted milk yield than expressing <6 times (on day four, 146.8g, 95% CI 47.4 to 246.1), but not in comparison to expressing 6–7 times (on day four, 82.1g, 95% CI -25.9 to 190.1).	
Fully breastfed or breastmilk feeding at hospital discharge: Retrospective case histories: early <6 hours vs. later >6 hours from birth	84 (1 non-randomised study)	⊕○○○ Very low ^{b,c,g}	-	Initiation of breastfeeding in the first 6 hours of life was associated with a relatively high probability of exclusive breastfeeding at hospital discharge (OR 2.38; 95% CI 1.19–4.75).	
Necrotising enterocolitis - not measured	-	-	-	-	-
Mortality - not measured	-	-	-	-	-
Neurodevelopmental impairment - not measured	-	-	-	-	-
Sepsis: proven or suspected - not measured	-	-	-	-	-
Time to full enteral feeds - not measured	-	-	-	-	-
Adverse effects - not measured	-	-	-	-	-
Faltering growth/body composition - not measured	-	-	-	-	-
Duration of initial hospital stay - not measured	-	-	-	-	-
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds - not measured	-	-	-	-	-

- a. Downgraded one level for concerns for risk of bias
- b. Downgraded one level for indirectness as evidence is only reported in a single study
- c. Downgraded one level for indirectness as not generalisable as no very preterm infants were included
- d. Downgraded one level for imprecision due to low sample numbers
- e. Downgraded one level for indirectness as study was in very preterm infants only
- f. Downgraded two levels for imprecision due to extremely wide confidence intervals
- g. Downgraded two levels for concerns with risk of bias

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Breastmilk expression within 6 hours of birth [1-3] Breastmilk supply/volume: RCT: For mothers who initiated early mother's own milk production over time was significantly lower through the 42 days ($p=0.045$). While the late expression group produced more others own milk during the first three days, there were no differences for days 4 to 7 or weekly for six weeks. Undesirable effects for Māori No additional evidence available	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Low to very low certainty of evidence overall. Certainty of evidence for Māori No additional evidence available	

Outcomes	Importance	Certainty of the evidence (GRADE)
Breastmilk supply/volume: RCT: Sequential vs. double pump assessed with: Weight (g)	CRITICAL	⊕○○○ Very low
Breastmilk supply/volume: RCT: Sequential vs. double pump assessed with: Weight (g)	CRITICAL	⊕⊕○○

		Low
Breastmilk supply/volume: RCT: 60 (early), 61–180 (intermediate) or 181–360 (late) minutes following delivery assessed with: Milk volume	CRITICAL	⊕⊕○○ Low
Breastmilk supply/volume: Cohort: (early <6 hours vs. later >6 hours from birth) assessed with: Milk yield (g)	CRITICAL	⊕○○○ Very low
Breastmilk supply/volume: Cohort: Frequent vs. less frequent expression	CRITICAL	⊕○○○ Very low
Fully breastfed or breastmilk feeding at hospital discharge: Retrospective case histories: early <6 hours vs. later >6 hours from birth	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis - not measured	CRITICAL	-
Mortality - not measured	CRITICAL	-
Neurodevelopmental impairment - not measured	CRITICAL	-
Sepsis: proven or suspected - not measured	CRITICAL	-
Time to full enteral feeds - not measured	CRITICAL	-
Adverse effects - not measured	IMPORTANT	-
Faltering growth/body composition - not measured	IMPORTANT	-
Duration of initial hospital stay - not measured	IMPORTANT	-
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Retinopathy of prematurity - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds - not measured	NOT IMPORTANT	-

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Frequent expression of breastmilk (≥ 8 times in 24 hours) after preterm birth - very low certainty evidence Increased milk yield Balance of effects for Māori No additional evidence	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Access to breast pumps Prenatal educational resources Access to breastfeeding support specialist and staff Resourcing for Māori No additional evidence available	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	A formal assessment of the certainty of evidence of the cost was not undertaken. Certainty of evidence of required costs for Māori No additional evidence available.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No studies reported on the cost effectiveness of breastmilk expression for mothers of preterm infants. Cost effectiveness for Māori No additional evidence available	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Māori mothers of preterm pēpi Māori face systemic barriers that affect their ability to establish and maintain breastfeeding. Early and frequent breastmilk expression is vital to improving milk supply and long-term breastfeeding success, yet pēpi Māori are less likely to be exclusively breastfed at discharge. Delayed or infrequent expression may worsen these outcomes and reinforce existing inequities. Given the impact of colonisation on health systems and whānau support, structured support for early and consistent expression can empower wāhine Māori. Prioritising these practices in neonatal care may enhance breastfeeding rates and promote culturally responsive care for whānau Māori with preterm pēpi. Equity for Pacific families Pacific mothers may face barriers to early and frequent milk expression due to limited support, inconsistent staff engagement or lack of culturally aligned guidance. Although Pacific infants had high rates of transition to mother's own milk only, 22% still received alternative nutrition by day three, suggesting gaps in consistent breastfeeding support. Delayed or less frequent breastmilk expression may contribute to reduced supply and interrupted feeding progress. Equity requires respectful education and proactive lactation support that affirms Pacific values and promotes confidence in maintaining milk supply from birth. Equity for underrepresented groups Mothers from migrant, rural or low-income backgrounds may experience delays in accessing pumps, lactation advice or culturally appropriate care. These barriers can reduce early expression and long-term supply. Equity demands timely resources, interpreter services and individualised support to ensure all mothers can establish and maintain breastmilk feeding. Promoting early and frequent expression can improve outcomes by creating more equitable opportunities for breastfeeding success. Ensuring access to equipment, culturally appropriate education and staff support across	

	all neonatal settings is essential to closing the gap in feeding disparities.	
Acceptability Is the intervention acceptable to key interest-holders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	While early, frequent breastmilk expression is clinically recommended to support milk supply for preterm infants, acceptability will vary across mothers and families depending on a range of personal, cultural and systemic factors. Emotional readiness: Parents of preterm infants are often under intense emotional stress. Some may feel overwhelmed by the expectation to express milk frequently and early, especially in the first hours after birth. Physical discomfort or health: Breastmilk expression—especially with a pump—can be physically uncomfortable. Some mothers recovering from a complicated birth or surgery may not feel able to express immediately. Time and capacity: Sequential and frequent expression is time intensive. Mothers caring for other children, managing work or without consistent support may struggle to commit to a strict schedule. Acceptability for Māori No additional evidence available	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Frequent expression is feasible if adequate equipment, education and support is available. Feasibility for Māori No additional evidence available.	Huang <i>et al</i> [15] reported on an implementation project to promote early, frequent and effective breastmilk expression. Breastmilk expression within 6 hours of birth of preterm infants (<37 weeks) increased from 23% to 87%. Compliance of expression for 8–12 times daily in the first 48 hours after delivery also experienced dramatic improvement from 0 to 50%. The volume of breastmilk expression in the first 24 hours increased from 2.1 +/- 5.5 to 7.7 +/-17.2 mL on average. In the following 24 h, the volume improved from 7.1 +/-13.0 to 43.8 +/-80.9 mL.

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	●	○

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EtD 43. Should the first feed for preterm infants be mother's expressed breastmilk vs. other milk to reduce the risk of mothers discontinuing optimal expressing or breastfeeding?

POPULATION:	Preterm infants
INTERVENTION:	First feed of mother's expressed breastmilk
COMPARISON:	other milk reducing risk of mothers discontinuing optimal expressing or breastfeeding
MAIN OUTCOMES:	Critical for making a decision Fully breastmilk feeding at hospital discharge Fully breastfeeding at hospital discharge Time to full enteral feeds Necrotising enterocolitis (NEC) Adverse effects Important but not critical Mortality Neurodevelopmental impairment Faltering growth / body composition Duration of initial hospital stay Bronchopulmonary dysplasia Sepsis: proven or suspected Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Of limited importance Time to full sucking feeds
SETTING:	Postnatal neonatal care
PERSPECTIVE:	
BACKGROUND:	Preterm infants often receive expressed breastmilk as their first feed. Early provision of a mother's own expressed breastmilk may support continued expressing and breastfeeding by enhancing maternal confidence and maintaining milk supply. Conversely, initial feeding with donor milk or infant formula may impact maternal motivation, lactation outcomes and breastfeeding continuation rates. Supporting mothers to provide their milk for their baby's first feed may be a key strategy for promoting optimal longer-term feeding outcomes. Equity considerations are critical because systemic barriers may prevent some mothers from accessing lactation support services or timely breastmilk expression opportunities after preterm birth. Ensuring that the first feed is a mother's own expressed breastmilk whenever possible could contribute to improving breastfeeding rates and long-term health outcomes, particularly for populations at higher risk of preterm birth, breastfeeding challenges and infant morbidity.
CONFLICT OF	The following DIAMOND cohort study authors are on the Guideline Development Group:

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	This is a narrative summary of evidence on whether the first feed being mothers' EBM compared with other milk reduces the risk of mothers discontinuing optimal expressing or breastfeeding. Fully breastfeeding at hospital discharge: Moderate to late preterm infants who successfully transitioned from parenteral fluids onto only mother's own milk were more likely to be exclusively breastmilk at discharge (Aotearoa New Zealand based RCT) [critical]. Fully breastmilk feeding at hospital discharge: A large study of infants <33 weeks' gestational age (n=6,404) found that feeding mother's own milk on/by day 3 was associated with higher odds of any breastmilk feeding at discharge. A delay in the initiation of supplementation was associated with higher breastfeeding at discharge rates (n=3,102) [critical]. Adverse effects: Receipt of formula as the first milk feed was associated with a reduction in exclusive breastfeeding at 6 weeks corrected age (n=279) [Critical]. Time to full enteral feeds: In one large study (n= 1273), there was no significant difference in days to reach full enteral feeds, days on which feeds were interrupted, discharge weight, or length between infants who received their mother's own milk, formula or donor milk [Important]. Length of hospital stay: In one study (n= 1273), there was no significant difference in length of stay, between infants who received their mother's own milk, formula or donor milk. In a smaller study (n=279), length of stay was 2.9 days longer for infants who received any formula compared with those receiving only breastmilk [Important]. No faltering growth/body composition: In one large study (n= 1273), there was no significant difference in discharge weight, or length between infants who received their mother's own milk, formula or donor milk [Important].	Aotearoa New Zealand: Cohort within a RCT [1]. Moderate to late preterm infants (32 to 35+6 weeks' gestational age). Australia/New Zealand/Singapore: Secondary analysis of an RCT [2]: <29 weeks' gestational age. Australia: Prospective cohort [3]: Late preterm infants. Ireland: Retrospective review [4]: Moderate-late preterm infants ≥1500g. Canada. Cohort study [5]: Infants <33 weeks' gestation. USA: Retrospective cohort [6]: ≥35 to 36+6 weeks' gestation.

	Further details are below: Alexander 2022 [1]: 93/151 (63%) successfully transition from parenteral fluids to mother's own milk only (43% Māori, 73% Pacific, 70% European). Receiving exclusively breastmilk at discharge was more likely for infants who successfully transitioned from IV fluids onto mother's own milk only OR 4.9; 95%CI 2.3–10.6; $P<0.0001$. Hilditch 2022 [2]: Of 1273 infants, 93.2% received mother's own milk as the first enteral feed, 3.7% received formula and 3.5% received donor milk as first feed. At discharge or estimated date of delivery 66.1% received mother's own milk, 42.1% formula and 0.4% donor milk. Infants born ≥ 27 weeks were more likely to receive mother's own milk as the first feed. There was no significant difference in days to reach full enteral feeds which varied from 17.7 days for mother's own milk, 15.1 for donor milk and 18.0 days for formula milk. There was no significant difference in the number of days on which feeds were interrupted; Mean 7.4 days for mother's own milk (donor milk 2.20 days fewer; 4.90 days fewer to 0.49 days more; $P=0.11$; formula milk 1.01 days fewer; 3.23 fewer to 1.20 more; $P=0.37$). Length of stay did not vary significantly between mother's own milk fed, donor milk fed or formula fed infants. Mean 97.1 days for mother's own milk group (donor milk 8.46 days fewer; 17.70 fewer to 0.78 more; $p=0.07$; formula milk 2.50 days fewer; 16.10 fewer to 11.09 more; $p=0.72$). There was no difference in discharge weight or length between infants who received their mother's own milk, formula or donor milk. Head circumference at discharge was larger in infants who received formula 0.59 cm more (0.06 more to 1.12 more; $P=0.03$). Mean head circumference for mother's own milk was 33.4 cm. Keir 2022 [3]: Of 270 infants, 78% received breastmilk only as their first feed. 83% received formula during hospitalisation. 74% of infants were exclusively breastfed at discharge, 41% at 6 weeks corrected age. The mean duration of hospitalisation was 2.9 days longer (95%CI 0.31-5.43; $p=0.03$) in infants who received any formula compared with those receiving only breastmilk. Receipt of formula as the first milk feed was associated with a reduction in exclusive breastfeeding at 6 weeks corrected age (OR 0.22; 95% CI 0.09 to 0.53). Piquet 2019 [4]: 110 infants. The number of infants receiving mother's milk exclusively remained consistent from the time of their first feed to when they were discharged from the unit (26% compared to 27%). Of the 29 infants who were given mother's milk on their first feed, 59% were fed exclusive mother's milk on discharge. A relatively small (14%) number of these were receiving all	
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	exclusive mother's milk feeds throughout their admission and on discharge. 20% of infants who received formula on first feeds were receiving exclusive breastmilk on discharge. Dharell 2021 [5]: 6,404 infants. Feeding mother's own milk on/by day 3 of age was associated with significantly higher odds of any breastmilk feeding at neonatal intensive care discharge (adj OR 3.61; 95%CI 3.17 to 4.12). Of infants who received formula only at discharge, 629/1947 (32.3%) had received breastmilk at day 3 of life. Of infants who were discharged, receiving any breastmilk 2773/4457 (62.2%) had received breastmilk at day 3 of life (P<0.001). Kumar 2024 [6]: 3,102 infants. Among the entire cohort, 1,031 (33.2%) were breastfed at discharge, and 2,071 (66.7%) were formula fed at discharge. Median time to first supplementation was 6.4 hours (2.2– 13.1 hours). This was earlier among late preterm infants, small-for-gestational age and infants of diabetic mothers (4.4 hours (1.5–10.3 hours). Overall, a delay in the initiation of supplementation was associated with higher breastfeeding at discharge rates. The adjusted odds of breastfeeding at discharge increased by 2.8% (95% CI 1.022, 1.035) for each hour of delay in the commencement of supplementation from time from birth. 223 (7.2%) received supplementation with expressed breastmilk (EBM) at least once. Even one EBM supplementation was associated with higher odds of breastfeeding at discharge (adj OR 9.8; 95%CI 7.2 - 13.3; p<0.001). Desirable effects for Māori No additional evidence available	
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Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies	None reported	

● Don't know		
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	These studies are observational and cohort studies or retrospective reviews of cases and are not judged as high quality. The certainty of evidence is judged as very low overall.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important variability	
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies	First feed of mother's own milk versus other milk for reducing the risk of mothers discontinuing optimal expressing or breastfeeding - Low certainty evidence Increase in breastfeeding at discharge Uncertain effect on growth, length of stay, time to full enteral feeding, and feed interruptions	

○ Don't know		
Resources required		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Minimal resources required.	
Certainty of evidence of required resources		
What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Reasonably certain.	
Cost effectiveness		
Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No studies were available.	
Equity		

What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Pēpi Māori are less likely to transition to enteral feeds with their mother's expressed breastmilk, with only 43% doing so compared to greater use of alternative sources such as formula (Alexander et al. 2022). Pēpi Māori are also significantly less likely to be exclusively breastfed at discharge (odds ratio 0.2, 95 % confidence interval 0.1 to 0.6, P <0.0006) (Hilditch et al. 2024). Ensuring pēpi Māori receive their mother's own milk for the first feed is critical for promoting breastfeeding continuation, supporting whakapapa and addressing entrenched inequities in neonatal and long-term health outcomes. Equity for Pacific families Pacific families may not be informed of how the first feed influences breastfeeding outcomes, especially if mother's milk is not immediately available. Without inclusive education, donor milk or formula may be used by default. Equity requires clear communication and culturally respectful support for expressing from the outset. Equity for underrepresented groups Families from underrepresented communities may have less access to donor milk or expressing support in the early hours after birth. If formula is offered without guidance, breastfeeding may be compromised. Equity means ensuring all families understand their options and are supported to provide their own milk when possible.	(Alexander et al., 2022): Alternative sources of milk, mostly formula, were used to transition from IV fluids onto enteral feeds more often in Māori, only 43% transitioned to mothers' own milk only. Receiving breastmilk exclusively at discharge was less likely for Māori than European infants OR 0.2; 95%CI 0.1–0.6, p<0.0006. (Hilditch et al., 2024) Infants were less likely to receive breastmilk as first feed if they were Indigenous (OR 0.25; 95%CI 0.07 to 0.86; p=0.03); Northeast Asian (OR 0.09; 95%CI 0.04 to 0.21; p<0.0001) or Southeast Asian (OR 0.19; 95%CI 0.07 to 0.50; p=0.0008).

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Probably acceptable for most.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Feasible	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies

	JUDGEMENT						
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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EtD 44. Should mothers of preterm infants have access to lactation consultant services vs. no access to lactation consultant services?

POPULATION:	Mothers of preterm infants
INTERVENTION:	Access to lactation consultant services
COMPARISON:	No access to lactation consultant services
MAIN OUTCOMES:	Critical for making a decision Exclusive breastmilk at hospital discharge Fully breastfeeding at hospital discharge any breastmilk at discharge Important but not critical Any breastmilk within 24 hours after birth Length of stay (days) Any breastmilk during hospital stay Time to full enteral feeds (days) Lactation consultant access
SETTING:	Postnatal neonatal setting
PERSPECTIVE:	Clinical guideline recommendation: patient perspective
BACKGROUND:	A preterm infant is born before the later stages of pregnancy which are important for the accretion of nutrients, resulting in nutrient deficiency and deficits in growth and neurodevelopment. Optimal nutrition plays a key role in growth, neurodevelopment, metabolism and the overall survival of preterm infants. Studies have shown that preterm infants fed their own mother's breastmilk experience considerable health benefits, a strengthened immune system, cognitive improvements and fewer complications compared to those who are not breastmilk fed. For this reason, mothers' breastmilk is considered an optimal source of nutrition. Despite mothers' breastmilk being so important, many mothers of preterm infants face a range of challenges when it comes to expressing breastmilk and breastfeeding; in particular, difficulties in establishing milk supply. Lactation consultants can provide education and support to improve breastfeeding outcomes, but they are a limited resource and some mothers do not have access to a lactation consultant so evidence of their impact is crucial. Important outcomes to consider are exclusive breastmilk at hospital discharge, fully breastfeeding at hospital discharge, any breastmilk at discharge and during hospital stay, as well as length of stay and time to full enteral feeds. Ensuring optimal breastmilk outcomes are achieved in a cost-effective way is critical in determining the overall health outcomes of the infant.
CONFLICT OF INTERESTS:	The following systematic review authors for this topic are on the Guideline Development Group: Chloe Bell and Luling Lin and Barbara Cormack

Assessment

Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know		[1] USA. Survey and audit. Babies in neonatal care including preterm and term infants. [2] USA. Cross-sectional study. 45% of infants were <37 weeks' gestation. [3] USA. Retrospective chart review. Early preterm non-Hispanic Black infants. [4] USA. Retrospective chart review. Babies <34 weeks' gestation. [5] USA. Quality improvement project. Mean gestational age 36.9 weeks. [6] USA. Retrospective chart review. Mean gestational by time period in study age 34-36 weeks. [7] USA. Retrospective observational study. Babies <30 weeks' gestation. [8] Slovenia. Retrospective observational study. Very low birthweight preterm infants. [9] USA. Retrospective chart review. 64% of infants were <37 weeks' gestation. [10] USA. Cross-sectional study. Very low birth weight infants. [11] Ireland. Retrospective chart review. Very low birth weight infants. [12] USA. Descriptive correlational study and follow-up. 33% of infants were <37 weeks' gestation.
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					[13] USA. Retrospective chart review. Very low birth weight infants. [14] USA. Retrospective cohort study. Babies </= 32 weeks' gestation. [15] France. National cohort. Babies 32-34 weeks' gestation. [16] USA. Quality improvement study. Very low birthweight infants. [17] Austria. Retrospective chart review. Very low birthweight infants. [18] USA. Retrospective study. Babies 23-41 weeks' gestation.
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Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with No Access to Lactation Consultant Services	Risk difference with Access to Lactation Consultant Services
Any Breastmilk within 24 hrs after Birth	262 (2 non-randomised studies)	⊕○○○ Very low ^{a,b}	OR 1.79 (1.05 to 3.03)	Study population	
				577 per 1,000	132 more per 1,000 (12 more to 228 more)
Lactation Consultant Access	735 (2 non-randomised studies)	⊕○○○ Very low ^{a,c,d}	OR 21.81 (4.11 to 115.73)	Study population	
				245 per 1,000	631 more per 1,000 (326 more to 729 more)
Length of Stay (days)	770 (6 non-randomised studies)	⊕○○○ Very low ^{a,d,e}	-	The mean length of Stay (days) was 49.49	MD 0.08 lower (4.06 lower to 3.91 higher)
Any Breastmilk during Hospital Stay	3413 (7 non-randomised studies)	⊕○○○ Very low ^a	OR 1.56 (1.14 to 2.13)	Study population	
				436 per 1,000	111 more per 1,000 (32 more to 186 more)
Exclusive Breastmilk at Discharge	616 (4 non-randomised studies)	⊕○○○ Very low ^{a,c,g}	OR 1.88 (0.88 to 4.02)	Study population	
				251 per 1,000	135 more per 1,000 (23 fewer to 323 more)
Time to Full Enteral Feeds (days)	270	⊕○○○	-	The mean time to Full Enteral Feeds	MD 1 lower

	(2 non-randomised studies)	Very low ^{a,b}		(days) was 12.84	(1.17 lower to 0.82 lower)
Fully breastfeeding at discharge - not reported	-	-	-	-	-
Any Breastmilk at Discharge	3629 (12 non-randomised studies)	⊕○○○ Very low ^{a,c,d}	OR 1.46 (0.93 to 2.27)	Study population	
				546 per 1,000	91 more per 1,000 (18 fewer to 186 more)

- a. Downgraded one level for risk of bias due to low quality of the studies.
b. Downgraded one level for imprecision due to insufficient sample size.
c. Downgraded two levels for inconsistency due to considerable heterogeneity.
d. Downgraded one level for imprecision due to wide confidence interval.
e. Downgraded one level for inconsistency due to substantial heterogeneity.
g. Downgraded two levels for imprecision due to insufficient sample size and wide confidence interval.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	No undesirable effects reported Undesirable effects for Māori No additional evidence available	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies		

Outcomes	Importance	Certainty of the evidence (GRADE)
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Any Breastmilk within 24 hrs after Birth	IMPORTANT	⊕○○○ Very low
Lactation Consultant Access	IMPORTANT	⊕○○○ Very low
Length of Stay (days)	IMPORTANT	⊕○○○ Very low
Any Breastmilk during Hospital Stay	IMPORTANT	⊕○○○ Very low
Exclusive Breastmilk at Discharge	CRITICAL	⊕○○○ Very low
Time to Full Enteral Feeds (days)	IMPORTANT	⊕○○○ Very low
Fully breastfeeding at discharge - not reported	CRITICAL	-
Any Breastmilk at Discharge	CRITICAL	⊕○○○ Very low

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Broom (2022) [1] included a staff survey in their cohort study, outlining that staff perceived that lactation consultants helped immensely in ensuring that mothers' educational needs around lactation were met and in mothers' confidence to continue breastfeeding post-discharge. There is no other qualitative research evidence available that discusses values regarding patient preferences, cultural values, or societal norms.	In an Aotearoa New Zealand context, it will need to be evaluated if mothers feel as though lactation consultant service support is valuable to their breastfeeding outcomes and overall hospital experience.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Lactation consultant services versus no lactation consultant services - very low certainty evidence Increase in any breastmilk within 24 hours after birth, lactation consultant access, any breastmilk during hospital stay Decrease time to full enteral feeds Uncertain effect on any breastmilk at discharge, duration of hospital stay, exclusive breastmilk at discharge Balance of effects for Māori No additional evidence	
Resources required		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Lactation Consultant Salary - Health New Zealand \$116,040 to \$127,674 per annum In Australian neonatal units, the recommended staffing level for International Board-Certified Lactation Consultants is 1 FTE (Full-Time Equivalent) per 235 infant admissions to neonatal intensive care. Therefore, the cost would be \$494 to \$543 per infant admission Starship Child Health, Auckland City Hospital has approx. 850 admissions per year. Additionally, some guidelines suggest 0.1 FTE per 1000 deliveries for program development/administration and education, and 0.1 to 0.2 FTE for research.	
Certainty of evidence of required resources		
What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Very low ○ Low ● Moderate ○ High ○ No included studies	Certain. Certainty of evidence of required resources for Māori No additional evidence available	
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Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	One cost-effectiveness study by Rice <i>et al</i> [19], in the UK, assessed the cost-effectiveness of providing <i>enhanced staff contact</i> to mothers of low-birth-weight infants in NICU, defined as providing individualised education, support and care plans by specially trained NICU staff. Compared to standard care, the intervention was found to lower overall costs and improve health outcomes across all weight groups, driven largely by increased breastmilk intake and reduced NEC. The model estimated savings of £66–£586 per infant and quality-adjusted life-years (QALYs) of +0.01 – +0.25, with the largest cost saving (£586 per infant) and health gain (+0.25 QALYs) in the 500–999 g group. These findings suggest that enhanced staffing focused on lactation support may be a cost-effective strategy, especially for infants under 1,750 g. However, the authors emphasised that this was the first economic evaluation in this field and highlighted the need for further research to confirm these findings with greater confidence. The only cohort study research evidence around the cost of access to lactation consultant services versus no access is from Gonzalez 2003 [9]. However, it would need to be considered that this data is from 2003 and from the USA. Data from Gonzalez, 2003, showed that: <u>Cost of NICU stay below \$10,000</u>: 27% before initiating lactation consultant services in a single hospital versus 33% after initiating lactation consultant services. <u>Cost of NICU stay between \$10,000-19,999</u>: 27% before initiating lactation consultant services in a single hospital versus 29% after initiating lactation consultant services. <u>Cost of NICU stay between \$20,000-29,999</u>: 14% before initiating lactation consultant services in a single hospital versus 11% after initiating lactation consultant services. <u>Cost of NICU stay at or above \$30,000</u>: 31% before initiating lactation consultant services in a single hospital versus 26% after initiating lactation consultant services. Cost effectiveness for Māori No evidence available.	A cost-effectiveness analysis may need to be undertaken in Aotearoa New Zealand.

Equity

What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Māori mothers of preterm pēpi face systemic barriers that affect their ability to establish and maintain breastfeeding. Early and frequent breastmilk expression is vital to improving milk supply and long-term breastfeeding success, yet pēpi Māori are less likely to be exclusively breastfed at discharge. Delayed or infrequent expression may worsen these outcomes and reinforce existing inequities. Given the impact of colonisation on health systems and whānau support, structured support for early and consistent expression can empower wāhine Māori. Prioritising these practices in neonatal care may enhance breastfeeding rates and promote culturally responsive care for whānau Māori with preterm pēpi. Equity for Pacific families Access to neonatal lactation consultants may be inconsistent for Pacific families, especially where services are not culturally grounded or translated. Delayed or missed referrals can impact breastfeeding outcomes. Equity requires timely access to trained consultants who understand and respond to the needs of Pacific mothers and infants. Equity for underrepresented groups Mothers in rural, migrant or underserved communities may not receive early referral to lactation support, especially if they face language or financial barriers. Without this, breastfeeding may not be established. Equity demands timely, accessible lactation care for all mothers of preterm infants, regardless of background or location. Promoting early and frequent expression can improve outcomes by creating more equitable opportunities for breastfeeding success. Ensuring access to equipment, culturally appropriate education and staff support across all neonatal settings is essential to closing the gap in feeding disparities.	
Acceptability		
Is the intervention acceptable to key interest-holders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Patients and whānau are likely to support the intervention, given the direct impact on infant health and wellbeing, and the absence of documented harms in the literature. Providers may place high value on the desirable outcomes but could have concerns about increased cost. However, improved early outcomes may reduce later complications and associated workload. Policymakers may be more likely to accept the resource implications if access to lactation consultant services is shown to reduce the overall cost of neonatal intensive care, as reported by Gonzalez (2003) in the Aotearoa New Zealand context. Autonomy and informed consent remain essential. Families should be supported to understand the purpose and implications of the intervention and be included in shared decision-making processes.	
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Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Financial, logistical, technical and organisational factors need to be taken into consideration in order to determine the overall feasibility of the intervention. Feasibility for Māori No additional data available	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			

	JUDGEMENT						
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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EtD 45. Should skin-to-skin care vs. no skin-to-skin care be used for mothers of preterm infants to improve breastfeeding?

POPULATION:	Preterm infants
INTERVENTION:	Skin-to-skin care
COMPARISON:	skin-to-skin care
MAIN OUTCOMES:	Critical outcomes Mortality Fully breastfed or breastmilk feeding at hospital discharge Adverse effects Breastmilk supply Initiation, establishment, and maintenance of breastfeeding (including readiness to breastfeed, sucking bursts, competent sucking and establishment of breastfeeding prior to discharge) Infant responsiveness and readiness to feed Important but not critical Time to full enteral feeds Faltering growth/body composition Duration of initial hospital stay Neurodevelopmental impairment Sepsis: proven or suspected Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation: patient perspective
BACKGROUND:	Skin-to-skin care (also called Kangaroo Mother Care or Pikau (baby wearing)) is a method of caring for preterm infants that involves holding them prone and upright on the chest of a parent or caregiver to give prolonged skin-to-skin contact between a mother and her infant and is recommended in neonatal care to promote breastfeeding and maternal-infant bonding. It is a simple and cost-effective intervention that decreases neonatal morbidity, mortality, hypoglycaemia, and the risk of infection in preterm infants. Initiating skin-to-skin care within the first 24 hours after birth and continuing throughout all levels of neonatal care may positively influence maternal milk supply by stimulating prolactin and oxytocin release, hormones critical for lactation. For preterm infants, kangaroo care has been associated with improved readiness to breastfeed, better sucking patterns, and more effective milk transfer. This close physical contact can also enhance maternal confidence in breastfeeding and foster an earlier and more successful establishment

and maintenance of breastfeeding prior to discharge. Mothers who practice kangaroo care are more likely to initiate and sustain breastfeeding due to increased milk production and confidence in their ability to provide for their infant. Skin-to-skin care initiated before a scheduled feed promotes preterm infants' physiological stability and responsiveness, preparing them for more effective feeding interactions. The skin-to-skin contact calms the infant, improves oxygen saturation, thermoregulation and primes the infant for active feeding behaviours, such as rooting and coordinated sucking bursts. This may enhance feeding readiness and support better feeding outcomes compared to infants who do not receive skin-to-skin care before feeding.

CONFLICT OF INTERESTS:

None

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know	Evidence based on a Cochrane review [1] and systematic reviews [2-6] Mortality: RCT: Very large reduction in mortality with skin-to-skin care (9 fewer per 1,000; 13 fewer to 4 fewer); effect was increased with earlier initiation (37 fewer per 1,000; 55 fewer to 15 fewer) [Critical]. Fully breastfed or breastmilk feeding at hospital discharge: RCT: Very large increase in being breastfed at discharge for skin-to-skin care (157 more per 1,000; 7 more to 354 more); discharge/28 days of life (262 more per 1,000; 240 more to 284 more); 1-3 months follow-up (RR 1.39, 95%CI 0.99 to 1.97); 28 days of age (RR 1.01; 0.98 to 1.04); exclusive breastfeeding at discharge (RR 1.12, 95%CI 1.07 to 1.16); (RR 1.09, 95%CI 0.83 to 1.44). Fully breastfed or breastmilk feeding at hospital discharge: RCT: Decrease in time to initiate exclusive breastfeeding for skin-to-skin care (MD 2.6 days lower; 3.96 lower to 1.23 lower) [Critical]. Breastmilk supply: RCT: Skin-to-skin care increased breastmilk supply and volume compared with standard care [Critical]. Infant responsiveness and readiness to feed: RCT: IBFAT scores increased for skin-to-skin care compared with standard care and infants receiving 2 hours of skin-to-skin care per day had higher scores than infants receiving 1 hour per day [Critical]. Adverse effects: RCT: Hypothermia: Very large effect for reduced risk of hypothermia for skin-to-skin care (140 fewer per 1,000; 186 fewer to 71 fewer) and (175 fewer per 1,000; 208 fewer to 121 fewer). Reduction in hypothermia also observed for early vs. later initiation of skin-to-skin care (RR 0.74, 95%CI 0.61 to 0.90) [Critical]. Adverse effects: RCT: Hypoglycaemia: Very large reduction in risk of hypoglycaemia for skin-to-skin care (96 fewer per 1,000; 122 fewer to 34 fewer) [Critical]. Time to full enteral feeds: RCT: One study found a reduced time until full enteral feeds for infants receiving skin-to-skin care as compared with standard care and one study found no difference [Important]. No faltering growth/body composition: RCT: Large effect for increased weight gain for skin-to-skin	Conde-Agudelo 2017 [1] Studies included LBW infants. Sivanandan 2023 [2]; Mekonnen 2019 [3] Low birthweight and/or preterm infants. Ghojazadeh 2019 [6] The average gestational age of all participants was 34.8 weeks. The mean birthweight was 2.31 in the skin-to-skin care group and 2.30 in the conventional care group. Clarke-Sather 2024 [4] Studies included LBW and VLBW infants, very preterm and moderate to late preterm infants.

	care (MD 4.08 g/day higher; 2.3 higher to 5.86 higher). Small increase in length (MD 0.21 higher; 0.03 higher to 0.38 higher) and head circumference (MD 0.18 higher; 0.09 higher to 0.27 higher). [Important] Duration of initial hospital stay: RCT: Reduction in initial hospitalisation (MD 2.37 days lower; 3.66 lower to 1.08 lower); (MD 0.3 days lower; 0.31 lower to 0.29 lower) [Important]. Neurodevelopmental impairment: RCT: No significant reduction in cerebral palsy (RR 0.65, 95%CI 0.21 to 2.02) and severe disability at 20 years (RR 0.34, 95%CI 0.09 to 1.24) for skin-to-skin care. No significant effect on cognitive scores for skin-to-skin care (MD 0.21 points higher; 1.84 lower to 2.26 higher) [Important]. Sepsis: RCT: Reduced risk of nosocomial sepsis for skin-to-skin care (32 fewer per 1,000; 45 fewer to 17 fewer) and for early initiation of skin-to-skin care (RR 0.85, 95%CI 0.75 to 0.95) [Important]. Cost: cost of intervention, cost of neonatal care and life-long cost: RCT: Reduced cost associated with skin-to-skin care [Important]. Desirable effects for Māori No additional evidence available	
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Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with no skin-to-skin care	Risk difference with skin-to-skin care
Mortality: RCT assessed with: hospitalisation or 28 days of life	10505 (12 RCTs)	⊕⊕⊕⊕ High	RR 0.68 (0.53 to 0.87)	Study population	
				28 per 1,000	9 fewer per 1,000 (13 fewer to 4 fewer)
Mortality: RCT: Early (within 24 hours) vs. late assessed with: hospitalisation or 28 days of life	3533 (3 RCTs)	⊕⊕⊕○ Moderate ^a	RR 0.77 (0.66 to 0.91)	Study population	
				161 per 1,000	37 fewer per 1,000 (55 fewer to 15 fewer)
Fully breastfed or breastmilk feeding at hospital discharge: RCT assessed with: 1-3 months' follow-up	8139 (7 RCTs)	⊕⊕⊕○ Moderate ^a	RR 1.39 (0.99 to 1.97)	Study population	
				Not reported	Not reported
Fully breastfed or breastmilk feeding at hospital discharge: RCT: assessed with: Time to initiate exclusive breastfeeding (days)	1900 (8 RCTs)	⊕○○○ Very low ^{b,c,d,e}	-	The mean fully breastfed or breastmilk feeding at hospital discharge: RCT: was not reported	MD 2.6 lower (3.96 lower to 1.23 lower)
Fully breastfed or breastmilk feeding at hospital discharge: RCT assessed with: exclusive breastfeeding rate at discharge/28 days of life	9983 (9 RCTs)	⊕⊕⊕○ Moderate ^a	RR 1.48 (1.44 to 1.52)	Study population	
				546 per 1,000	262 more per 1,000 (240 more to 284 more)

Fully breastfed or breastmilk feeding at hospital discharge: RCT/quasi RCT	1341 (10 RCTs)	 Very low ^{c,f,g}	RR 1.24 (1.01 to 1.54)	Study population	
				656 per 1,000	157 more per 1,000 (7 more to 354 more)
Fully breastfed or breastmilk feeding at hospital discharge: RCT	Not reported (3 RCTs)	 Very low ^{b,f}	-	One study found that breastfeeding within 24 hours post-birth, being brought to the breast within 72 hours post-birth, and full breastfeeding within 7 days post-birth were all higher for skin-to-skin care groups compared with standard care groups. A second study found an increased percentage of infants breastfed at discharge for skin-to-skin care compared with standard care and the third study found no difference in the time to full breastfeeding between groups.	
Fully breastfed or breastmilk feeding at hospital discharge: RCT: Early vs. late assessed with: Exclusive breastfeeding at 28 days of age	2841 (3 RCTs)	 Moderate ^a	RR 1.01 (0.98 to 1.04)	Study population	
				Not reported	Not reported
Fully breastfed or breastmilk feeding at hospital discharge: RCT: Early vs. late assessed with: Exclusive breastfeeding at discharge	2841 (3 RCTs)	 Moderate ^a	RR 1.12 (1.07 to 1.16)	Study population	
				Not reported	Not reported
Fully breastfed or breastmilk feeding at hospital discharge: RCT:	Not reported (13 RCTs)	 Very low ^{f,k}	RR 1.09 (0.83 to 1.44)	Study population	
				Not reported	Not reported
Adverse effects: RCT assessed with: Hypothermia by discharge or 40 weeks' PMA or 28 days after birth	1169 (11 RCTs)	 Moderate ^a	RR 0.32 (0.19 to 0.53)	Study population	
				257 per 1,000	175 fewer per 1,000 (208 fewer to 121 fewer)
Adverse effects: RCT/quasi RCT: assessed with: Hypothermia	2873 (23 RCTs)	 Very low ^{c,f,g,i}	RR 0.49 (0.32 to 0.74)	Study population	
				274 per 1,000	140 fewer per 1,000 (186 fewer to 71 fewer)
Adverse effects: RCT: Early vs. late assessed with: Hypothermia at discharge or by 28 days	3553 (3 RCTs)	 Moderate ^a	RR 0.74 (0.61 to 0.90)	Study population	
				Not reported	Not reported
Adverse effects: RCT/quasi RCT: assessed with: Hypoglycaemia	922 (7 RCTs)	 Low ^{f,g}	RR 0.32 (0.13 to 0.76)	Study population	
				141 per 1,000	96 fewer per 1,000 (122 fewer to 34 fewer)
Breastmilk supply: RCT	42 (1 RCT)	 Very low ^{i,e,m}	-	One study found that skin-to-skin care helped in increasing and building milk supply and milk volume expressed, but standard care did not.	
Infant responsiveness and readiness to feed: RCT assessed with: Infant Breastfeeding Assessment Tool (IBFAT)	40 (1 RCT)	 Very low ^{i,e,m}	-	IBFAT scores increased for skin-to-skin care compared with standard care and infants receiving 2 hours of skin-to-skin care per day had higher scores than infants receiving 1 hour per day.	

Time to full enteral feeds: RCT	143 (2 RCTs)	⊕○○○ Very low ^{a,f,m}	-	One study found a reduced time until full enteral feeds for infants receiving skin-to-skin care as compared with standard care and one study found no difference.	
Faltering growth/body composition: RCT assessed with: Weight gain at latest follow-up (g/d)	1198 (11 RCTs)	⊕⊕○○ Low ^{a,b}	-	The mean faltering growth/body composition: RCT was 17 g/day	MD 4.08 higher (2.3 higher to 5.86 higher)
Faltering growth/body composition: RCT: Early v late assessed with: Weight gain at 28- day follow- up (g/d)	204 (1 RCT)	⊕○○○ Very low ^{i,k}	-	The mean faltering growth/body composition: RCT: Early v late was not reported	MD 2.2 lower (5.26 lower to 0.86 higher)
Faltering growth/body composition: RCT assessed with: Length gain at latest follow-up (cm/week)	377 (3 RCTs)	⊕○○○ Very low ^{a,b,e}	-	The mean faltering growth/body composition: RCT was not reported	MD 0.21 higher (0.03 higher to 0.38 higher)
Faltering growth/body composition: RCT assessed with: Head circumference gain at latest follow- up (cm/week)	652 (5 RCTs)	⊕⊕○○ Low ^{a,b}	-	The mean faltering growth/body composition: RCT was not reported	MD 0.18 higher (0.09 higher to 0.27 higher)
Duration of initial hospital stay: RCT assessed with: Days	3437 (31 RCTs)	⊕○○○ Very low ^{c,b,g,i}	-	The mean duration of initial hospital stay: RCT was 23.23 days	MD 2.37 lower (3.66 lower to 1.08 lower)
Duration of initial hospital stay: RCT assessed with: Days	3498 (3 RCTs)	⊕⊕⊕○ Moderate ^a	-	The mean duration of initial hospital stay: RCT was not reported	MD 0.3 lower (0.31 lower to 0.29 lower)
Neurodevelopmental impairment : RCT assessed with: Cerebral palsy at 12 months' corrected age	588 (1 RCT)	⊕○○○ Very low ^{e,j,k}	RR 0.65 (0.21 to 2.02)	Study population	
				Not reported	Not reported
Neurodevelopmental impairment: RCT assessed with: Severe disability at 20 years	264 (1 RCT)	⊕○○○ Very low ^{e,j,k}	RR 0.34 (0.09 to 1.24)	Study population	
				Not reported	Not reported
Neurodevelopmental impairment: RCT assessed with: 12 months of age using BSID- III - Cognitive score Scale from: 1 to 100	516 (1 RCT)	⊕○○○ Very low ^{a,h,j}	-	The mean neurodevelopmental impairment: RCT: Bayley III Cognitive score was not reported	MD 0.21 higher (1.84 lower to 2.26 higher)
Neurodevelopmental impairment: RCT assessed with: 12 months of age using BSID- III - Motor score Scale from: 1 to 100	516 (1 RCT)	⊕○○○ Very low ^{a,h,j}	-	The mean neurodevelopmental impairment: RCT: Bayley III Motor score was not reported	MD 0.85 lower (2.65 lower to 0.95 higher)
Neurodevelopmental impairment: RCT assessed with: 12 months of age using BSID- III - Language score Scale from: 1 to 100	516 (1 RCT)	⊕○○○ Very low ^{a,h,j}	-	The mean neurodevelopmental impairment: RCT: Bayley III Language score was not reported	MD 0.91 lower (2.46 lower to 0.64 higher)
Sepsis: proven or suspected: RCT: Early vs.	3415		RR 0.85	Study population	

late assessed with: Nosocomial sepsis	(2 RCTs)	⊕⊕⊕○ Moderate ^a	(0.75 to 0.95)	Not reported	Not reported
Sepsis: proven or suspected: RCT assessed with: nosocomial clinical sepsis	9847 (9 RCTs)	⊕⊕⊕○ Moderate ^a	RR 0.85 (0.79 to 0.92)	Study population 215 per 1,000	32 fewer per 1,000 (45 fewer to 17 fewer)
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost: RCT assessed with: US\$	334 (2 RCTs)	⊕○○○ Very low ^{a,b,l}	-	One study reported the overall cost was "about 50% less for KMC" (US\$19,289 for skin-to-skin care and US\$39,764 for conventional care). Another study reported "costs of neonatal care were greater in the control than in the skin-to-skin group." Overall, the cost of hospital stay and post-neonatal care at five months was US\$741 greater for the control than the skin-to-skin group. However, data were available for only 49 infants (24 skin-to-skin, 25 control) at six months' follow-up.	
Time to full sucking feeds - not measured	-	-	-	-	-

- a. Downgraded one level for inconsistency
- b. Downgraded two levels for risk of bias
- c. Downgraded two levels for inconsistency as I²>80%
- d. Downgraded one level for indirectness as studies were conducted in India, Bangladesh and Brazil and included preterm and low birthweight infants
- e. Downgraded one level for imprecision due to wide confidence intervals or low sample numbers
- f. Downgraded one level for risk of bias
- g. Downgraded one level for indirectness as included both term and preterm infants

- a. Downgraded one level for imprecision as confidence intervals cross the line of no effect
- b. Downgraded one level for evidence of publication bias - significant Egger's test
- c. Downgraded one level for indirectness as evidence is based on a single study
- d. Downgraded two levels for imprecision due to wide confidence intervals that cross the line of no effect
- e. Downgraded one level for indirectness as the review is based on low birthweight infants and not generalisable
- f. Downgraded two levels for imprecision as based on very low numbers

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies	Faltering growth/body composition: RCT: No significant decrease in weight gain with early initiation of skin-to-skin care (MD 2.2 g/day lower; 5.26 lower to 0.86 higher) [Important]. Neurodevelopmental impairment: RCT: No significant effect on motor scores (MD 0.85 points lower; 2.65 lower to 0.95 higher) and language scores (MD 0.91 points lower; 2.46 lower to 0.64 higher) for skin-to-skin care [Important].	

○ Don't know	Undesirable effects for Māori No additional evidence available	
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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	High to very low certainty of evidence overall Certainty of evidence for Māori No additional evidence available.	

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT assessed with: hospitalisation or 28 days of life	CRITICAL	⊕⊕⊕⊕ High
Mortality: RCT: Early (within 24 hours) vs. late assessed with: hospitalisation or 28 days of life	CRITICAL	⊕⊕⊕○ Moderate
Fully breastfed or breastmilk feeding at hospital discharge: RCT assessed with: 1-3 months' follow-up	CRITICAL	⊕⊕⊕○ Moderate
Fully breastfed or breastmilk feeding at hospital discharge: RCT: assessed with: Time to initiate exclusive breastfeeding (days)	CRITICAL	⊕○○○ Very low
Fully breastfed or breastmilk feeding at hospital discharge: RCT assessed with: exclusive breastfeeding rate at discharge/28 days of life	CRITICAL	⊕⊕⊕○ Moderate
Fully breastfed or breastmilk feeding at hospital discharge: RCT/quasi RCT	CRITICAL	⊕○○○ Very low
Fully breastfed or breastmilk feeding at hospital discharge: RCT	CRITICAL	⊕○○○ Very low ⁱ
Fully breastfed or breastmilk feeding at hospital discharge: RCT: Early vs. late assessed with: Exclusive breastfeeding at 28 days of age	CRITICAL	⊕⊕⊕○ Moderate
Fully breastfed or breastmilk feeding at hospital discharge: RCT: Early vs. late assessed with: Exclusive breastfeeding at discharge	CRITICAL	⊕⊕⊕○ Moderate

Fully breastfed or breastmilk feeding at hospital discharge: RCT:	CRITICAL	⊕○○○ Very low
Adverse effects: RCT assessed with: Hypothermia by discharge or 40 weeks' PMA or 28 days after birth	CRITICAL	⊕⊕⊕○ Moderate
Adverse effects: RCT/quasi RCT: assessed with: Hypothermia	CRITICAL	⊕○○○ Very low
Adverse effects: RCT: Early vs. late assessed with: Hypothermia at discharge or by 28 days	CRITICAL	⊕⊕⊕○ Moderate
Adverse effects: RCT/quasi RCT: assessed with: Hypoglycaemia	CRITICAL	⊕⊕○○ Low
Breastmilk supply: RCT	CRITICAL	⊕○○○ Very low
Infant responsiveness and readiness to feed: RCT assessed with: Infant Breastfeeding Assessment Tool (IBFAT)	CRITICAL	⊕○○○ Very low
Time to full enteral feeds: RCT	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Weight gain at latest follow-up (g/d)	IMPORTANT	⊕⊕○○ Low
Faltering growth/body composition: RCT: Early v late assessed with: Weight gain at 28- day follow- up (g/d)	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Length gain at latest follow- up (cm/week)	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Head circumference gain at latest follow- up (cm/week)	IMPORTANT	⊕⊕○○ Low
Faltering growth/body composition	IMPORTANT	-
Duration of initial hospital stay: RCT assessed with: Days	IMPORTANT	⊕○○○ Very low
Duration of initial hospital stay: RCT assessed with: Days	IMPORTANT	⊕⊕⊕○ Moderate
Neurodevelopmental impairment: RCT assessed with: Cerebral palsy at 12 months' corrected age	IMPORTANT	⊕○○○ Very low

Neurodevelopmental impairment: RCT assessed with: Severe disability at 20 years	IMPORTANT	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: 12 months of age using BSID- III - Cognitive score	IMPORTANT	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: 12 months of age using BSID- III - Motor score	IMPORTANT	⊕○○○ Very low
Neurodevelopmental impairment: RCT assessed with: 12 months of age using BSID- III - Language score	IMPORTANT	⊕○○○ Very low
Sepsis: proven or suspected: RCT: Early vs. late assessed with: Nosocomial sepsis	IMPORTANT	⊕⊕⊕○ Moderate
Sepsis: proven or suspected: RCT assessed with: nosocomial clinical sepsis	IMPORTANT	⊕⊕⊕○ Moderate
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Retinopathy of prematurity - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost: RCT	IMPORTANT	⊕○○○ Very low
Time to full sucking feeds (<0.5 days) - not measured	NOT IMPORTANT	-

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ Don't know	Skin-to-skin care vs. no skin-to-skin care - high certainty evidence Reduced mortality Skin-to-skin care vs. no skin-to-skin care - moderate certainty evidence Reduced mortality, hypothermia, duration of initial hospitalisation, sepsis (early initiation) Increase in exclusive breastfeeding at discharge Uncertain effect for fully breastfed or breastmilk feeding at hospital discharge/28 days of age, exclusive breastfeeding at 28 days of age Skin-to-skin care vs. no skin-to-skin care - low certainty evidence Reduced hypoglycaemia Increase in weight gain and head circumference at latest follow-up Skin-to-skin care vs. no skin-to-skin care - very low certainty evidence Decrease in time to initiate exclusive breastfeeding Reduced hypothermia; duration of initial hospitalisation, cost Increase in exclusive breastfeeding at discharge; breastmilk supply and volume; Infant Breastfeeding Assessment Tool (IBFAT) score; length Uncertain effect for fully breastfed or breastmilk feeding at hospital discharge; time to full enteral feeds; weight gain (early initiation); neurodevelopmental impairment (cerebral palsy, severe disability at 20 years, cognitive score, motor score, language score) Balance of effects for Māori No additional evidence available.	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings	Parents' time Space in the neonatal unit Resources required for Māori	

○ Large savings ● Varies ○ Don't know	No additional evidence available.	
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Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	A formal assessment of the certainty of evidence of the cost was not undertaken. Certainty of evidence of required costs for Māori No additional evidence available.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	Very low certainty evidence reported in one study that the overall cost was "about 50% less for skin-to-skin care" (US\$19,289 for skin-to-skin care and US\$39,764 for conventional care). Another study reported "costs of neonatal care were greater in the control than in the skin-to-skin care group. " Overall, the cost of hospital stay and post neonatal care at five months was US\$741 greater for the control than the skin-to-skin group. However, data were available for only 49 infants (24 skin-to-skin, 25 control) at six months' follow-up.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced	Equity for Māori	

○ Probably reduced ○ Probably no impact ○ Probably increased ● Increased ○ Varies ○ Don't know	Pēpi Māori experience higher rates of preterm birth, sepsis and neurodisability and are less likely to survive compared to other ethnicities. They transition off parenteral fluids faster than others yet are less likely to receive mother's own milk only. By day three, over half of pēpi Māori receive alternative nutrition not based on mother's own milk. At discharge, they are significantly less likely to be exclusively breastfed. Colonisation continues to affect Māori health outcomes. Promoting skin-to-skin care may support breastfeeding success and help reduce existing disparities in early nutrition and bonding for Māori mothers and their preterm pēpi. Equity for Pacific families Pacific infants had the highest rate of transition to mother's own milk only, yet over one in five still received alternative nutrition by day three. Pacific families may not receive adequate support or information to practise skin-to-skin care regularly, especially in busy units with limited space or staffing. When culturally appropriate support is lacking, opportunities to support breastfeeding through skin-to-skin may be lost. Equity requires enabling safe, supported kangaroo care for all families. Equity for underrepresented groups Families who are migrants, live rurally or lack transport may find it difficult to provide frequent skin-to-skin care. Without flexible visiting policies or logistical support, participation may be limited. Equity calls for inclusive NICU policies and resources to ensure all families can benefit from early skin-to-skin contact. In the DIAMOND RCT, Asian infants also showed varied access to exclusive breastfeeding. These differences reflect broader systemic inequities in healthcare delivery and cultural support. Implementing skin-to-skin care across all settings may offer a culturally inclusive, low-cost method to enhance bonding and breastfeeding rates. Standardising this practice could help reduce ethnic disparities by ensuring consistent support for all mothers and infants. Promoting skin-to-skin care can particularly benefit underrepresented groups by supporting equitable early feeding outcomes and maternal wellbeing.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Probably acceptable to most families. Acceptability for Māori No additional evidence available.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☐ Varies ☐ Don't know	Barriers may include a lack of private spaces (this has been reported in our interviews), staffing to support parents or clinician hesitation in unstable infants or with umbilical catheters. Feasibility for Māori No additional evidence available.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies

	JUDGEMENT						
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ●
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EtD 46. Should additional staff-related interventions vs. standard care be used for improving breastfeeding outcomes in whānau of preterm infants in NICU?

POPULATION:	Mothers and preterm infants
INTERVENTION:	Additional staff-related interventions
COMPARISON:	Standard care
MAIN OUTCOMES:	Critical outcomes Time to first express Milk supply volumes Time to establish breastfeeding Time to reach full sucking feeds Breastfeeding or maternal breastmilk feeding at discharge Other breastfeeding outcomes as described by authors Important but not critical Mortality Neurodevelopmental impairment Adverse effects Time to reach full enteral feeds Duration of initial hospital stay Necrotizing enterocolitis Faltering growth/body composition Sepsis Bronchopulmonary dysplasia Retinopathy of prematurity Less important for decision making Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost
SETTING:	Neonatal care
PERSPECTIVE:	Parents / staff
BACKGROUND:	Breastmilk feeding is a critical factor in neonatal care, providing essential nutrients and immunological protection that support growth and development. However, mothers of preterm infants often face significant challenges in initiating and maintaining milk supply. Some of these challenges are compounded by systemic issues such as understaffing, high workloads, competing clinical priorities, or a lack of specialised training in lactation and breastfeeding establishment following preterm birth. Long-standing racial inequities within healthcare may also present additional

	challenges and can affect access to culturally appropriate lactation support and the quality of communication between families and healthcare providers. Staff-related interventions may help address these gaps and improve breastfeeding outcomes for mothers and their preterm infants in NICU. In this review, we explore hiring dedicated staff to assist with breastfeeding, implementing targeted training programs, or increasing the involvement of existing NICU staff as staff-related interventions.
CONFLICT OF INTERESTS:	None

Assessment

Desirable Effects					
How substantial are the desirable anticipated effects?					
JUDGEMENT	RESEARCH EVIDENCE			ADDITIONAL CONSIDERATIONS	
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	Evidence based on 12 studies: 6 non-randomised [1] (Aydemir 2019; Cornell 2016 [2]; Maastrup 2021 [3]; Montgomery 2008 [4]; Oza-Frank 2024 [5]; Tanaka 2021 [6]), 1 observational (Parker 2018) [7] and 5 qualitative (McInnes 2010 [8] ; McLeish 2024a [9]; McLeish 2024b [10]; Morelius 2021 [11]; Ong 2022 [12]) studies.			○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with standard care	Risk with Additional staff-related interventions			
Timing of first expression - first breastmilk expression <6h post birth	Study population		OR 1.51 (1.11 to 2.04)	727 (1 non-randomised study)	⊕○○○ Very low ^a
	328 per 1,000	425 per 1,000 (499 to 352)			
Exclusive breastfeeding at discharge	Study population		OR 1.33 (1.07 to 1.66)	1406 (3 non-randomised studies)	⊕⊕○○ Low
	494 per 1,000	565 per 1,000 (618 to 511)			
Any maternal breastmilk at discharge	Study population		OR 1.26 (0.85 to 1.86)	413 (1 non-randomised study)	⊕○○○ Very low ^{a,b}
	559 per 1,000	615 per 1,000 (702 to 519)			
Duration of breastfeeding	The mean duration of breastfeeding was 6,1	MD 2.3 months more (0.73 fewer to 5.33 more)	-	78 (1 non-randomised study)	⊕○○○ Very low ^{a,c}

	months				
Exclusive breastmilk use during first 7 days of feeding	Study population		OR 1.99 (1.19 to 3.33)	245 (1 non-randomised study)	⊕○○○ Very low ^{a,c,d}
	331 per 1,000	496 per 1,000 (622 to 370)			
Any maternal breastmilk during NICU stay	Study population		OR 1.58 (1.04 to 2.39)	413 (1 non-randomised study)	⊕○○○ Very low ^{a,b}
	631 per 1,000	730 per 1,000 (803 to 640)			
Time to reach full enteral feeds	The mean time to reach full enteral feeds was 27,3 days	MD 8.6 days fewer (15.34 fewer to 1.86 fewer)	-	78 (1 non-randomised study)	⊕○○○ Very low ^{a,c}
Growth - daily weight gain	The mean growth - daily weight gain was 25,7 grams/day	MD 2.8 grams/day more (0.77 fewer to 6.37 more)	-	78 (1 non-randomised study)	⊕○○○ Very low ^{a,c}
Growth- weight at discharge	The mean growth- weight at discharge was 2288 grams	MD 46 grams more (99.09 fewer to 191.09 more)	-	245 (1 non-randomised study)	⊕○○○ Very low ^{a,e}
BPD	Study population		OR 0.68 (0.23 to 2.07)	78 (1 non-randomised study)	⊕○○○ Very low ^{a,c}
	237 per 1,000	174 per 1,000 (391 to 67)			

- a. Downgraded one level for indirectness as evidence is based on a single study
- b. Downgraded one level for imprecision due to small sample size and confidence intervals crossing the line of no effect
- c. Downgraded one level for imprecision due to small sample size
- d. Downgraded one level for risk of bias due to concerns about poor reporting
- e. Downgraded two levels for imprecision due to small sample size and wide confidence intervals that cross the line of no effect

From the 5 qualitative studies (McInnes 2010; McLeish 2024a; McLeish 2024b; Morelius 2021; Ong 2022), we found:

Time to First Expression (McLeish 2024a; McLeish 2024b)

Timely, clear information from staff helped mothers understand the importance of early and frequent expressing (within hours of birth).

Early encouragement and reassurance from staff increased confidence to start expressing despite doubts around it.

Dedicated staff or designated contact points improved consistency and reduced confusion.

Staff acknowledging mothers' challenges (e.g. travel, family commitments) and offering encouragement supported adherence to expressing breastmilk.

Milk Supply (McInnes 2010; McLeish 2024a; McLeish 2024b; Morelius 2021)

Specialist staff who proactively checked progress and offered support improved mothers' confidence and milk supply.

Counselling and in-person /physical demonstrations by health workers facilitated successful expression and adequate milk volumes.

Skilled advice on maintaining/increasing supply (e.g. pumping at night, power pumping, domperidone, tracking sessions) was valued.

Time to Breastfeeding (McInnes 2010; McLeish 2024a; McLeish 2024b)

Intensive support from specialist staff enabled earlier introduction to breastfeeding and longer learning periods.

Consistent encouragement from staff helped mothers persist with breastfeeding attempts.

Breastfeeding at Discharge (McLeish 2024a)

Staff spending time to prepare mothers for home feeding increased confidence.

Rooming-in before discharge and ongoing outreach support were highly valued. These likely contribute to adherence to breastfeeding after discharge from NICU, although this is not certain.

Breastmilk Expression (Incidence and Duration) (Ong 2022; Tanaka 2021)

Dedicated, well-trained infant feeding teams increased rates and duration of expressing.

Staff counselling and demonstrations improved adherence and success with expression.

Other – Long-Term Expression

Neonatal-specific feeding training for all staff was seen as crucial for supporting prolonged expressing.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	From the 5 qualitative studies (McInnes 2010; McLeish 2024a; McLeish 2024b; Morelius 2021; Ong 2022), we found: Time to First Expression Heavy workloads and staff shortages delayed initiation, reduced monitoring, and led to inconsistent feeding intervals. Milk Supply Difficulty accessing specialist staff when needed created gaps in support around maintaining milk supply. Time to Breastfeeding Contradictory advice from different nurses caused insecurity and inconsistent practices Overstretched staff made mothers reluctant to ask for help, fearing they were a burden.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low	Certainty of evidence at the outcome level:	

○ Low ○ Moderate ○ High ○ No included studies		
Outcomes	Importance	Certainty of the evidence (GRADE)
Timing of first expression - first breastmilk expression <6h post birth	CRITICAL	⊕○○○ Very low
Timing of first expression	CRITICAL	⊕○○○ Very low
Milk supply - Breastmilk volume on day 4 post birth	CRITICAL	⊕○○○ Very low
Milk supply - Breastmilk volume on day 10 post birth	CRITICAL	⊕○○○ Very low
Milk supply - mothers that reached ≥140ml/day expressed breastmilk on day 4 post birth	CRITICAL	⊕○○○ Very low
Milk supply - mothers that reached ≥500ml/day expressed breastmilk on day 10 post birth	CRITICAL	⊕○○○ Very low
Timing of first breastfeeding- Postmenstrual age when breastfeeding was established	CRITICAL	⊕○○○ Very low
Exclusive breastfeeding at discharge	CRITICAL	⊕⊕○○ Low
Any breastfeeding at discharge	CRITICAL	⊕○○○ Very low
Any maternal breastmilk at discharge	CRITICAL	⊕○○○ Very low
Duration of breastfeeding	CRITICAL	⊕○○○ Very low
Exclusive breastmilk use during first 7 days of feeding	CRITICAL	⊕○○○ Very low
Exclusive maternal breastmilk during NICU stay	CRITICAL	⊕○○○

		Very low
Any maternal breastmilk during NICU stay	CRITICAL	⊕○○○ Very low
Frequency of milk expression during 10 days post birth (times/day)	CRITICAL	⊕○○○ Very low
Time to reach full enteral feeds	CRITICAL	⊕○○○ Very low
Duration of hospital stay	IMPORTANT	⊕○○○ Very low
NEC	IMPORTANT	⊕○○○ Very low
Growth - daily weight gain	IMPORTANT	⊕○○○ Very low
Growth- weight at discharge	IMPORTANT	⊕○○○ Very low
Sepsis	IMPORTANT	⊕○○○ Very low
Retinopathy of prematurity	IMPORTANT	⊕○○○ Very low
Bronchopulmonary dysplasia	IMPORTANT	⊕○○○ Very low
Quality of the qualitative studies was Moderate/high: Qualitative studies: Critical appraisal skills programme (CASP) checklist Table 3. CASP checklist for appraisal of qualitative studies		

	McLeish 2024 (mothers)	McLeish 2024 (staff)	McInnes 2010	Morelius 2021	Ong 2022
<i>Section A: Are the results valid?</i>					
1. Was there a clear statement of the aims of the research?	2	2	2	2	2
2. Is a qualitative methodology appropriate?	2	2	2	2	2
3. Was the research design appropriate to address the aims of the research?	2	2	2	2	0
4. Was the recruitment strategy appropriate to the aims of the research?	2	2	2	2	1
5. Was the data collected in a way that addressed the research issue?	2	1	2	2	2
6. Has the relationship between researcher and participants been adequately considered?	2	0	2	2	0
<i>Section B: What are the results?</i>					
7. Have ethical issues been taken into consideration?	2	2	2	2	2
8. Was the data analysis sufficiently rigorous?	2	2	2	1	2
9. Is there a clear statement of findings?	2	2	2	2	2
<i>Section C: Will the results help locally?</i>					
10. How valuable is the research?	2	2	2	2	2
Overall quality assessment (High, Moderate, Low)	High 20/20	Moderate 17/20	High 20/20	Moderate/High 19/20	Low 15/20

Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	Whānau value consistent, skilled support for breastfeeding and milk expression, especially given the unique challenges of preterm feeding. They often expect staff to be available and knowledgeable, yet this may be difficult in NICU settings where workloads are high and specialised training is limited. Interventions that improve staff capacity or skills to provide breastfeeding support are likely to align with these priorities.	Critical outcomes of this question are: Time to first express Milk supply volumes Time to establish breastfeeding Time to reach full sucking feeds Breastfeeding or maternal breastmilk feeding at discharge Other breastfeeding outcomes as described by authors

Balance of effects		
Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Additional staff-related interventions vs. standard care - low certainty evidence Increased exclusive breastfeeding at discharge (surpasses threshold) Increased maternal breastmilk feeding during NICU stay Reduced BPD (surpasses threshold) Additional staff-related interventions vs. standard care - very low certainty evidence Increased incidence of first breastmilk expression <6h post birth, duration of breastfeeding, exclusive breastmilk use during first 7 days of feeding, maternal breastmilk feeding at discharge, daily weight gain and weight at discharge Decrease in time to reach full enteral feeds (surpasses threshold) Decrease in breastmilk volume on day 4 and 10 post birth and mothers that reached ≥140 mL/day expressed breastmilk up to day 4 post birth and ≥500 mL/day up to day 10, any breastfeeding at discharge, exclusive maternal breastmilk during NICU stay and daily frequency of milk expression during 10 days post birth Increase in time of first breastmilk expression, postmenstrual age when breastfeeding was established and duration of hospital stay Increase in NEC, sepsis and ROP (surpasses threshold) Additional staff-related interventions vs. standard care - moderate/high quality evidence from QUALITATIVE STUDIES Improved time to first expression, milk supply and duration with timely, proactive, skilled support and structured advice Improved time to breastfeeding with targeted specialist involvement Improved motivation to express and long-term expression with dedicated, well-trained feeding teams and counselling Longer time to first expression and milk supply due to delayed or contradictory advice, staff shortages and lack of designated feeding specialists Delayed time to breastfeeding and decreased rates of breastfeeding at discharge when support was limited or conflicting and under conditions of understaffing and heavy workloads Worse long-term expression when monitoring wasn't consistent and staff lacked neonatal-specific training	Additional staff-related interventions: hiring peer counsellors/nutrition nurses, additional targeted staff training and increased involvement in NICU breastfeeding support.
Resources required		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ● Moderate costs	Salary - hiring a dedicated person to provide additional breastfeeding support Educators to deliver training to staff	

○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Additional staff time to provide more breastfeeding information and support	
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Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	We are relatively certain of what would be needed for the intervention, however not as certain about how much it would cost to each unit, and each type of intervention would have a different cost (hiring new staff vs. training an existing member of staff)	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention	No evidence found	

○ Varies ● No included studies		
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori: Whānau Māori navigating neonatal care often face systemic barriers that limit access to culturally safe breastfeeding support. Standard care may not adequately reflect mātauranga Māori or prioritise relational approaches that build trust. Staff-related interventions—such as dedicated personnel or training that incorporates cultural safety—could help ensure breastfeeding support is delivered in ways that honour Māori values and empower whānau to advocate for and realise their breastfeeding aspirations. Equity for Pacific families: Pacific families bring strong collective caregiving traditions to neonatal care yet often encounter gaps in culturally relevant breastfeeding support. Standard care may overlook the importance of family involvement and accessible communication. Staff interventions that include cultural safety training or approaches co-designed with Pacific lead knowledge and use of Pacific health frameworks can improve confidence and support informed feeding decisions, ensuring care aligns with their values and breastfeeding aspirations. Equity for Underrepresented groups: Families from migrant, low-income, or rural backgrounds may struggle to access consistent breastfeeding support due to language barriers, digital exclusion, transport limitations, or staff shortages. Staff-related interventions that increase availability and responsiveness—such as dedicated personnel or targeted training—can help bridge these gaps. Equity requires ensuring all families receive timely, skilled breastfeeding support tailored to their circumstances and strengths.	
Acceptability Is the intervention acceptable to key interest-holders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Likely acceptable to most stakeholders, as improving breastfeeding support aligns with priorities for whānau-centred care. However, NICU staff may have concerns about increased workload or time pressures associated with implementing these interventions.	
Feasibility		

Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☐ Probably yes ☐ Yes ☒ Varies ☐ Don't know	Potential issues around hiring additional personnel. Increasing involvement of existing staff or providing training may also be hindered by workload and competing priorities.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the	Probably favours the intervention	Favours the intervention	Varies	No included studies

	JUDGEMENT						
EFFECTIVENESS			comparison				
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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EtD 47. Should mana-enhancing tikanga practices be incorporated to support whānau Māori breastfeeding?

POPULATION:	Preterm infants
INTERVENTION:	Mana enhancing tikanga practices that support whānau Māori breastfeeding
COMPARISON:	Standard care
MAIN OUTCOMES:	Critical outcomes Upholding tikanga Māori Breastmilk supply/volume Fully breastfed or breastmilk feeding at hospital discharge and/or at 6 months post-partum Important but not critical Time to full enteral feeds Time to full sucking feeds Faltering growth/body composition Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Adverse effects Necrotising enterocolitis Mortality Neurodevelopmental impairment Sepsis: proven or suspected Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity
SETTING:	Neonatal care
PERSPECTIVE:	Clinical guideline recommendation. Patient perspective
BACKGROUND:	Breastmilk is the optimal source of nutrition for pēpi, providing essential nutrients, immune protection and developmental benefits. Exclusive breastfeeding is recommended for the first six months of a pēpi's life. Statistics show a high rate of breastfeeding in pēpi Māori at discharge from hospital. However, the rates of breastfeeding subsequently decrease, and the rate of breastfeeding at five months postpartum is lower in pēpi Māori than in other infants. Yet, breastfeeding is considered a tikanga (correct cultural practice) and a tika tūāpapa (a fundamental right) in te ao Māori. This discrepancy suggests barriers to ongoing breastfeeding after discharge. Understanding those barriers, identifying mana-enhancing practices and implementing effective breastfeeding strategies tailored to whānau Māori are all necessary steps in addressing this equity gap. Mana enhancing practices involve enhancing the mana of all those involved particularly mama and pēpi. We are all connected at a fundamental level so to enhance the mana of others enhances your own. Empowerment, tino rangatiratanga and effective communication practices are critical in ensuring the mana of the whanau.

CONFLICT OF INTERESTS:

The following co-author for Harris, S *et al* (reference 8) is on the Guideline Development Group:
Frank Bloomfield

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	The evidence was based on six qualitative publications [1-6], newborn infants. There were no studies specifically about preterm pēpi Māori. The mana-enhancing tikanga practices that were identified included: The promotion of breastfeeding as a tikanga Māori (correct way of doing things from a Māori perspective) rather than a perceived lifestyle choice was critical and the relationship was seen as being important in developing this as a 'norm'. The normalisation of breastfeeding within whānau members, including tāne Māori, provided wāhine Māori with encouragement and support. The influence of and involvement of maternal grandmothers and sisters played an important role in supporting breastfeeding, especially when they had breastfed their own pēpi Māori. Identification of breastfeeding as an enjoyable experience that could be associated with intimacy and closeness with the pēpi Māori. A need for positive and sufficient maternity support to promote breastfeeding through antenatal and postnatal education. The prevention or minimisation of interruptions in establishing breastfeeding through physical separations (e.g. admission to neonatal intensive care) or physical factors such as sore/cracked nipples or discomfort through engorgement. Wāhine Māori found a lot of support from linking to breastfeeding support networks. Improvements in knowledge about breastfeeding, such as latching and positioning, as well as how breastfeeding changes over time (e.g. some wāhine Māori switched to infant formula at 4 months as they thought their milk wasn't sufficient anymore) Emotional and informational support was perceived as being of higher importance than instrumental support. In Bennett <i>et al</i>, of the 1,060 pēpi Māori who were breastfed at discharge, 12% were still exclusively breastfed at six or more months [1]. Using the Te Anga o	Proportion of Māori in included studies: [1] 100% [4] 100% [5] 100% [6] 0.5% [3] Born in Aotearoa New Zealand 11.2%; born in Australia 0.3% [2,7] 10% Definitions of breastfeeding: Exclusive breastfeeding: The infant has never, to the mother's knowledge, had any water, formula or other liquid or solid food. Only breastmilk, from the breast or expressed, and prescribed medicines have been given from birth. Fully breastfeeding: The infant has taken breastmilk only, no other liquids or solids except a minimal amount of water or prescribed medicines, in the past 48 hours. Manhire <i>et al</i> extracted information obtained from a RCT that compared the risks and benefits of a wahakura and a bassinet [6]. In the questionnaires administered during pregnancy and at one, three and six months postpartum, several questions related to breastfeeding. Manhire <i>et al</i> pooled the data from both groups and reported on predictors of extended breastfeeding duration: Strong support from the mother's partner (OR 3.64, 95% CI 1.76, 7.55) or mother for breastfeeding (OR 2.47, 95% CI 1.27, 4.82) Older age (OR 1.07, 95% CI 1.02, 1.12).

ngā Horopaki Māori* model, several variables were identified as statistically significant positive influencers for continued exclusive breastfeeding:

In domain **Mahi Arataki** (Policy and Strategy): wāhine Māori were more likely to exclusively breastfeed for six-or- more months if they had thought, antenatally, that it was best to breastfeed for longer than six months (aOR 1.94, 95% CI 1.05–3.78).

The authors concluded that breastfeeding promotion should start early in the pregnancy and include mothers, whānau Māori and health professionals. The dissemination of breastfeeding information antenatally, in a culturally safe and accessible way would help support whānau ora (family health and development) and ongoing breastfeeding post-discharge.

Also in domain **Mahi Arataki** (Policy and Strategy), wāhine Māori who thought breastfeeding would not be limited by their return to work (aOR 2.17, 95% CI 1.17–4.24) or who thought it would "maybe" be limited (aOR 4.25, 95% CI 1.86–9.85) by their return to work were more likely to continue exclusively breastfeeding by six month compared to wāhine Māori who responded "yes, breastfeeding duration will be limited by return to work". The study was conducted before the extension of paid parental leave from 13 weeks to 26 weeks, and before the broadening of inclusion criteria (e.g. some casual workers). While this extension may have positively influenced the above variable, it was noted by the authors that many wāhine Māori are still not eligible for paid parental leave - a change in policy ensuring universal paid parental leave may positively impact breastfeeding rates.

In domain **Whanaungatanga** (Family and Home), multiparous Māori mothers were more likely to exclusively breastfeed for six-or-more months compared to primiparous Māori mothers (aOR 2.55, 95% CI 1.35–5.06).

First time Māori mothers may benefit from additional breastfeeding support from whānau, community and healthcare providers.

* Te Anga o ngā Horopaki Māori is a contemporary Māori model of health and wellbeing developed by Māori researchers specifically for the *Growing Up in New Zealand* Māori cohort, comprising of six domains. A lack of face-to-face support (especially during the COVID-19 pandemic) was associated with decreased confidence in breastfeeding. A lack of information, education and ongoing at-home lactation support during the first six weeks of the pēpi Māori decreased breastfeeding. Primiparity significantly reduced breastfeeding self-efficacy, i.e. their perceived ability to breastfeed. This population was more likely than multiparous wāhine Māori to have stopped breastfeeding in the first

	six weeks post-partum and may require additional support. A lack of whanau support and encouragement to bottle-feed decreased breastfeeding.	
Undesirable Effects		
How substantial are the undesirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Using the Te Anga o ngā Horopaki Māori model, Bennett <i>et al</i> identified several variables as statically significant negative influencers for continued exclusive breastfeeding [1]: In domain Te Ao Māori (Cultural identity): wāhine Māori who rated maintaining cultural traditions and practices as “fairly important” were less likely to exclusively breastfeed for six-or-more months, compared with women who rated these as “very important” (aOR 0.53, 95% CI 0.27–0.99). Yet, wāhine Māori who answered "not very/not at all important" (aOR 1.20, 95% CI 0.55–2.51) or "somewhat important" (aOR 1.00, 95% CI 0.51–1.91) were not less likely to exclusively breastfeed for six-or-more months compared to participants who answered "very important". Although breastfeeding is a fundamental aspect of tikanga, the evidence regarding the influence of cultural traditions and practices on breastfeeding is conflicted. It remains that, for many, access to te ao Māori is limited by the legacy of colonisation, poverty, and systemic racism. In domain Hauora (Health and Wellbeing), wāhine Māori who experienced depression during pregnancy (aOR 0.47, 95% CI 0.20–0.99) were less likely to exclusively breastfeed for six-or-more months than those without depressive symptoms. Routine perinatal depression screening in a culturally safe and appropriate setting is necessary. Where needed, screening must be followed by provision of culturally sensitive mental health support. No screening tool validated in a Māori perinatal population was identified in our evidence search. The Hua Oranga questionnaire, which focuses on various aspect of wellbeing, could be considered as an alternative. Also, in domain Hauora (Health and Wellbeing), wāhine Māori who remained	In (6), non-Māori breastfed their infants for longer than Māori (OR 2.22; 95% CI 1.17, 4.21). The sample was 70% Māori. The predictors (for all ethnicities) of reduced breastfeeding duration were: Pacifier use (OR 0.28, 95% CI 0.17, 0.46), Daily cigarette smoking (OR 0.51, 95% CI 0.37, 0.69), Alcohol use (OR 0.54, 95% CI 0.31, 0.93) Living in a deprived area (OR 0.40, 95% CI 0.22, 0.72).

	undecided about their child's infant immunisations were more likely to exclusively breastfeed for six or more months than mothers who had decided about immunisation (aOR 3.16, 95% CI 1.55– 6.39). While this variable was associated with increased breastfeeding rates, low infant immunisation rates is a public health issue. This variable further highlights the interconnectedness of the domains of health as well as the broad impact wariness towards healthcare providers and institutions may have.	
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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	The overall certainty of evidence is low because the evidence is indirect and the quantitative evidence from the studies by (Bennett et al., 2022) (Manhire et al., 2018) was downgraded to very low but the qualitative evidence was of moderate certainty. The evidence was indirect to the PICO: no study focused on tikanga practice that support Māori breastfeeding in the context of NICU/preterm birth. However, rich qualitative evidence was available on the experience of whanau Māori breastfeeding in the general population. Two studies [1,6] provided statistical analysis of factors associated with longer duration of breastfeeding, based on interviews or questionnaires. The evidence started at a low level of certainty: - the study by Bennett, gathered data from the cohort study Growing Up in New Zealand - the study by Manhire was a secondary analysis of data from a RCT comparing the use of a wahakura to a bassinet. Data was gathered through questionnaires and Manhire pooled the data from both arms regarding breastfeeding: the study was therefore not considered a RCT but an observational study. The evidence was further downgraded to very low certainty due to: - serious risk of bias (recall bias). In the study by Bennett et al, the OR were adjusted for the age of food introduction, which may slightly mitigate the risk of bias- for some outcomes, serious imprecision (low number of participants) - for some outcomes, wide confidence intervals - for some outcomes, the confidence intervals almost reached the null (0.99).	* CASP criteria: 1. Was there a clear statement of the aims of the research? 2. Is a qualitative methodology appropriate? 3. Was the research design appropriate to address the aims of the research? 4. Was the recruitment strategy appropriate to the aims of the research? 5. Was the data collected in a way that addressed the research issue? 6. Has the relationship between researcher and participants been adequately considered? 7. Have ethical issues been taken into consideration? 8. Was the data analysis sufficiently rigorous? 9. Is there a clear statement of findings? 10. How valuable is the research? CASP critical score: a) Criterion is completely met = 2; b) criterion is partially met = 1; c) criterion not applicable, not met, or not mentioned = 0; Total score 20 = high quality; 16–19 moderate quality; ≤ 15 low quality

	The Critical Appraisal Skills Programme (CASP) checklist* for qualitative studies was used to assess the quality of the studies conducting interviews/focus groups. Overall, the studies scored high on the checklist, and the evidence was of moderate quality. Results of the CASP checklist were as follow: Alianmoghaddam <i>et al.</i>, 2017: 19/20 (moderate quality) [criterion relationship between researcher and participants not met] Glover <i>et al.</i>, 2007: 18/20 (moderate quality) [criterion relationship between researcher and participants not met] Glover <i>et al.</i>, 2009: 16/20 (moderate quality) [criterion research design and criterion data collection partially met, criterion relationship between researcher and participants not met]	
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Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Within te ao Māori, breastfeeding is tika tūāpapa (a fundamental right). This tikanga has been impacted by colonialism. The included qualitative studies on Māori breastfeeding report that most participants value breastfeeding and believe that it improves the pēpi health, mother's wellbeing and helps with mother-child bonding. When supported by their whānau and by healthcare providers (in the form of breastfeeding information in the antenatal and postnatal phase), wāhine Māori favoured prolonged exclusive breastfeeding. Factors that prevented breastfeeding to 6 months or more were mostly modifiable, external factors (e.g. lack of information, lack of support, work-related, belief that breastfeeding in public is not acceptable/legal).	Harris et al conducted a survey (n= 496) of parents and healthcare practitioners on the use of breastmilk donation in New Zealand [8]. While Harris' study is not representative of a Māori population specifically (the study included 7.6% Māori), it gives evidence of parents' preferences for human breastmilk, when given the option. In the study cohort, 59.3% of pēpi were exclusively fed mother's milk for the first six months of their life, and 17.3% were fed both mother's milk and donated breastmilk. Mother's milk combined with infant formula only came third (11.3%).

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ● Probably favours	Evidence (mainly qualitative and from broader Māori populations) suggests tikanga-aligned practices support breastfeeding, strengthen whānau involvement and improve cultural safety. No major harms were identified,	

the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	but the effectiveness in preterm infants is uncertain. In the two studies that provided statistical data [1,6], factors associated with increased duration of breastfeeding were reported but specific interventions were not tested.	
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Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Cultural training of staff is required for healthcare providers to better understand te ao Māori, to ensure whānau-centred care and to improve the quality of interactions and information delivery with whānau Māori. Ongoing quality assessments and improvement programmes (e.g. Plan-Do-Study-Act [PDSA] cycles) involving champions of Māori-centred care may be necessary to improve outcomes and increase equity.	There is also a cost for not implementing the intervention.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No included studies	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No included studies	Evidence from Reid and colleagues on the economic costs of Māori health inequities demonstrates that the cost of inaction is substantial and enduring [9]. While incorporating mana-enhancing tikanga practices that support whānau Māori breastfeeding and embed Te Ao Māori values such as whanaungatanga and manaakitanga may require moderate investment in workforce capability, service redesign and time, these costs are likely outweighed by the consequences of not acting. Failure to provide culturally safe, mana-affirming breastfeeding support risks lower breastfeeding rates, poorer maternal and infant health outcomes and the perpetuation of inequities, all of which carry significant downstream health system and societal costs.

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	The Aotearoa New Zealand 2024 national infant exclusively breastfeeding rate at discharge in 2024 was 76.5%. The rate of exclusively breastfeeding at discharge for pēpi Māori was 80.7%, which is higher than the national rate. However, the percentage of pēpi Māori exclusively breastfed decreases by three months and more. At 5 months of age, the rate of exclusively breastfeeding in Māori population is lower than the national rate: 24.3% versus 35.4% [10].	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes	Promoting mana enhancing tikanga practices that increase Māori breastfeeding is acceptable, equitable, and is necessary to fulfil the Crown's obligations under the Te Tiriti o Waitangi.	

☐ Yes ☐ Varies ☐ Don't know		
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☐ Varies ☐ Don't know	There is a lack of available evidence and research on specific interventions to increase mana enhancing tikanga practices. The included studies are mostly qualitative and/or observational studies that report on likely influencers of breastfeeding. Opportunities exist to explore how breastfeeding can be supported from a cultural perspective in a mana enhancing way alongside implementation science to support implementation of support for whānau. Māori leadership in mana enhancing tikanga practices will increase feasibility and support these practices based on the evidence provided for positive and negative influencers. Eg: hapūtananga wananga for whānau Māori, are feasible.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know

	JUDGEMENT						
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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Appendix H.4 – Evidence to Decision: Monitoring Nutrition and Growth

EtD 51. What is the definition of faltering growth that requires attention or nutritional intervention for preterm infants?

POPULATION:	Preterm infants
INTERVENTION:	What is the definition of faltering growth that requires attention or nutritional intervention
COMPARISON:	(no comparison)
MAIN OUTCOMES:	Critical outcomes Mortality Faltering growth/body composition Neurodevelopmental impairment Adverse effects Fully breastmilk feeding at hospital discharge Important but not critical Time to full enteral feeds Necrotising enterocolitis Sepsis: proven or suspected Duration of initial hospital stay Time to full sucking feeds Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	Whilst growth is considered a critical measure of preterm infant progress and development, faltering growth is poorly defined with significant variation in definition, method of assessment, and threshold for intervention. Evaluating the evidence in relation to defining faltering growth is important to establish a consensus definition to guide clinical practice.
CONFLICT OF INTERESTS:	The following authors of the secondary analysis within a RCT (Nyakotey <i>et al</i>) are guideline group members: Barbara Cormack and Frank Bloomfield

Assessment

Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	There is no direct evidence to answer this clinical question. We provide a narrative summary of some additional supporting evidence. Growth assessment Serial measurements of weight, length and head circumference and knowledge of expected growth patterns are crucial for making accurate growth assessments in preterm infants. Z-scores and changes in z-scores are useful for standardising and quantifying infants' sizes, losses and growth, and for determining at which threshold faltering growth is associated with adverse outcomes. Expected growth patterns ESPGHAN [1] and the American Academy Pediatrics [2] agree that after early postnatal weight loss, the best goal for preterm infant growth is growth similar to the fetus and then term-born infants, which translates to growth approximately parallel to growth chart curves. A large, international longitudinal observational study [3] reported that even infants with uncomplicated postnatal adaptation transitioned to a weight gain trajectory 0.8 z-scores below birthweight at day 21 after birth. Maximum weight loss was 11% for infants with gestational age of 25-29 weeks and 7% for those between 30-34 weeks' gestation. This means that if an infant loses weight, as expected after birth, and then grows parallel to the growth chart, their weight z-score will be 0.8 z-score below their birth z-score, which may also apply to their length and head circumference. If an infant's growth is slower than growth chart curves, further investigation is needed to explore nutrition, morbidity, intrauterine or genetic reasons, with the actions required depending on the cause [4,5]. Existing consensus faltering growth/malnutrition criteria 1. American Academy of Dietetics: Consensus faltering growth/malnutrition criteria for preterm infants or neonates up to age 1 month were developed by eight experienced neonatal dietitians [4]. They proposed:	Evidence of benefit from nutrition and growth studies A systematic review of 6 clinical trials by Ong [7] showed consistent positive associations between postnatal weight or head growth and neurodevelopmental outcomes. For ELBW infants, achievement of head circumference z-score ≥ -2 by term-equivalent age is associated with better cognitive outcome at 5.5 years of age when compared with those with a head circumference z-score < -2 [8]. For preterm infants, head circumference growth is more closely related to neurodevelopment than weight gain [9,10]. In VLBW infants assessed at 25 years of age, it was found that, after adjustment for demographic factors and neonatal complications, only faster head circumference growth between birth and term-corrected age was significantly associated with improvements in IQ and its components, performance and verbal IQ, with effect sizes ranging between 0.33-0.42 standard deviations per z-score increase in head growth [11]. There were no statistically significant associations with faster weight or length growth. Aotearoa New Zealand: Secondary analysis of RCT [12]: Extremely low birthweight infants (n=327). Canada: Cohort study [3]: Gestational age 25-29 weeks and 30-34 weeks (n=981).
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Table 1. Primary indicators of neonatal malnutrition

Indicator	Mild malnutrition	Moderate malnutrition	Severe malnutrition	Use of indicator
Primary indicators requiring 1 indicator				
Decline in weight-for-age z score ^a	Decline of 0.8-1.2 SD ^b	Decline of >1.2-2 SD	Decline of >2 SD	Not appropriate for first 2 wk of life
Weight gain velocity ^a	<75% of expected rate of weight gain to maintain growth rate	<50% of expected rate of weight gain to maintain growth rate	<25% of expected rate of weight gain to maintain growth rate	Not appropriate for first 2 wk of life
Nutrient intake	≥3-5 consecutive days of protein/energy intake ≤75% of estimated needs	≥5-7 consecutive days of protein/energy intake ≤75% of estimated needs	>7 consecutive days of protein/energy intake ≤75% of estimated needs	Preferred indicator during the first 2 wk of life
Primary indicators requiring 2 or more indicators				
Days to regain birth weight	15-18	19-21	>21	Use in conjunction with nutrient intake
Linear growth velocity ^a	<75% of expected rate of linear gain to maintain expected growth rate	<50% of expected rate of linear gain to maintain expected growth rate	<25% of expected rate of linear gain to maintain expected growth rate	Not appropriate for first 2 wk of life May be deferred in critically ill, unstable infants Use in conjunction with another indicator when accurate length measurement available
Decline in length-for-age z score ^a	Decline of 0.8-1.2 SD	Decline of >1.2-2 SD	Decline of >2 SD	Not appropriate for first 2 wk of life May be deferred in critically ill, unstable infants Use in conjunction with another indicator when accurate length measurement is available

^aExpected weight gain velocity, expected linear growth velocity, and z scores can be determined using the online calculator PediTools (www.peditools.org).

^bSD=standard deviation.

2. NICE Recommendations: The National Institute for Health and Care Excellence (NICE) published recommendations in 2017 on a similar question to ours for *term infants* [6]. Consider using the following as thresholds for concern about faltering growth in infants and children (a centile space being the space between adjacent centile lines on a growth chart):

- a fall across 1 or more weight centile spaces, if birthweight was below the 9th centile
- a fall across 2 or more weight centile spaces, if birthweight was between the 9th and 91st centiles
- a fall across 3 or more weight centile spaces, if birthweight was above the 91st centile

current weight is below the 2nd centile for age, whatever the birthweight

The 10th percentile in a growth chart equates to a z score of -1.28 points. The 90th percentile also corresponds to a z-score of 1.28 points.

Undesirable Effects

How substantial are the undesirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Research indicates a link between faltering growth in preterm infants and subsequent neurodevelopment up to age 19 years [4,5]. Evidence from observational studies In a cohort born at <28 weeks' gestation [13] tested the predictive performance of 36-week gestational age weight measures <10th percentile, <3rd percentile, >1 z -score loss from birth and >2 z-scores loss from birth. Only a loss of >2 z-scores for weight related to adverse neurodevelopmental outcomes at 18-24 months CA. A secondary analysis within a RCT [12] examined associations between faltering growth and neurodevelopment in Aotearoa New Zealand and Australian extremely low birthweight infants. Faltering growth was defined as a z-score decrease ≥ 0.8 for weight/length, >1 for head circumference between birth, 4 weeks', 36 weeks' postmenstrual age and 2 years' corrected age. Faltering growth in all measures between 4–36 weeks (OR 2.0–4.7) compared with other time intervals (OR 1.7–2.7) were more strongly associated with developmental delay, particularly motor delay (OR 2.0–4.7) but faltering growth was poorly predictive of developmental delay at 2 years (AUC ≤ 0.62). In 168 VLBW infants [14] reported every 1-point loss in weight z-score to 36 weeks was associated with a 5.6 point (95% CI 1.7 to 9.4) decrease in the Bayley- II Mental Development Index. However, a weight z-score < -1.5 at 36 weeks was not associated with a worse mental or psychomotor result. In a USA cohort study [15], infants who lost >1 z-score for length from birth to discharge or 120 days had no difference in Bayley-III cognitive scores but had lower Bayley-III language scores. In summary, several studies have observed associations between losses of z-scores in neonatal care with suboptimal neurodevelopment [7,10,14,16,17]. Single studies that examined associations between z-score losses and neurodevelopmental outcomes found that losses of >1 z-scores for head circumference [10,17,18], weight [19] or length [20] or >2 z-scores for weight [21,22] were predictive. However, determining an appropriate z-score loss guideline that requires nutrition intervention requires further validation.	Over diagnosing faltering growth could lead to overfeeding preterm infants, which could increase their risks for obesity and cardiovascular disease in later life, doubt among practitioners about the adequacy of current preterm infant nutrition recommendations and damaging messages to parents about their infant's growth. If parents are told that their infant has faltering growth, distress on the part of parents could lead to discontinuing breastmilk feeding and possibly to inappropriate nutrition intervention. Nutrition intervention to limit perceived faltering growth, e.g. decrease of <0.8 z-scores from birthweight after the first 21 days after birth, especially if this involves increasing energy intake without the addition of protein and other nutrients. This type of intervention may not be beneficial because increasing fat mass without increasing fat-free mass may be harmful for later cardiovascular health outcomes.

Certainty of evidence

What is the overall certainty of the evidence of effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ○ No included studies	No included studies	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability	
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies	Definition of faltering growth that requires attention or nutritional intervention - moderate certainty evidence Until there is a clearer definition of when nutritional intervention is required with faltering growth in preterm infants, it is reasonable to use the recommendations suggested by (Goldberg et al., 2018) [4] and NICE to screen for and characterise faltering growth.	Head circumference growth may be more important than weight or length growth for neurodevelopment

☐ Don't know		
Resources required		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ Large costs ☐ Moderate costs ☒ Negligible costs and savings ☐ Moderate savings ☐ Large savings ☐ Varies ☐ Don't know	Negligible costs and savings	
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ Very low ☒ Low ☐ Moderate ☐ High ☐ No included studies	No studies were identified	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ Favours the comparison ☐ Probably favours the comparison ☐ Does not favour either the intervention or the comparison	No included studies	

○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies		
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Preterm pēpi Māori are more likely to experience challenges that contribute to faltering growth, due to the cumulative impact of social determinants of health, including colonisation, racism, income inequality, education, employment and housing. These factors may affect access to antenatal care, the quality of postnatal nutrition, breastfeeding support and continuity of care after discharge. Whānau Māori may face systemic barriers to timely identification and response to growth concerns, particularly if definitions are inconsistently applied or not communicated clearly. A lack of culturally grounded engagement can delay trust and limit opportunities for early intervention. A clear, equitable and nationally consistent definition of faltering growth is critical to ensuring that pēpi Māori receive timely and appropriate nutritional support. Equity for Pacific families Pacific infants are overrepresented in the preterm population and may be at greater risk of growth faltering due to overlapping clinical and social vulnerabilities. These include higher rates of early hospital discharge, limited culturally relevant post-discharge support and variability in how growth concerns are identified or addressed. Standardising the definition of faltering growth that requires intervention, alongside culturally appropriate engagement, can support equitable recognition and management of growth issues for Pacific infants. Equity for underrepresented groups Indian infants and infants from other underrepresented groups (including Middle Eastern and Asian backgrounds) are increasingly present in the preterm population in Aotearoa New Zealand. Risk factors for faltering growth may be compounded by language barriers, low health literacy, cultural food practices (such as vegetarianism or veganism) and limited familiarity with the New Zealand health system. Migrant, refugee and rural families may not consistently receive timely explanations or follow-up regarding growth patterns, particularly if the definition of faltering growth is not well understood across settings. An inclusive, clearly defined approach to identifying faltering growth is essential to enable consistent nutritional care and empower all families to participate meaningfully in their	

	infant's growth and care planning.	
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☐ Probably yes ☐ Yes ☐ Varies ☐ Don't know	Nutrition intervention when there is faltering growth - probably yes	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☐ Probably yes ☐ Yes ☐ Varies ☐ Don't know	Nutrition intervention when there is faltering growth - yes if there is a neonatal dietitian	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			

	JUDGEMENT						
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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EtD 54. Does access to a specialist neonatal dietitian vs. no access improve preterm infant outcomes?

POPULATION:	Preterm infants
INTERVENTION:	Access to a specialist neonatal dietitian
COMPARISON:	No access
MAIN OUTCOMES:	Critical for making a decision Mortality Neurodevelopmental impairment Adverse effects Faltering growth/body composition Fully breastmilk feeding at hospital discharge Important but not critical Fully breastfeeding at hospital discharge Duration of initial hospital stay Time to full enteral feeds Bronchopulmonary dysplasia Necrotising enterocolitis (NEC) Sepsis: proven or suspected Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Of limited importance Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	Preterm infants are born with increased nutritional needs due to interrupted <i>in-utero</i> growth and immature organ function. They are at high risk of faltering growth, feeding intolerance, nutrient deficiencies and long-term neurodevelopmental impairment. Meeting these needs through individualised, timely and carefully balanced nutrition is critical to improving both short- and long-term outcomes. Despite this, the availability of specialist neonatal dietitians varies widely across Aotearoa New Zealand, contributing to inconsistent care and widening inequities. Neonatal dietitians are trained to assess nutritional requirements, monitor feeding progression and support breastmilk feeding, the safe use of fortifiers, supplements and specialised formulas. Their involvement leads to more accurate nutrient delivery, earlier achievement of full enteral feeds, reduced rates of complications such as necrotising enterocolitis, and improved growth and neurodevelopment. The inclusion of a dietitian means there is consistent team member whose focus is nutrition which also strengthens team decision-making, supports culturally responsive care and helps guide parents through complex feeding journeys. International standards recommend minimum staffing ratios to ensure consistent care across neonatal units. The absence of these roles in some hospitals highlights a gap in service delivery that may contribute to avoidable harm. Addressing this gap through equitable, national implementation of neonatal dietitian services has the potential to significantly improve outcomes for preterm infants and their whānau.
CONFLICT OF	The following Guideline Development Group members are neonatal dietitians: Barbara Cormack and Tanith Alexander.

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	A non-systematic search found a rapid review [1] and two implementation studies [2,3] exploring the effect of the introduction of a multidisciplinary team that included a registered dietitian in the neonatal intensive care unit (NICU). Note that the two implementation studies were also included in the rapid review. No faltering growth/body composition: Pre-post implementation study: Weight gained per day from birth to discharge was significantly greater in the 2004 group (24 g; 95%CI 22 to 25) compared with the 2001 group (20 g; 95%CI 19 to 21; $P < 0.05$). Weight gain/day from birth to start of enteral feeds was significantly higher in the 2004 group (1.29 g; 95%CI 0.08 to 1.6) compared with the 2001 group (-8 g; 95%CI -5 to 0.0; $P < .05$). Weight gain/day from birth to full feeds was significantly higher in the 2004 group (17 g; 95%CI 13 to 20) compared with the 2001 group (6 g; 95%CI 3 to 9; $P < .05$). There was no difference in total length growth (2001: 8 cm; 95%CI 6 to 10 vs. 2004: 9 cm; 95%CI 8 to 11). Total head circumference growth was higher in the 2004 group (8 cm; 95%CI 7 to 9; $P < .05$) compared with the 2001 group (6 cm; 95%CI 5 to 7; $P < .05$). Another study reported a borderline significant decrease of weight Z-scores change between discharge and admission in the post-implementation period (-1.13 ± 0.99 vs. -0.91 ± 0.74, $p = 0.055$) [Critical] Duration of initial hospital stay: Pooled analysis from four studies ($n=785$) showed no difference in length of Neonatal Intensive Care Unit stay (MD 2.58 days; 9.04 less to 14.20 more) [Important]. Time to full enteral feeds: Pooled analysis from three studies ($n=680$) showed no difference in time to oral or enteral feeding (MD 16.43 days; 14.29 fewer to 47.15 more) [Important]. Bronchopulmonary dysplasia: Pre-post implementation study: No difference in bronchopulmonary dysplasia between pre-implementation (39/107; 37.5%) and post-implementation (49/122; 41.5%) [Important]. Necrotising enterocolitis (NEC): Pre-post implementation study: No difference in NEC (2001: 2/42 (5%) vs. 2004: 2/63 (3%). A second study also found no difference in NEC between pre-implementation (7/107; 10.7%) and post-implementation (11/122; 9%) [Important].	[1] UK; Rapid review: Infants admitted to Neonatal Intensive Care. The review included four non-randomised studies that included infants with gastroschisis, short bowel syndrome or very low birthweight. [2] USA: Implementation study. Infants with birthweights ≤ 1500g. Charts were reviewed for 42 infants in 2001 and 63 infants in 2004. [3] South Korea: Implementation study. Infants < 30 weeks' gestation or < 1250 g. Charts reviewed for 107 infants pre-intervention and 122 post-intervention. Key benefits of specialist neonatal dietitians: Improved nutrient intakes: Neonatal dietitians ensure infants receive the appropriate nutrients through strategies like breastmilk fortification, optimal macronutrient composition and tailored feeding plans. Enhanced growth and development: Early and optimal nutrition support, guided by dietitians, can lower the risk of adverse health outcomes and improve cognitive development in later life. Dietitians play a key role in detecting, diagnosing, and treating malnutrition and other nutritional issues in neonates. Reduced length of stay and costs: By optimising nutrition support, dietitians help to reduce the need for parenteral nutrition, decrease prescription errors and shorten hospital stays, leading to cost savings. Standardised practice and improved research: In Aotearoa New Zealand, there is substantial variation in neonatal nutrition practice. Neonatal dietitians contribute to the development of standardised practices and the improvement of the quality of research in neonatal nutrition, leading to more effective and equitable care for all infants. Expert nutrition support for parents and healthcare teams: Dietitians provide consistent, holistic support to parents and other members of the multi-disciplinary team, ensuring they have the

	Sepsis: Pre-post implementation study: No difference in sepsis between pre-implementation (26/107; 24.3%) and post-implementation (36/122; 29.5%) [Important]. Retinopathy of prematurity: Pre-post implementation study: No difference in retinopathy of prematurity requiring surgery between pre-implementation (23/107; 21.5%) and post-implementation (25/122; 21.4%) [Important].	knowledge and resources to provide optimal care. Addressing variations in practice: Neonatal dietitians help identify and address variations in neonatal nutrition practice, leading to more consistent and effective care. Early intervention: Early administration of optimal nutrition can significantly improve outcomes for preterm infants, lowering the risk of long-term health problems.
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Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Mortality: Pooled analysis from four studies (n=785) showed no difference in mortality (0 fewer per 1,000; 37 fewer to 93 more) [Critical].	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Overall certainty of evidence is very low. However, the importance of the neonatal dietitian is increasingly recognised in international guidance: National Institute for Health and Care Excellence (NICE 2022) clearly state that dietitians should be established members of the neonatal nutrition care team, with responsibilities that include the provision and management of parenteral nutrition (NICE NG154), 2020 [4]; NICE QS205, 2022) [5]. These roles are essential not only for ensuring high standards of nutritional care but also for improving outcomes and reducing variation across neonatal services. National Health Service (NHS) England and NHS Improvement (2021: In their neonatal transformation review) [6], the NHS acknowledged the essential role of specialist neonatal dietitians and highlighted the need to address under-resourcing in many neonatal units. The British National Health Service, National Quality Board recommends “all units have access to a neonatal or paediatric dietitian competent in neonatal nutrition and who can access a specialist neonatal dietitian if required”.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Access vs. no access to a specialist neonatal dietitian on infant outcomes - very low certainty evidence Probable increase in head circumference Uncertain effect on mortality, weight gain, length, duration of hospitalisation, time to reach full enteral feeds, bronchopulmonary dysplasia, NEC, sepsis, retinopathy of prematurity	Evidence is based on two implementation studies. There are unlikely to be randomised trials of access to a specialist neonatal dietitian versus no access. Providing access to a specialist neonatal dietitian is aligned with national and international best practice, is cost-effective and supports health equity across regions and ethnic groups. The role enhances multidisciplinary care and ensures safe, consistent and culturally respectful nutrition for our most vulnerable infants.

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Neonatal Dietitian Salary Advanced Practitioner \$130,295 to \$151,410 Advanced Clinician \$119,995 to \$127,720 Optimal neonatal dietetic staffing levels can be calculated using recommendations published by the neonatal specialist subgroup of the British Dietetic Association (BDA), which have been endorsed by the British Association of Perinatal Medicine (BAPM) and by the Australasian Neonatal Dietitians Network (ANDiN).	Resources such as job descriptions, specifications for neonatal dietitian skill requirements according to unit level and an <i>Australasian Neonatal Dietitians Network (ANDiN) Neonatal Dietitian Mentoring and Training</i> pathway already exist.

	https://www.bapm.org/resources/service-and-quality-standards-for-provision-of-neonatal-care-in-the-uk British Dietetic Association guidelines recommend: 0.1 full-time equivalent (FTE) per intensive care cot (Level 3) 0.05 FTE per high-dependency cot (Level 2) 0.033 FTE per special care/transitional cot (Level 1)	
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Reasonably certain Certainty of evidence of required resources for Māori No additional evidence available	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No studies assessed the cost-effectiveness of neonatal dietitians. As an integral member of the neonatal team, the specialist neonatal dietitian plays a vital role ensuring the delivery of consistent, individualised nutritional care, supported by evidence-based protocols and robust monitoring tools. This specialist input contributes to enhanced clinical effectiveness and reduces the risk of nutrition-related complications, which in turn is associated with shorter hospital stays and cost savings for healthcare services. Cost effectiveness for Māori No additional evidence available	Savings result from: Fewer days on parenteral nutrition Improved growth trajectories Reduced need for surgical or specialist follow-up for nutrition-related complications
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	A 2020 survey in Aotearoa New Zealand neonatal units [7] showed access to a neonatal dietitian was inconsistent. This has not changed. Evidence also shows that neonatal units with access to a dedicated specialist neonatal dietitian deliver more consistent and proactive nutritional care. Dietitians provide a clear point of consistent daily oversight for tracking nutritional progress and are more likely to implement early, optimal nutrition strategies and regular growth monitoring, improving the overall quality and safety of care. Rural hospitals and lower-resourced units are less likely to have access to specialist neonatal dietitians. Implementation of standard staffing across all units, supported by telehealth and equity-based workforce development, can help reduce disparities experienced by Māori, Pacific peoples and other underrepresented families.	
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Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Families and clinicians value early, consistent feeding guidance and support. Dietitians contribute to culturally responsive care, improve team confidence and ensure safer feeding practices. Their role is well-accepted by parents and professionals alike. Acceptability for Māori No evidence available	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Potential implementation challenges include: - Initial cost of employing new staff - Integration into existing clinical teams - Ensuring equitable access to training and resourcing across smaller or rural hospitals These challenges are outweighed by substantial benefits to patient outcomes and system-level efficiency.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know

	JUDGEMENT						
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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Appendix H.5 – Evidence to Decision: Whānau Education and Involvement

EtD 55. How do whānau Māori prefer to engage in discussions and receive information when making shared decisions about the care of their preterm pēpi?

POPULATION:	Preterm infants
INTERVENTION:	Whānau Māori engaged in discussions and receive information when making decisions about the nutrition care of their pēpi?
COMPARISON:	Standard care
MAIN OUTCOMES:	Critical outcomes Clear and culturally safe communication Upholding tikanga Māori Less important for decision making Faltering growth/body composition Fully breastfed or breastmilk feeding at hospital discharge Time to full sucking feeds Time to full enteral feeds Breastmilk supply/volume Duration of initial hospital stay Cost: cost of intervention, cost of neonatal care and life-long cost Mortality Neurodevelopmental impairment
SETTING:	Neonatal care
PERSPECTIVE:	Clinical guideline recommendation. Patient perspective
BACKGROUND:	Literature on the experience of the public health system by whānau Māori highlight experiences of racism and discrimination, including a lack of information provision and a lack of positive communication with healthcare providers. In the often-unfamiliar context of neonatal intensive care units (NICU), whānau Māori may feel particularly vulnerable and unsure how to provide for the specific needs of their preterm pēpi. Pēpi Māori have the highest overall rate of admission to SCBU/NICU and it is therefore paramount to ensure information is relayed to their whānau in a culturally appropriate way so that they can engage confidently in the care of their pēpi and bond with their pēpi. Studies show that, when faced with a lack of essential health information, whānau Māori find it difficult to ask questions and may fear that they are disturbing the staff. Within this power differential, it is the healthcare providers' duty of care to ensure they provide the necessary medical information in a way that is understood by the recipient. This would be described as mana enhancing behaviour from the medical staff, ensuring the parents are feeling empowered by the medical discussion not disempowered. Getting this right will contribute to increasing equity in Māori and is part of culturally safe care.
CONFLICT OF INTERESTS:	The following qualitative research (references 1 and 4) co-author is on the Guideline Development Group: Liza Edmonds

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	The evidence was based on two qualitative studies [1,2] Adcock <i>et al</i> [1] followed 19 whānau of preterm pēpi Māori (19 mothers, 9 fathers and 13 non-parents whānau Māori). The study followed their journey from birth to one year, with the majority of the interviews occurring while the pēpi Māori were in NICU. Themes that emerged from the interviews, regarding communication with healthcare providers were: The importance of having supportive providers who encouraged whānau Māori to not only take part but also lead the care of their pēpi. This was supported by clear communication around the need of the pēpi, with the opportunity to ask for more information and follow-up questions. Good communication involved information delivered at an understandable level, often involving playfulness and jokes, thus making participants feel at ease. Being involved in the care of the pēpi allowed whānau Māori to gain autonomy, to become familiar with the NICU environment and to become experts in the needs of their pēpi. Supportive healthcare providers were those who provided culturally safe care, with loving and empathetic communication. Continuity of care was seen as a key component of culturally safe care and allowed for whakawhanaungatanga (process of establishing relationships). Such providers became like family and participants often used familial terms to describe them. Of note the majority of healthcare providers identified as champions were non-Māori. The need to acknowledge the importance and legitimacy of extended whānau rather than only allowing the mother and father to participate in the care of the preterm pēpi. The need for healthcare providers to build relationship with the wider whānau was seen as a cultural imperative. Whānau Māori felt respected when healthcare providers made an effort to pronounce their name and their pēpi's name	In Adcock's 2021 study [1]: Not being involved in the care of the pēpi and having to follow the hospital schedule and routine made whānau Māori feel as if their pēpi was not really theirs. Being told by healthcare providers who could hold the pēpi Māori and when the pēpi could be held fostered feelings of fear and guilt. Whānau Māori reported feeling scared to hurt the pēpi, who, as a preterm pēpi, was already seen as fragile. Those feelings were enhanced when healthcare providers did not allow non-parents whānau members to hold the pēpi. The lack of understanding of the extended whānau and wide support system felt isolating to the parents. Giving too much information during the early days in NICU was described as overwhelming. Conflicting advice was also an issue that left whānau frustrated and unfairly treated. Communication was hindered when providers made assumptions about the participants, such as their smoking status, parental skills, age or relationship status. In the Masters-Awatere study [2], the whānau Māori who did not receive the Harti tool but instead received usual care said negative experiences that occurred were due to: Feeling shamed by healthcare providers rather than helped Feeling rushed and as if they were intruding on the hospital staff's time when they wanted to ask questions. This left them feeling isolated and alone Participant's expectation of hospital care was very low, with some participants feeling happy as long as their tamariki received clinical care and were still alive at the end of their hospital stay In another study, Adcock <i>et al</i> interviewed 10 healthcare providers (7 nurses, 1 medical officer, 1 kaiāwhina and 1 counsellor) identified as champions of culturally safe neonatal care by whānau of preterm pēpi Māori [4]. Themes that emerged from those interviews with champions were similar to those described by whānau Māori: The importance of collaboration between whānau Māori and healthcare provider in NICU, with mutual trust and respect. This included ensuring correct use of te reo Māori by healthcare providers. The need to ensure extended whānau Māori were involved in the care of the pēpi and in the decision-making processes. Champions of culturally safe care adapted their level of communication to the health literacy of the whānau and checked understanding with strategies such as open questions

	correctly. The study by Masters-Awatere <i>et al</i> [2] yielded similar themes. In this study, 15 whānau who had experienced the Harti tool* during their child's hospital stay were interviewed about their experience. The child were aged 0-5 years old. The Harti tool allowed for positive communication based on: Culturally appropriate and respectful interactions, facilitated by the use of te reo Māori and by cultural matching between the healthcare provider and whānau Māori. Kaupapa Māori practices such as whakawhanaungatanga (process of establishing relationships): this was facilitated by health practitioners creating a calm and relaxing environment, taking the time to listen to whānau Māori concerns and to answer their queries, and offering information and practical advice that promoted confidence and self-autonomy. Connection based on genuine care and practical actions to address identified needs. * The Harti Hauora Tamariki Tool (The Harti tool) is a tamariki and whānau-based need assessment tool, developed at the Waikato Hospital and designed to reduce health inequities [3].	or teach-back method. Champions believed their role was not just taking care of the preterm pēpi but also to spend time with the extended whānau and build a relationship with them through everyday conversation and through continuity of care. Culturally safe communication is based on aroha (love), compassion and empathy and an understanding that childbirth and care of the preterm pēpi are sacred time and spaces for whānau Māori. Culturally safe care did not rest on technological performances but on genuine and respectful relationship building between healthcare providers and whānau Māori. In a qualitative study by Abel <i>et al</i> [5] on the experience of 12 wāhine Māori using a wahakura, it was noted that the making of the wahakura was an opportune time for healthcare providers to engage with whānau Māori on safe sleep recommendations. The activity was perceived as having cultural value and a way to connect or reconnect with "being Māori". This culturally safe environment facilitated engagement of whānau Māori with healthcare providers and their messages.
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Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	No undesirable effects were identified	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low	The evidence provided is rich qualitative data, that amplifies whānau Māori experience of health. The methodology used	* CASP criteria: 1. Was there a clear statement of the aims of the research? 2. Is a qualitative methodology appropriate? 3. Was the research design appropriate to

○ Moderate ● High ○ No included studies	to analyse the data includes, for example kaupapa Māori methodologies and grounded theory. Nine references were included, which is significant for this area of research. The Critical Appraisal Skills Programme (CASP) checklist* for qualitative studies was used to assess the strength of the including qualitative studies. Overall, included studies ranked high on the checklist (high to moderate quality). The majority of the included studies directly or closely answered the PICO, meaning the information was not extrapolated from indirect evidence. Results of the CASP checklist were as follow: ●Adcock et al., 2021: 20/20 (high quality) [1] ●Masters-Awatere et al., 2019: 20/20 (high quality) [2] ●Malek et al., 2018: 18/20 (moderate quality) [6] [criteria for both recruitment strategy and relationship between research and participants partially met]	address the aims of the research? 4. Was the recruitment strategy appropriate to the aims of the research? 5. Was the data collected in a way that addressed the research issue? 6. Has the relationship between researcher and participants been adequately considered? 7. Have ethical issues been taken into consideration? 8. Was the data analysis sufficiently rigorous? 9. Is there a clear statement of findings? 10. How valuable is the research? CASP critical score: a) Criterion is completely met = 2; b) criterion is partially met = 1; c) criterion not applicable, not met, or not mentioned = 0; Total score 20 = high quality; 16–19 moderate quality; ≤ 15 low quality
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Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	A review by Wilson <i>et al</i> noted that Māori worldviews consider people's physical, psychosocial, spiritual and, importantly, relational needs [7] Relational care is defined as the deliberate nurturing of respectful and meaningful relationships with Māori and their whānau. The review therefore highlighted the key elements for a Māori-centred model of care: Whanaungatanga (connectedness) and whakawhanaungatanga (the process of building relationships) using tikanga (cultural protocols and processes). Informed by cultural values of aroha (compassion and empathy), manaakitanga (kindness and hospitality), mauri (binding energy) and wairua (importance of spiritual wellbeing). In the 2022 New Zealanders' Experiences and Perceptions of	In the Malek <i>et al</i> study, Australian and New Zealand parents of children aged <12 months, who were using infant formula were interviewed in focus groups [6]. Among the 136 participants, 30 were Māori/Pacific People (no distinction made in the study). The authors noted that healthcare providers were rarely able to answer parents' query on the best infant formula to choose and that parents were therefore left to their own devices when making a decision. The focus group highlighted parents thought process regarding the selection of an infant formula. In the three Māori/Pacific People focus groups, the main themes that emerged around communication of information were: Lack of understanding of the ingredients listed - parents would rather see layman's terms and/or visual explanations (e.g. pictures). Lack of understanding of nutrient claims - nutrition information was deemed important if the pēpi had specific nutritional needs. Parents therefore preferred claims that stated health benefits, as they found those easier to understand. Parents sometimes checked the sugar, fat and/or salt content. Parents were sometimes swayed by specific claims such as "for hungrier babies".

	the Maternity and Perinatal System Report, whānau Māori reported that not having their cultural needs met was a source of dissatisfaction. This included: Cultural needs being assumed, based on their physical appearance. No help to meet cultural needs. A general lack of awareness amongst hospital staff about what was culturally appropriate and respectful.	
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Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ Don't know	Studies are primarily qualitative data summarising experiences and not the effect of an intervention. There is clear qualitative evidence supporting the inclusion of whānau as essential team members.	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies	The evidence presented highlight that the barriers to information delivery in the context of caring for preterm pēpi Māori are not technical but relational. Cultural training of staff is therefore required for healthcare providers to better understand te ao Māori, to ensure whānau-centred care and to improve the quality of interactions and information delivery with whānau Māori. Ongoing quality	

○ Don't know	assessments and improvement programmes (e.g. Plan-Do-Study-Act cycles) involving champions of Māori-centred care may be necessary to improve outcomes and increase equity.	
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Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No included studies	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No included studies	Evidence from Reid and colleagues on the economic costs of Māori health inequities demonstrates that the cost of inaction is substantial and enduring [8]. While incorporating mana-enhancing tikanga practices that support whānau Māori breastfeeding and embed Te Ao Māori values such as whanaungatanga and manaakitanga may require moderate investment in workforce capability, service redesign and time, these costs are likely outweighed by the consequences of not acting. Failure to provide culturally safe, mana-affirming breastfeeding support risks lower breastfeeding rates, poorer maternal and infant health outcomes and the perpetuation of inequities, all of which carry significant downstream health system and societal costs.

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ● Increased ○ Varies ○ Don't know	In 2023, 8.5% of pēpi Māori were born before 37 weeks' gestation, compared to 7% of NZ European/other pēpi and 7.8% of pēpi Māori were born weighing less than 2500 g compared to 5.5% of NZ European/other pēpi. In the 2019 review of neonatal care in New Zealand pēpi Māori had the highest overall rate of admission to SCBU/NICU, accounting for 28% although pēpi Māori had lower occupancy in level 3 units compared with pēpi from other ethnic groups [9]. The review noted that the NICU staff did not reflect the population it supports, as Māori staff represented 4% of the workforce in 2019 compared to 73% for NZ European staff. Adcock <i>et al</i> [1] also noted that many pēpi Māori were transferred to a NICU far from home. This had various consequences: Financial consequences, with many parents not knowing about or having difficulties accessing government-funded travel assistance, needing to take unpaid time off work, needing to access accommodation Loss of whānau support. When parents had other pēpi, the mother was often transferred alone to NICU - many participants reported on the subsequent feeling of isolation in a foreign environment, making whakawhanaungatanga with healthcare providers even more important Lack of access to spiritual practices such as whenua ki te whenua (returning the placenta to the earth) due to the placenta being lost/destroyed during transfer.	A systematic review by Graham <i>et al</i> on Māori experiences of the public health system reported on institutional level barriers, including racism and discrimination [10]. Experiences from whānau Māori described in the review included: Being aware of negative perceptions by healthcare providers, through the provider's body language, facial expressions and mispronunciation of their name. Inability to build a relationship with and absence of warmth from healthcare providers. When in an unfamiliar setting, information provision was poor, leaving whānau Māori unsure of what to ask. When information was provided, it was often in an inappropriate form, such as a pamphlet. Access to additional resources and ancillary support services was rare and difficult. Unwillingness to "disturb" busy healthcare providers and "waste their time", leading to whānau Māori downplaying their pain and symptoms. Having to focus on physical health only and having to ignore mental and spiritual health.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No	Promoting culturally safe communication and healthcare	

○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	delivery is acceptable, equitable, and is necessary to fulfil the Crown's obligations under the Te Tiriti o Waitangi.	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Culturally appropriate initiatives such as the wellbeing needs assessment tool Harti Hauora Tamariki Tool (The Harti tool) show that whānau-centred approaches are feasible. The Harti tool is currently being assessed in a randomised controlled trial conducted at the Waikato hospital. Early qualitative results highlight an improvement in whānau Māori experiences of communication with healthcare providers [2,3].	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know

	JUDGEMENT						
REQUIRED							
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ●
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EtD 56. How do Pacific peoples and families prefer to engage in discussions and receive information when making shared decisions about the care of their preterm pēpi?

POPULATION:	Preterm infants
INTERVENTION:	Pacific peoples and families engaged in discussions and receiving information when making decisions about the nutrition care of their preterm pēpi
COMPARISON:	Standard care
MAIN OUTCOMES:	Critical outcomes Clear and culturally safe communication Upholding Yavu – Foundations of Pacific Engagement Policy Faltering growth/body composition (<0.5 z-score or %FFM) Fully breastfed or breastmilk feeding at hospital discharge (<20 per 1000) Less important for decision making Time to full sucking feeds (<0.5 days) Time to full enteral feeds (<0.5 days) Breastmilk supply/volume Duration of initial hospital stay (<0.5 days) Cost: cost of intervention, cost of neonatal care and life-long cost (<NZD\$10 per baby) Mortality (<1 per 1000) Neurodevelopmental impairment (<10 per 1000)
SETTING:	Neonatal care
PERSPECTIVE:	Clinical guideline recommendation. Patient perspective
BACKGROUND:	The rate of preterm birth in Pacific families in Aotearoa New Zealand was 8.8% in 2023, and Pacific families are disproportionately represented in the NICU. Yet, only 1% of NICU staff identify as Pacific Peoples and there is a significant lack of research on the experiences of Pacific families in the SCBU/NICU, particularly regarding culturally appropriate essential medical information provision and health communication. To increase equity and provide culturally safe care, health providers must prioritise identifying and delivering medical information in a culturally safe manner and demonstrate behaviours that empower Pacific families. This would increase Pacific families bonding and caring for their pēpi as well as be able to engage confidently with staff".
CONFLICT OF INTERESTS:	None

ASSESSMENT

Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial	There is a clear evidence gap when it comes to the care of Pacific	In a third study [3] study, parents of infants in NICU were interviewed

○ Small ● Moderate ○ Large ○ Varies ○ Don't know	families in the context of preterm birth. Only sparse indirect evidence was available, extracted from qualitative studies. In Walsh et al [1], 10 Pacific families of pēpi (four Samoan, four Tongan, one Cook Island and one Māori mother married to a Samoan man) with neonatal hypoglycaemia were interviewed about their experience. Infants were not necessarily in NICU, nor were they necessarily born preterm. Enablers of positive experiences were: • Teu Le Vā (the building and nurturing of relationships) was the most important theme identified during the care pathway. Participants recalled positive experiences with healthcare practitioners who provided time and loving care. On the other hand, participants felt disrespected when faced with healthcare providers they did not know and who did not take the time to build a relationship. This was viewed as an invasion of their sacred space. • Faith and spirituality were important to many participants, and the opportunity to have a space and the opportunity to pray while in the hospital, especially before a procedure, was appreciated. Most participants also wished to express their faith without fear of judgement from hospital staff. In a study by Abel et al [2], 150 participants were divided into six focus groups to discuss infant care practices. Among the 150 participants, 25 were Tongan, 28 were Samoan, 30 were Cook Island and 14 were Niuean. The study was conducted in 1998 which could prevent the generalisation of the findings to today's population. Themes that emerged were: • The importance of community support during the postpartum period. In the Pacific Island groups, support from the extended family, especially female members (mother, mother-in-law, sisters and aunts) was expected and readily offered. Support was practical, financial and emotional. The extended family is very much involved in the care of the infant and therefore has a strong impact on infant care practices. • When support from family/community was not available, Pacific Island participants tended to rely more on healthcare providers for information. However, few attended antenatal classes or sought postnatal support from professional organisations as they perceived those services to be developed for Pākehā families. • Information from healthcare providers sometimes clashed with information and traditional practices promoted by elders in the	about their experience. Of the 83 parents interviewed, 7 were Pacific families (8.6%). Challenges that emerged were: • Feeling of disempowerment due to a lack of control, of information and of involvement in the care of the infant. • Power imbalance between NICU staff and parents, with NICU staff acting as gatekeeper to the infant and parents feeling that they needed to ask permission to touch, care for and spend time with their infant. Parents also did not want to disturb the staff with questions. • Lack of space for the fathers, who felt they had a secondary role to the mother and felt they were in the way while in NICU, even though they were described as the main support person for the mother. In a study by Pio et al [4], 20 Samoan mothers were interviewed about their experience with their general practitioners (GP). The study reported that: • Mothers' experiences with their GP influenced their decisions and care of their children. • Participants valued positive feedback on their care of their children and being acknowledged as the expert of their child's health. • Participants often felt rushed during their consultation and received closed answers that prevented true communication with the GP, trust and relationship building. • Participants often felt inferior to the GP and too intimidated to ask questions or disagree. • Limited English of some participants was a barrier to communication with the GP. The use of medical jargon was also a barrier, whether or not the participant understood English. Instead, participants wished user-friendly resources were available, written in both Samoan and English, and using imaging as much as possible. In another study [5], seven grandparents who had provided at least five meals per week to their grandchild (infant <24 months) in the previous three months were interviewed. Two participants were Samoan and five were Māori. Of the two Samoan participants, one was the primary caregiver or had a substantive role for their six grandchildren. The other participant had a substantive caregiver role to one grandchild. Themes that emerged were: • Participants wanted more infant nutrition resources developed
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	community, especially those who had been raised outside of New Zealand. • An example of conflict was around the introduction of solids, with healthcare providers recommending (at the time) to wait until four months old before introducing some solids. Some Cook Islands participants believed that Pacific infants were hungrier than Pākehā infants and that the recommendation therefore did not apply to them. Some Pacific family participants introduced solids at 6-8 weeks, and several participants started at 3 months. Solids were pureed fruits, vegetables and cereals and/or sua alaisa (a special Samoan soup), pia (arrowroot starch) and mokomoko (coconut milk). • Most participants, especially those raised in New Zealand, adopted some Western recommendations and modified them to integrate traditional practices. • Most participants favoured breastfeeding although some ceased to breastfeed due to challenges such as having difficulty establishing breastfeeding, experiencing cracked nipples, conflicting advice between healthcare providers and thinking they did not have enough milk. • Bedsharing with the infant was the norm amongst Pacific family participants. Bedsharing was believed to have practical, psychological and spiritual benefits for the infant. • The traditional practice of milimili during pregnancy (gentle rubbing of the abdomen), as well as traditional baby massage were also identified as very important to most Pacific families.	specifically for them (e.g. written in Samoan), readily available and easy to understand (e.g. through the use of lay terms). • Strong support for breastfeeding, considered the healthiest option but also the most cost-efficient. • Limited income and high cost of food (especially fresh fruits and vegetables) were identified as significant barriers to ensuring optimal feeding practices for the children in their care. • Participants were identified as community advisors, carers and cultural custodians. As such, they shared key information and experiences around childcare and infant feeding practices with other members of the community. Many also had gardens and knowledge around plants that they shared with others. Participants were exposed to social scrutiny, with some feeling ashamed or guilty if their grandchildren were perceived as 'skinny' by others.
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Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	No undesirable effects were identified.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	The overall certainty of evidence is low due to indirectness: no information was available for Pacific families and the care of their preterm pēpi. No statistical analysis was provided in any of the included studies and the evidence is therefore purely narrative. However, the included evidence, while indirect to the PICO, ranked high on the Critical Appraisal Skills Programme (CASP) checklist* for qualitative studies. Overall, the strength of the including qualitative studies was high to moderate. Two of the included studies used a Pacific family/ies centred framework when developing their study methodology/epistemology (e.g. use of the Fonofale Model in George 2021) or when reporting on study findings (e.g. use of the Seitapu Framework of Cultural and Clinical Competency in Walsh 2025). Results of the CASP checklist were as follow: • Walsh et al., 2025: 20/20 (high quality) [1] • Abel et al., 2001: 20/20 (high quality) [2] • Tapera et al., 2016: 20/20 (high quality)[5] • George et al., 2021: 19/20 (moderate quality) [6] [criteria statement of aims partially met] • Pio et al., 2020: 18/20 (moderate quality) [4] [criterion for relationship between researcher and participants not met] • Serlachius et al., 2018: 17/20 (moderate quality) [3] [criterion for recruitment strategy partially met; criterion for relationship between researcher and participants not met]	* CASP criteria: 1. Was there a clear statement of the aims of the research? 2. Is a qualitative methodology appropriate? 3. Was the research design appropriate to address the aims of the research? 4. Was the recruitment strategy appropriate to the aims of the research? 5. Was the data collected in a way that addressed the research issue? 6. Has the relationship between researcher and participants been adequately considered? 7. Have ethical issues been taken into consideration? 8. Was the data analysis sufficiently rigorous? 9. Is there a clear statement of findings? 10. How valuable is the research? CASP critical score: a) Criterion is completely met = 2; b) criterion is partially met = 1; c) criterion not applicable, not met, or not mentioned = 0; Total score 20 = high quality; 16–19 moderate quality; ≤ 15 low quality

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important	Two models of health for Pacific Island whānau were identified during the search: In George <i>et al</i> [6] in which 17 Pacific Island households were interviewed around their sleep patterns and habits, the Fonofale Model was used. In this model, family is considered the foundation for health. Wellbeing involves several posts such body, mind, spirit and culture, all occurring within the broader context of time and environment. In Walsh <i>et al</i>, the Seitapu Framework of Cultural and Clinical Competency was used [1]. It is based on four principals of Seitapu	

uncertainty or variability	(sacred flower): Family, Language, Tapu (sacred religion and cultural beliefs), and Community.	
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	The studies are primarily qualitative data summarising experiences and not the effect of an intervention. The limited available evidence shows that Pacific families place the highest value on relationship-centred care, where trust, time, respect and spirituality are honoured, and where extended family are included in decision-making.	
Resources required		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	No information is available. Resources are first needed to bridge the evidence gap and find out the best communication strategies and practices to engage with Pacific Island whānau in the context of premature birth.	
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Very low ○ Low ○ Moderate ○ High ● No included studies	No included studies.	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No included studies.	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased	In 2023, 8.8% of Pacific Island pēpi were born before 37 weeks' gestation, compared to 7% of NZ European/other pēpi. In the 2019 Review of neonatal care in New Zealand pēpi of Pacific peoples accounted for 7% of level 2 unit, 4% of level 2a unit and 16% of level 3 unit. The review noted that the NICU staff did not reflect the population it	

○ Increased ○ Varies ○ Don't know	supports, as Pacific Island staff represented 1% of the workforce in 2019 compared to 73% for NZ European staff.	
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ● Don't know	This evidence gap is an issue, especially considering the significant percentages of preterm infants from Pacific families in NICU. To be acceptable, interventions would also need to consider the specificity of each Pacific Island (e.g. Samoa, Tonga, Cook Islands) as Pacific People are not a completely homogenous group, but each Pacific Island has its own cultural identity.	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	While there is no evidence, it is feasible in Aotearoa New Zealand to improve the way we engage with Pacific peoples and families in shared decision-making about the care of their preterm pēpi, but doing so will require intentional, culturally grounded changes in how health services communicate and build relationships. The Yavu – Foundations of Pacific Engagement Policy offers a practical framework for this. Yavu is a Pacific engagement tool developed by the Ministry for Pacific Peoples to help guide engagement with Pacific communities in ways that are meaningful, culturally responsive, sustainable, and relationship based. The word yavu refers to “foundation” and incorporates Pacific values and worldviews into engagement processes. These principles overlay the usual engagement steps and remind health professionals and systems that effective engagement with Pacific peoples is not just about information transfer – about connection, respect and shared understanding.	Key principles of Yavu include: • Understanding context – know the Pacific peoples you are engaging with, including cultural backgrounds, languages, family systems and health-related beliefs. • Environment – invest time and space to connect genuinely, rather than treating engagement as transactional. • Responsibility – recognise the contribution and expertise Pacific families bring, especially in caring for pēpi. • Teu le va – build, nurture and strengthen relationships over time; va refers to the relational space between people.

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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EtD 57. Should whānau-led tikanga around food be integrated into supporting whānau Māori in the nutritional care of pēpi Māori?

POPULATION:	Preterm infants
INTERVENTION:	Integrating whānau-led tikanga around food to support whānau Māori in the nutritional care of pēpi Māori
COMPARISON:	Standard care
MAIN OUTCOMES:	Critical outcomes Upholding whānau-led tikanga Māori Breastmilk supply/volume Fully breastfed or breastmilk feeding at hospital discharge and/or at 6 months post-partum Necrotising enterocolitis Mortality Neurodevelopmental impairment Sepsis: proven or suspected Time to full enteral feeds Important but not critical Adverse effects Faltering growth/body composition Duration of initial hospital stay Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical guideline recommendation. Patient perspective
BACKGROUND:	The concept of kai as rongoa and critical to the healing of the patient is a concept widely shared in indigenous traditions. There is currently no national-level policy on provision of meals for the primary caregiver of a hospitalised pēpi. Whānau Māori often report feeling hungry during their stay in NICU due to the lack of food provision and few affordable options nearby. In te ao Māori, kai (food) is a source of connection, and the gifting of kai is a mark of manaakitanga (respect, hospitality) and is important to create an environment that is noa (free from tapu). Whānau Māori with a preterm pēpi often describe NICU as an inhospitable environment where they feel stressed, isolated and alone. The wellbeing of the pēpi is dependent on the wellbeing of the whānau and integrating whānau-led tikanga around food may improve whānau wellbeing and ultimately benefit everyone.
CONFLICT OF INTERESTS:	The following qualitative study (reference 3) co-authors are on the Guideline Development Group: Lisa Kremer, Liza Edmonds

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	No evidence was found that addresses the benefits of integrating whānau-led tikanga around food into the care of Māori preterm pēpi. However, in a study by Smith <i>et al</i> [1] the findings of the Kai Atua project were presented. Kai Atua is a three-year Kaupapa Māori research project revolving around Māori understandings of food and traditional Māori food practices. The study reported that: Kai (food) is connected to te taiao (the environment) and tūpuna (ancestors) Māori food system is based on respect for the environment and connection between people and nature Kai binds communities and environments across generations Kai is rongoā (medicine), a source of wellbeing and connection Integrating tikanga practices around food in the care of preterm pēpi may therefore mean ensuring that the whole whānau is provided for, and that healthcare providers are involved in tikanga around food, as the sharing of kai and company, mātauranga (knowledge), pūrākau (storytelling) and manaakitanga (showing respect, generosity and care) are all connected. Examples of family Integrated Care (FICare) models for whānau Māori are still rare but a tamariki and whānau-based need assessment tool, the Harti Hauora Tamariki Tool (The Harti tool) was developed at the Waikato Hospital and designed to reduce health inequities [2]. The Harti tool is a co-design tool grounded in Māori worldview: It emphasises the existence and validity of Mātauranga Māori (Māori knowledge) It promotes mana motuhake (self-determination) and whānau-centred care, with the understanding that the whānau is "a source of strength, support, security, and identity" The tool is based on tikanga practices such as whakamana (empowerment), whakawhanaungatanga (process of establishing relationships), manaakitanga (showing respect, generosity and care). A qualitative study by Masters-Awatere [3] including whānau Māori of a child aged 0-5 who had experienced the Harti tool during the child's hospital stay reported that the tool fostered culturally appropriate and respectful interactions, facilitated by the use of te reo Māori and by cultural matching between the healthcare provider and whānau Māori. The role of kai and the possible ways to integrate tikanga around food in the hospital environment were however not discussed.	In a study by Rogers <i>et al</i>, 10 whānau Māori with a pēpi at risk of neonatal hypoglycaemia were interviewed [4]. Themes that emerged were: Whānau found it easier to accept medical interventions such as heel prick tests if this was preceded by a tikanga led process (e.g. karakia) Whānau want to take an active part in the care of their pēpi, and health decision are often taken collectively by the whānau Deep connection of the whānau and the pēpi to whakapapa - this was highlighted by tikanga practices such as using karakia before hypoglycaemia testing/treatment to connect to tipuna (ancestors).

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	In a master's thesis work by Brown [5], eight whānau Māori caring for a pēpi in NICU were interviewed. Participants reported that: Kai is central to the wellbeing of whānau Māori in NICU. Receiving kai fulfils a basic need and is therefore paramount in the care of whānau Māori caring for their pēpi Kai connects people and creates a noa (free from tapu) environment However, participants' experience of meals provided by the hospital did not allow for these positive feelings and connections to occur. Participants described the food as limited, 'gross' and 'uneatable' and not kai that whānau Māori would eat in their everyday life Participants who breastfed their pēpi relied on nutritious and appetising kai as well as a dedicated space to eat to ensure milk supply, neither of which was provided by the hospital On the other hand, participants recalled feeling respected and cared for when staff offered extra meals to caretakers other than the mother, such as during Father's Day. Experiences of hunger is often reported in the literature around NICU. In Adcock's study of 19 whānau of preterm pēpi Māori, several participants reported going without food as this was not provided or it was overly difficult to access during their stay in NICU [6]. This led to participants describing NICU as an inhospitable space. When it comes to kai, the support of non-parent whānau members was therefore essential as they delivered food to parents of preterm pēpi and advocated for parents to receive entitlements in the hospital, such as meal vouchers. This was particularly important as the majority of parents in the study lived far from NICU and therefore had to stay in hospital accommodations or in hotels. However, some units prevented non-parents whānau to visit outside of visiting hours, which limited their ability to provide practical support called for a meal to be provided to whānau caring for a child in hospital [7]. Provision of food and/or kitchen facilities currently varies in different hospitals with many whānau having to bring or buy their own meals. Fifteen whānau Māori participants of hospitalised tamariki aged 0-4 were interviewed. Themes that emerged were: Participants often had to rush to the hospital and did not have time/did not think to bring food. Having to pay for food, alongside other expenses (such as reduced work hours, parking/transport) was a financial burden, especially for low-income whānau Māori. Some participants reported having no money to pay for food	

	On-site hospital cafés were often too expensive, meaning participants had to find more affordable options outside of the hospital, thus having to leave their child's side which many described as unacceptable, especially if no one else was there to care for the tamariki Parents, especially mothers, of tamariki were often away from their extended whānau (especially for participants who lived rurally and who had no local support near the hospital) which left them feeling isolated and without emotional and material support such as food being brought to them. Whānau extended network was therefore not always available or able to provide food to the caregiver (either due to cost or/and transport and/or time constraint such as being at work or taking care of the sibling of the hospitalised tamariki) Participants therefore experienced hunger during their hospital stays ("I was starving") but some felt whakamā (embarrassed) and were reluctant to ask for help. Some were also wary of mentioning their situation to healthcare providers, for fear of "getting in trouble" with government agencies Hunger increased anxiety and worry in participants, in a situation that was already stressful.	
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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	No statistical analysis was provided in the included studies. The evidence is therefore narrative and qualitative in nature, but the majority of included studies used a kaupapa Māori approach. While only two studies provided direct information relevant to the PICO (Brown 2023, Masters-Awatere 2020), the evidence provided is rich in themes and valuable insights from whānau Māori with a pēpi in NICU. The remaining studies included indirect evidence that gave some additional insights into tikanga practices around kai. The judgement of moderate certainty was based on the first critical outcome: "upholding whānau-led tikanga Māori. The Critical Appraisal Skills Programme (CASP) checklist* for qualitative studies was used to assess the strength of the including qualitative studies. Overall, the evidence was of high quality. Results of the CASP checklist were as follow: • Masters-Awatere et al., 2019: 20/20 (high quality) [3] • Rogers et al., 2025: 20/20 (high quality) [4] • Brown, 2023: 20/20 (high quality)	* CASP criteria: 1. Was there a clear statement of the aims of the research? 2. Is a qualitative methodology appropriate? 3. Was the research design appropriate to address the aims of the research? 4. Was the recruitment strategy appropriate to the aims of the research? 5. Was the data collected in a way that addressed the research issue? 6. Has the relationship between researcher and participants been adequately considered? 7. Have ethical issues been taken into consideration? 8. Was the data analysis sufficiently rigorous? 9. Is there a clear statement of findings? 10. How valuable is the research? CASP critical score: a) Criterion is completely met = 2; b) criterion is partially met = 1; c) criterion not applicable, not

	- Adcock et al., 2021: 20/20 (high quality) [6] - Masters-Awatere et al., 2020: 16/20 (moderate quality) [7] (criterion data collection and criterion data analysis partially met, criterion ethical issues not completed)	met, or not mentioned = 0; Total score 20 = high quality; 16–19 moderate quality; ≤ 15 low quality
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Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	It is important to not treat Māori as a homogenous group who have the same values; however, most Māori will value upholding tikanga in healthcare.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	The studies are primarily qualitative data summarising experiences and not the effect of an intervention.	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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● Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Masters-Awatere et al [7] provided a quick cost analysis in their call for universal meal provision of caregivers of a hospitalised child. The analysis was conducted in 2020 and is therefore not up to date. At the time, they calculated that: The cost of patient meals as provided by in-house catering services was NZ\$1.83 per patient meal Across Aotearoa New Zealand, 143,710 children under the age of 5 were discharged from a public hospital for the year ended 30 June 2017 The national mean length of stay was 2.5 days Based on these figures, they calculated that the delivering a lunch and a dinner meal to one caregiver of all admitted children (aged 0-4) in a public hospital would cost around \$1 million per annum (\$1,051,957.20) on what was, at the time, an annual health expenditure of \$6 billion. This analysis only accounted for meal provision for one caregiver. Studies show the importance of the extended whānau in the care of the preterm pēpi. Available literature also emphasises the community aspect of kai - a truly culturally appropriate approach would therefore need to encompass more than one caregiver. It may for example mean ensuring kitchen and communal places dedicated to cooking and eating are available in every NICU wards. It would also mean reconsidering and adapting the existing visiting policies to enable the presence of the extended whānau.	
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Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	The analysis conducted by Masters-Awatere [7] is out of date as the study was published in 2020. No recent cost-analysis could be found.	In December 2025, the cost of parent meals as provided by hospital contracted catering services is NZ\$12.00 per lunch meal and NZ\$13.50 per dinner meal.

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the	In the Masters-Awatere [7] study, the meal delivery service was described as more cost-effective than providing meal vouchers to be used at the hospital café.	

intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies		
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Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Studies show that whānau Māori often experience hunger while caring for their pēpi in the hospital. Pēpi may need to stay in NICU for several weeks or months, which means whānau Māori face many long-term costs, especially if the pēpi is cared for in a hospital away from home (in the available literature, many study participants lived more than 90 minutes away from the hospital). These costs include loss of work income, cost of transport/parking, accommodations, food. For those of lower income status, those costs are often prohibitive: several participants recall going without food during their stay. When kai is provided by the hospital, it is often described in the literature as very different to what whānau Māori would usually eat, highlighting that meals are designed for a non-Māori population.	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	In the 2019 Review of neonatal care in New Zealand pēpi Māori had the highest overall rate of admission to SCBU/NICU [8]. Adapting the NICU environment to provide culturally appropriate care to whānau Māori is paramount to fulfil the Crown's obligations under the Te Tiriti o Waitangi. In the Masters-Awatere [7] study, providing meals through the hospital was described as: More nutritious and healthier than making whānau buy food outside Communicating a sense of care to the parent(s) Enabling the caregiver to stay in the room with their tamariki.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know	Masters-Awatere [7] identified several barriers to providing meals to caregiver of hospitalised tamariki. This included: - Financial cost - Staff and kitchen capacity - Need to comply with hygiene requirements - Lack of space in hospitals. To address those barriers, they called for increased resources and support allocated to this issue as well as reshaping processes. They note that nurses currently need to fill in paperwork to provide meal to eligible primary caregivers, which is a time-consuming task and can be off-putting to both staff and whānau. Universal meal provision would address this issue. However, Masters-Awatere called for provision of meal to one caregiver, which does not necessarily reflect the need of whānau Māori as described in the available literature. When food is provided, it is sometimes not appropriate, with kai that is described as unappealing, as well as very different to what whānau Māori would usually eat. The extended family is involved in the care of the pēpi and a culturally safe approach would need to consider more than one caregiver. As highlighted by Brown <i>et al</i> [5], such an approach may need to include whānau Māori in the co-design of NICU, to allow for shared spaces in which whānau Māori can cook, share a meal, connect and socialise.	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			

	JUDGEMENT						
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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References

1. Smith, J.; Hutchings, J. Feeding Indigenous Aotearoa better. *Journal of the Royal Society of New Zealand* **2025**.
2. Scott, N.; Atatoa Carr, P.E.; Jones, A.R.; Sandiford, P.; Masters-Awatere, B.; Clark, H. Harti Hauora Tamariki: randomised controlled trial protocol for an opportunistic, holistic and family centred approach to improving outcomes for hospitalised children and their families in Aotearoa, New Zealand. *Frontiers in Paediatrics* **2024**.
3. Masters-Awatere, B.; Graham, R. Whānau Māori explain how the Harti Hauora Tool assists with better access to health services. *Australian Journal of Primary Health* **2019**.
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5. Brown, M.K. What is the experience of whānau Māori caring for their pēpi in a neonatal setting? **2023**.
6. Adcock, A.; Cram, F.; Edmonds, L.; Lawton, B. He Tamariki Kokoti Tau: Families of Indigenous Infants Talk about Their Experiences of Preterm Birth and Neonatal Intensive Care. *Int. J. Environ. Res. Public Health* **2021**, *18*, doi:10.3390/ijerph18189835.

7. Masters-Awatere, B.; Graham, R.; Scott, N.; Atatoa Carr, P. *Meal provision needed for caregivers who stay with a child in hospital*; American Psychological Association: 2020.
8. Malatest International. Review of neonatal care in New Zealand. Wellington: Ministry of Health; 2019/2020.

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EtD 58. Should early breastfeeding education vs. standard care be used for mothers of preterm infants?

POPULATION:	Preterm infants
INTERVENTION:	Early breastfeeding education
COMPARISON:	Standard care
MAIN OUTCOMES:	Critical outcomes Breastmilk supply/volume Fully breastfed or breastmilk feeding at hospital discharge Necrotising enterocolitis Mortality Neurodevelopmental impairment Sepsis: proven or suspected Time to full enteral feeds (<0.5 days) Important but not critical Adverse effects Faltering growth/body composition Duration of initial hospital stay Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical guideline recommendation. Patient perspective
BACKGROUND:	Early education and communication about a preterm infant's nutrition plan, feeding methods and growth are essential to enhance parental understanding and engagement in their infant's care. Structured educational programmes for parents have demonstrated significant improvements in breastfeeding initiation and continuation rates, as well as in parents' confidence in supporting their infants' nutritional needs. Group-based early parent education has also been linked to positive developmental outcomes in preterm infants. Such interventions empower parents to actively participate in their infant's care and foster stronger parent-infant bonding, which is crucial in the neonatal care setting. In the NICU, early education provided either prior to or shortly after birth about the importance of breastmilk has been shown to significantly influence parental approaches to feeding. Early breastfeeding education may improve maternal milk supply, exclusive breastfeeding rates adherence to feeding plans and positively impact growth and health outcomes in preterm infants. However, while fortification and nutritional supplements play a critical role in the care of preterm infants, the specific impact of early education on parental understanding and decision-making around these topics remains underexplored. This question explores the evidence on Early feeding education:

CONFLICT OF INTERESTS:	How do early education and communication about a preterm infant's nutrition plan, mode of feeding and growth impact parents' understanding and engagement in their child's care? How does early education (prior to birth or just after) on the importance of breastmilk, fortification, and nutritional supplements influence parents' approach to feeding, breastfeeding practices and overall outcomes for preterm infants?
	None

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence is based on six RCTs [1-6] two quasi-RCTs [7,8] and three observational/implementation pre- post studies [9-11]. Breastmilk supply/volume: RCT: No significant increase in breastmilk volume in education group on Day 7/1 week (MD 56.1 mL higher; 265.4 lower to 377.5 higher); Day 14/2 weeks (MD 46.0 mL higher; 401.6 lower to 493.5 higher); Day 21/3 weeks (MD 247.1 mL higher; 76.1 lower to 570.3 higher) and at week 4 (MD 352.3 mL higher; 256.1 lower to 960.6 higher) [Critical]. Breastmilk supply/volume: Quality improvement pre-post studies: One study reported a significant increase in breastmilk volume in the education group in the first and third 24 hours. A second study also reported an increase in breastmilk volume following an education intervention for Day 1, Day 2/3, Day 7 and Day 14 [Critical]. Fully breastfed or breastmilk feeding at hospital discharge: RCT: No significant increase in exclusive breastfeeding at discharge/end of study in the education group (324 more per 1,000; 66 fewer to 1,217 more) [Critical]. Fully breastfed or breastmilk feeding at hospital discharge: Pre- post-study: Rates of exclusive breastfeeding of preterm newborns increased from 1.8% pre-intervention to 4.1% post-intervention [Critical]. Understanding and engagement: RCT: Little or no difference in <i>Breastfeeding Knowledge Questionnaire</i> (MD 0.1 points higher; 1.39 lower to 1.59 higher). No significant increase in <i>Breastfeeding Self-Efficacy Scale</i> (MD 7.99 points higher; 9.17 lower to 25.16 higher) [Critical]. Understanding and engagement: Implementation study/pre- post study: Maternal lactation skills increased from 56.5 +/- 3.5 (n=36) at the preintervention audit to 92.1 +/- 1.9 (n=34) after the intervention ($P < .01$). No change in beliefs or attitudes but significant improvement in practical knowledge and use of breast pump [Critical].	Population information for included evidence [1] USA. RCT. <35 weeks. Antenatal education on benefits of mother's own milk. [2] India. RCT. 28-34 weeks' gestation. Ante/post-natal counselling to improve exclusive breastmilk feeding. [3] Bangladesh. RCT. Low birthweight infants <2500 g. Nutrition education on breastfeeding. [4] Iran. RCT. Babies 34-36 weeks' gestation. Four training sessions focused on breastfeeding patterns based on the Theory of Planned Behaviour. [5] Canada. RCT. Breastmilk expression education and support intervention. Very and extremely preterm infants. [6] Australia. RCT pilot. Education on breast massage and hand expressing. Babies 28-35 weeks' gestation. [7] Iran. Quasi-random study. Exclusive breastfeeding education. Babies 36 -36.6 weeks' gestation, birthweight 2,500-2,999 g. [8] China. Quasi-random study. Online breastfeeding education and support program. Babies <37 weeks'

	Necrotising enterocolitis (NEC): RCT: There were no events of NEC reported in either group. [Important] Mortality: RCT: No significant reduction in mortality in the education group (43 fewer per 1,000; 82 fewer to 87 more) [Important]. No faltering growth/body composition: RCT: No significant increase in weight at discharge (MD 179.1 g higher; 65.8 lower to 424.0 higher). Increase in length at 2 months (MD 1.5 cm higher; 1.08 higher to 1.92 higher) [Important]. Duration of hospital stay: RCT: No significant effect in duration of hospital stay (MD 0.1 days lower; 3.3 lower to 3.1 higher) [Important]. Desirable effects for Māori No additional evidence available	gestation, <2,500 g. [9] China. Preterm infants <37 weeks' gestation. Breastfeeding implementation project. Observational. [10] Kenya. pre/post intervention study. Breast pump education. Preterm and sick infants in special care. [11] India. Quality improvement project to increase mother own milk usage. Mean gestational age 30.3 weeks, mean birthweight 1,176 g.
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Outcomes	No of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with control	Risk difference with early education
Breastmilk supply/volume: RCT assessed with: Day 1 (mL)	92 (2 RCTs)	⊕○○○ Very low ^{a,b,c}	-	The mean breastmilk supply/volume: RCT was 13.2 mL	MD 8.64 lower (18.99 lower to 1.72 higher)
Breastmilk supply/volume: RCT assessed with: Day 7/1 week (mL)	272 (4 RCTs)	⊕○○○ Very low ^{a,b,c,d}	-	The mean breastmilk supply/volume: RCT was 363.28 mL	MD 56.05 higher (265.37 lower to 377.46 higher)
Breastmilk supply/volume: RCT assessed with: Day 14/2 weeks (mL)	272 (4 RCTs)	⊕○○○ Very low ^{a,b,c,d}	-	The mean breastmilk supply/volume: RCT was 624.79 mL	MD 45.98 higher (401.58 lower to 493.54 higher)
Breastmilk supply/volume: RCT assessed with: Day 21/3 weeks (mL)	241 (3 RCTs)	⊕○○○ Very low ^{a,b,c,e}	-	The mean breastmilk supply/volume: RCT was 656.39 mL	MD 247.13 higher (76.08 lower to 570.34 higher)
Breastmilk supply/volume: RCT assessed with: Week 4 (mL)	180 (2 RCTs)	⊕○○○ Very low ^{a,b,c,d}	-	The mean breastmilk supply/volume: RCT was 722.84 mL	MD 352.27 higher (256.06 lower to 960.6 higher)
Breastmilk supply/volume: Quality improvement pre-post studies	352 (2 non-randomised studies)	⊕○○○ Very low ^{f,g}	-	Breastmilk volume: Study 1 First 24 hours: pre-intervention 0.15 +/- 1.17 mL (n=36) vs. post-intervention 5.74 +/- 2.80 mL (P<0.01) Third 24 hours: pre-intervention 5.285 +/- 2.29 mL (n=36) vs. post-intervention 19.56 +/- 4.91 mL (P<0.01) Breastmilk volume: Study 2 Day 1 Baseline phase 1.6 +/- 2.8 mL (n=87) vs. intervention phase 4.0 +/- 5.7 mL (n=195) Day 2/3 Baseline phase 24 +/- 43 mL (n=87) vs. intervention phase 29 +/- 53 mL (n=195) Day 7 Baseline phase 204 +/- 219 mL (n=87) vs. intervention phase 287 +/- 284 mL (n=195) Day 14 Baseline phase 642 +/- 653 mL (n=87) vs. intervention	

				phase 909 +/-555 mL (n=195)	
Fully breastfed or breastmilk feeding at hospital discharge: RCT	444 (4 RCTs)	⊕○○○ Very low ^{a,d,h}	RR 1.89 (0.82 to 4.34)	Study population	
				364 per 1,000	324 more per 1,000 (66 fewer to 1,217 more)
Fully breastfed or breastmilk feeding at hospital discharge: Pre-post study	70 (1 non-randomised study)	⊕○○○ Very low ^{a,j,j}	-	Rates of exclusive breastfeeding of premature newborns increased from 1.8% pre-intervention to 4.1% post-intervention.	
Maternal lactation skills: Implementation study	70 (1 non-randomised study)	⊕○○○ Very low ^{a,i,k}	-	Maternal lactation skills increased from 56.5 +/-3.5 (n=36) at the preintervention audit to 92.1 +/- 1.9 (n=34) after the intervention. The increase was statistically significant (p < .01).	
Breast pump attitudes and beliefs: pre-post study	40 (1 non-randomised study)	⊕○○○ Very low ^{i,k,l,m}	-	No change in beliefs or attitudes but significant improvement in practical knowledge and use of breast pump Breastmilk pumping beliefs score (Not significant) Pretest 22.7 +/- 2 Post-test 22.5 +/- 1.5 Breastmilk pumping attitude score (Not significant) Pretest 8.5 +/- 0.8 Post-test 8.6 +/- 0.7 Practical knowledge (P<0.001) Pretest 1.8 +/-0.9 Post-test 4.6 +/- 0.9 Nurses' observations of pump use activities (P<0.001) Pretest 0.08 +/- 0.5 Post-test 4.8 +/- 0.7	
Breastfeeding Knowledge Questionnaire: RCT	50 (1 RCT)	⊕○○○ Very low ^{i,k,n,o}	-	The mean breastfeeding Knowledge Questionnaire: RCT was -1.1 points	MD 0.1 higher (1.39 lower to 1.59 higher)
Breastfeeding Self-Efficacy: RCT	150 (2 RCTs)	⊕○○○ Very low ^{d,h,n}	-	The mean breastfeeding Self-Efficacy: RCT was 23.15 points	MD 7.99 higher (9.17 lower to 25.16 higher)
Necrotising enterocolitis: RCT	140 (1 RCT)	⊕○○○ Very low ^{a,i,k,p}	not estimable- no events	Study population	
				0 per 1,000	0 fewer per 1,000 (0 fewer to 0 fewer)
Mortality: RCT	140 (1 RCT)	⊕○○○ Very low ^{a,i,k,o}	RR 0.57 (0.18 to 1.87)	Study population	
				100 per 1,000	43 fewer per 1,000 (82 fewer to 87 more)
Neurodevelopmental impairment - not measured	-	-	-	-	-
Sepsis: proven or suspected: RCT assessed with: Culture positive sepsis	140 (1 RCT)	⊕○○○ Very low ^{a,b,i,k}	RR 4.00 (0.46 to 34.90)	Study population	
				14 per 1,000	43 more per 1,000 (8 fewer to 484 more)

Time to full enteral feeds - not measured	-	-	-	-	-
Adverse effects - not measured	-	-	-	-	-
Faltering growth/body composition: RCT assessed with: Weight at discharge (g)	313 (2 RCTs)	⊕○○○ Very low ^{a,b,d}	-	The mean faltering growth/body composition: RCT was 2442.5 g	MD 179.11 higher (65.76 lower to 423.97 higher)
Faltering growth/body composition: RCT assessed with: Length: 2 months (cm)	184 (1 RCT)	⊕○○○ Very low ^{a,i,k}	-	The mean faltering growth/body composition: RCT was 48.7 cm	MD 1.5 higher (1.08 higher to 1.92 higher)
Duration of hospital stay: RCT assessed with: Days	240 (3 RCTs)	⊕⊕○○ Low ^{a,o}	-	The mean duration of hospital stay: RCT was not calculated	MD 0.1 lower (3.3 lower to 3.11 higher)
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Retinopathy of prematurity - not measured	-	-	-	-	-
Retinopathy of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds (<0.5 days) - not measured	-	-	-	-	-

- a. Downgraded one level for concerns for risk of bias
- b. Downgraded three levels for imprecision as extremely wide confidence intervals that cross the line of no effect
- c. Downgraded one level as funnel plots suggest publication bias
- d. Downgraded two levels for inconsistency with I²>80%
- e. Downgraded one level for inconsistency as I² >50% and <80%
- f. Downgraded two levels for risk of bias as these are uncontrolled studies
- g. Downgraded one level for imprecision due to wide variation in the data
- h. Downgraded two levels for imprecision with very wide confidence intervals crossing the line of no effect
- i. Downgraded one level for inconsistency as evidence only reported in a single study
- j. Downgraded one level as unable to judge imprecision
- k. Downgraded one level as evidence is based on a single study
- l. Downgraded two level for risk of bias as uncontrolled study, confounding variables not investigated including number of sessions and milk volume
- m. Downgraded one level for indirectness as study included sick term infants as well as preterm infants.
- n. Downgraded two levels for concerns for risk of bias
- o. Downgraded one level for imprecision due to wide confidence intervals crossing the line of no effect
- p. Downgraded two levels for imprecision due to very low event rate

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small	Breastmilk supply/volume: RCT: No significant effect in milk volume in education group on Day 1 (MD 8.64 mL lower; 18.99 lower to 1.72 higher) [Critical].	

○ Moderate ○ Large ○ Varies ○ Don't know	Sepsis: RCT: No significant increase in culture-proven sepsis in the education group (43 more per 1,000; 8 fewer to 484 more) [Important]. Undesirable effects for Māori No additional evidence available	
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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Low to very low certainty evidence overall. Certainty of evidence for Māori - No additional evidence available	

Outcomes	Importance	Certainty of the evidence (GRADE)
Breastmilk supply/volume: RCT assessed with: Day 1 (mL)	CRITICAL	⊕○○○ Very low ^a
Breastmilk supply/volume: RCT assessed with: Day 7/1 week (mL)	CRITICAL	⊕○○○ Very low
Breastmilk supply/volume: RCT assessed with: Day 14/2 weeks (mL)	CRITICAL	⊕○○○ Very low
Breastmilk supply/volume: RCT assessed with: Day 21/3 weeks (mL)	CRITICAL	⊕○○○ Very low
Breastmilk supply/volume: RCT assessed with: Week 4 (mL)	CRITICAL	⊕○○○ Very low
Breastmilk supply/volume: Quality improvement pre-post studies	CRITICAL	⊕○○○ Very low
Fully breastfed or breastmilk feeding at hospital discharge: RCT	CRITICAL	⊕○○○ Very low
Fully breastfed or breastmilk feeding at hospital discharge: Pre-post study	CRITICAL	⊕○○○ Very low
Maternal lactation skills: Implementation study	CRITICAL	⊕○○○ Very low

Breast pump attitudes and beliefs: pre-post study	CRITICAL	⊕○○○ Very low
Breastfeeding Knowledge Questionnaire: RCT	CRITICAL	⊕○○○ Very low
Breastfeeding Self-Efficacy: RCT	CRITICAL	⊕○○○ Very low
Necrotising enterocolitis: RCT	CRITICAL	⊕○○○ Very low
Mortality: RCT	CRITICAL	⊕○○○ Very low
Neurodevelopmental impairment - not measured	CRITICAL	-
Sepsis: proven or suspected: RCT assessed with: Culture positive sepsis	CRITICAL	⊕○○○ Very lo
Time to full enteral feeds - not measured	CRITICAL	-
Adverse effects - not measured	IMPORTANT	-
Faltering growth/body composition: RCT assessed with: Weight at discharge (g)	IMPORTANT	⊕○○○ Very low
Faltering growth/body composition: RCT assessed with: Length: 2 months (cm)	IMPORTANT	⊕○○○ Very low
Duration of hospital stay: RCT assessed with: Days	IMPORTANT	⊕⊕○○ Low
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Retinopathy of prematurity - not measured	IMPORTANT	-
Retinopathy of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	IMPORTANT	-
Time to full sucking feeds (<0.5 days) - not measured	NOT IMPORTANT	-

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Some people may not value the breastfeeding outcomes if they want to bottle-feed their infant. Values for Māori No additional evidence available.	
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Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Early education vs. no education on breastfeeding - very low certainty evidence Uncertain effect on breastmilk volume, fully breastfed or breastmilk feeding at hospital discharge, understanding and engagement, NEC, mortality and sepsis. Balance of effects for Māori No additional evidence	There is a lot of heterogeneity between the studies, primarily due to the type of intervention, duration of intervention and gestational age of infants. Studies rarely took into account confounding variables such as when expressing started and how many times a day women expressed.

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Cost of staff to provide education Breast pumps, if required	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low	A formal assessment of the certainty of evidence of the cost	

○ Low ○ Moderate ○ High ● No included studies	was not undertaken. Certainty of evidence of required resources for Māori No additional evidence available	
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Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No economic studies were identified to address the cost-effectiveness of the intervention or the comparison. Cost effectiveness for Māori No evidence available.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Wahine Māori caring for preterm pēpi often face systemic barriers that limit early involvement in feeding decisions and breastfeeding support. Education provided before or shortly after birth about the importance of breastmilk and fortification can improve understanding and increase engagement. However, without culturally grounded and timely communication, whānau Māori may feel excluded from their pēpi's nutrition plan. Colonisation continues to impact trust in healthcare and access to consistent support. Equity-focused education that honours mātauranga Māori and includes whānau in all aspects of care can support stronger breastfeeding outcomes and build confidence in navigating complex neonatal environments. Equity for Pacific families Pacific families value strong familial roles in infant care but often experience communication gaps in neonatal settings. Without early and culturally appropriate education about nutrition and feeding practices, parents may struggle to advocate for the use of breastmilk or understand the reasons behind fortification. While	

	some Pacific pēpi show high rates of transition to mother's own milk, many still receive early formula due to a lack of support or access to resources. Equity means delivering consistent information in accessible ways and ensuring staff are trained to engage Pacific families with respect and cultural understanding throughout the infant's care journey. Equity for underrepresented groups Families from migrant backgrounds, lower-income communities or rural areas may face logistical and language barriers that limit their access to early education about preterm nutrition. Parents may feel unprepared to participate in feeding decisions, leading to reduced confidence and suboptimal breastfeeding outcomes. Without equitable access to interpreters, transport, digital tools or culturally relevant materials, their ability to engage is significantly reduced. Early education that is individualised, accessible and inclusive of diverse family needs can improve feeding practices and health outcomes. Promoting equity means not only offering information, but ensuring families are supported to understand and act on it effectively.	
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Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☐ Varies ☐ Don't know	No evidence Acceptability for Māori No evidence	Acceptability for Māori More acceptable if the education was based on Te Ao Māori values and kaupapa Māori development.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☐ Varies ☐ Don't know	No evidence Feasibility for Māori No evidence available	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	●	○

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EtD 59. Should additional education around the nutrition and/or care of their preterm infants throughout their NICU stay be delivered through different methods (face-to-face, written, online) vs. standard care be used for families of preterm infants?

POPULATION:	Preterm infants and their parents
INTERVENTION:	Additional education delivered through different methods (face-to-face, written, online)
COMPARISON:	Standard care
MAIN OUTCOMES:	Critical outcomes -Whānau preferences for sources of information around the nutrition and/or care of their preterm infants throughout their NICU stay -Whānau decision-making experiences -Whānau wellbeing, as defined by authors -Parental understanding of information received: self-reported and measured -Other lived experiences of receiving information throughout their infants' NICU journey Important but not critical - Fully breastfed or breastmilk feeding at hospital discharge - Mortality - Neurodevelopmental impairment - Adverse effects - Time to reach full enteral feeds - Duration of initial hospital stay - Necrotising enterocolitis - Faltering growth/body composition - Sepsis - Bronchopulmonary dysplasia - Retinopathy of prematurity Less important for decision making - Anaemia of prematurity - Cost: cost of intervention, cost of neonatal care and life-long cost
SETTING:	Neonatal care
PERSPECTIVE:	Patient/parent perspective
BACKGROUND:	The neonatal intensive care unit (NICU) is a challenging environment for parents, especially those with preterm infants. Infants' parents and wider support system (whānau) often struggle with stress, uncertainty, decreased parenting confidence, and disrupted bonding with the infant, all of which can impact their psychological health and ability to make informed decisions about their infant's care and nutrition. Preterm infants have unique needs compared to full-term infants, including difficulties with breathing, feeding, and maintaining body temperature, which usually necessitates specialised care and support, crucial to their healthy development in neonatal care. The provision of accurate and accessible information to parents and families at these times is crucial, and educational methods can play a significant role in supporting parents of preterm infants. The method of delivering information can directly impact not only their understanding of the challenge at hand and subsequent decision-making, but their personal wellbeing and lived experiences of NICU. Different modes of information delivery, such as face-to-face, written materials

CONFLICT OF INTERESTS:	(in physical form) and online sources may influence parental understanding, decision-making, and overall wellbeing throughout the infants' NICU journey.
	None

Assessment

Desirable Effects How substantial are the desirable anticipated effects?						
JUDGEMENT	RESEARCH EVIDENCE			ADDITIONAL CONSIDERATIONS		
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	Evidence based on 21 studies: • 8 randomised controlled trials (Beheshtipour 2014, Franck 2011, Hoffenkamp 2014, Jaywant 202, Kongsakenkaew 2024, Nekavand 2014, Sabzevari 2019, Tiryaki 2024) [1-8] • 3 non-randomised (Jang 2020, Pourkhani 2017, Zhang 2024) [9-11] • 6 observational (Araque Salazar 2013, Brown 2013, Bueno 2018, Chivers 2016 [abstract only], Harrison 2017, Jones 2009) [12-17] • 4 qualitative (Booth 2014 [abstract only], Boucher 2011, Franck 2024, Tada 2020) [18-21]			Most studies included a wide range of infant gestational age (GA), however: Only 3 (Brown 2013, Franck 2024, Hoffenkamp 2014) included extremely preterm infants (<28 weeks) 3 (Boucher 2011, Jang 2020, Nekavand 2014) only included moderate-to-late preterm infants 7 (Araque Salazar 2013, Jones 2009, Kongsakenkaew 2024, Zhang 2024) included all hospitalised infants (preterm and LBW, potentially) Studies' settings: globally diverse sample from urban hospitals across high-, middle-, and low-income countries, including both urban and tertiary care hospitals. Notably, no studies originate from Australasia, limiting direct applicability to Aotearoa New Zealand's context		
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Standard care	Risk with additional education delivered through different methods (face-to-face, written, online)				
Whānau preferences - Acceptability/usefulness of education	Video education Bueno 2018 (questionnaire): All parents (100%) declared they would recommend the video to other parents. None of the included parents expressed discomfort by watching the video or indicated any negative aspects related to the video and its content. The video was considered as useful, easy to understand, easy to apply in clinical settings by the totality of the included parents.		-	246 (4 non-randomised studies)	-	

	Harrison 2017 (survey): 44 of the 50 parents (88%) said they would recommend the video to other parents Written education Jones 2009 (questionnaire): 46 of 69 parents (67%) said the written education was very useful, 17 out of 69 parents (25%) said it was useful, 2 out of 69 parents (2%) didn't answer. Combination education Chivers 2016 (questionnaire): phone App and written information were the most useful methods of information delivery: 55.3% Using a smartphone App (26 respondents); 51% access to medical notes (24 respondents); 48.9 % regular progress charts (23 respondents)					
Whānau preferences - Satisfaction with care assessed with: Questionnaire after face-to-face + written education Scale from: 0 to 232	The mean whānau preferences - Satisfaction with care was 217.6	MD 59.42 higher (51.05 higher to 67.79 higher)	-	100 (1 RCT)	⊕⊕○○ Low ^{a,b,c}	
Decision-making - Perceived ability to make care decisions assessed with: Survey after all educational methods Scale from: 0 to 100	The mean decision-making - Perceived ability to make care decisions was 71.31	MD 11.37 higher (0.25 higher to 22.49 higher)	-	42 (1 RCT)	⊕⊕○○ Low ^{b,d}	
Decision-making, other outcomes	Video education Harrison 2017 (questionnaire): After viewing the video, 47 of 49 (95.92%) parents intended to advocate for breastfeeding, skin-to-skin, or giving sucrose.		-	49 (1 non-randomised study)	-	
Whānau wellbeing - Maternal stress assessed with: PSS:NICU scale (different versions) after face-to-face + written/video	The mean whānau wellbeing - Maternal stress was 0 SD	SMD 0.58 SD lower (1.29 lower to 0.12 higher)	-	429 (4 RCTs)	⊕○○○ Very low ^{a,e}	
Whānau wellbeing - Paternal stress assessed with: PSS:NICU scale (different versions) after face-to-face + written/video	The mean whānau wellbeing - Paternal stress was 0 SD	SMD 0.94 SD lower (1.37 lower to 0.5 lower)	-	186 (2 RCTs)	⊕⊕○○ Low ^{c,f}	
Whānau wellbeing - Stress assessed with: Questionnaire after face-to-face + written Scale from: 0 to 63	The mean whānau wellbeing - Stress was 30.42	MD 2.46 lower (4.64 lower to 0.28 lower)	-	100 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
Whānau wellbeing - stress at discharge assessed with: Depression Anxiety and Stress Scale DASS-21 Scale from: 0 to 21	The mean whānau wellbeing - stress at discharge was 8.65	MD 5.45 lower (7.34 lower to 3.56 lower)	-	80 (1 non-randomised study)	⊕○○○ Very low ^{b,c,f}	
Whānau wellbeing - Stress	Face-to-face and video education Brown 2013 (Case study, PSS:NICU 14-70 scale): 26 right after intervention, 20.5 at discharge. <u>Lower stress</u>		-	2 (1 non-randomised study)	-	
Whānau wellbeing - Maternal depression assessed with: EPDS after face-to-face & face-to-face+video		MD 5.74 lower (15.53 lower to 4.04 higher)	-	346 (2 RCTs)	⊕⊕○○ Low ^{c,f}	

Scale from: 0 to 30						
Whānau wellbeing - Depression assessed with: DASS-21 scale after face-to-face + written Scale from: 0 to 21		MD 3.05 lower (4.23 lower to 1.81 lower)	-	80 (1 non-randomised study)	⊕○○○ Very low ^{b,c,f}	
Whānau wellbeing - Depression assessed with: CES-D: Center for Epidemiological Studies—Depression questionnaire (Scale 0-60)	Face-to-face and video education Brown 2013 (Case study): 24.5 right after intervention, 2.5 at discharge. <u>Lower</u> depression		-	2 (1 non-randomised study)	-	
Whānau wellbeing - Parenting confidence at discharge assessed with: Pharis's Self-confidence Scale (Korean adaptation) after face-to-face + written Scale from: 38 to 190	The mean whānau wellbeing - Parenting confidence at discharge was 110.33	MD 17.17 higher (4.48 higher to 29.86 higher)	-	53 (1 non-randomised study)	⊕○○○ Very low ^{b,c}	
Whānau wellbeing - confidence	Written education, reassurance Jones 2009 (cross-sectional, questionnaire): 10 respondents (11%) found the <u>leaflet reassuring</u>		-	10 (1 study)	-	
Whānau wellbeing - Parental anxiety assessed with: State-Trait Anxiety Inventory STAI after face-to-face + video		0.31 lower (0.58 lower to 0.03 lower)	-	294 (1 RCT)	⊕○○○ Very low ^{b,c,f}	
Whānau wellbeing - Anxiety at discharge assessed with: Depression Anxiety and Stress Scale DASS-21 after face-to-face + written Scale from: 0 to 21	The mean whānau wellbeing - Anxiety at discharge was 6.1	MD 4.63 lower (6.24 lower to 3.02 lower)	-	80 (1 non-randomised study)	⊕○○○ Very low ^{b,c,f}	
Whānau wellbeing - Anxiety	Face-to-face and video education Brown 2013 (Case study, State-Trait Anxiety Inventory STAI): 79 right after intervention, 50.5 at discharge. <u>Lower</u> anxiety		-	2 (1 non-randomised study)	-	
Whānau wellbeing - Maternal worry assessed with: My Baby and I Questionnaire (MBI) after face-to-face + video Scale from: 3 to 15		MD 0.04 lower (0.15 lower to 0.07 higher)	-	150 (1 RCT)	⊕○○○ Very low ^{b,c,f}	
Whānau wellbeing - Hope assessed with: Miller Hope Scale (MHS) after face-to-face + written Scale from: 40 to 200		MD 27.18 higher (20.67 higher to 33.69 higher)	-	100 (1 RCT)	⊕⊕○○ Low ^{a,b,c}	
Breastfeeding knowledge assessed with: Breastfeeding knowledge questionnaire (BKQ) after online education Scale from: 0 to 18	The mean breastfeeding knowledge was 15	MD 0.33 higher (1.22 lower to 1.88 higher)	-	41 (1 non-randomised study)	⊕○○○ Very low ^{b,d}	
Parental knowledge	Face-to-face education, knowledge on taught concepts relating to KMC Araque Salazar (cohort): 6.67% pre intervention vs. 58.33% post intervention		-	10 (1 non-randomised study)	-	
Other lived experiences - Maternal self-efficacy		MD 17.24 higher	-	42	⊕⊕○○	

assessed with: Questionnaire after all educational methods Scale from: 0 to 100		(7.43 higher to 27.05 higher)		(1 RCT)	Low ^{b,d}	
Other lived experiences - Breastfeeding self-efficacy assessed with: BSES scale (different ranges) after face-to-face + written		SMD 1.69 SD higher (0.77 higher to 2.6 higher)	-	152 (2 RCTs)	⊕⊕○○ Low ^{d,g}	
Other lived experiences - Breastfeeding self-efficacy assessed with: BSES (Chinese adaptation) after online Scale from: 30 to 150		MD 3.68 higher (12.09 lower to 19.45 higher)	-	41 (1 non-randomised study)	⊕○○○ Very low ^{b,f}	
Other lived experiences - Readiness for discharge assessed with: Questionnaire after face-to-face Scale from: 20 to 154		MD 33.4 higher (28.53 higher to 38.26 higher)	-	68 (1 RCT)	⊕⊕○○ Low ^{a,b,c}	
Time to reach full enteral feeds after face-to-face	The mean time to reach full enteral feeds after face-to-face was 20.26 days	MD 3.67 days fewer (10.04 fewer to 2.7 more)	-	68 (1 RCT)	⊕○○○ Very low ^{a,b,d}	
Duration of hospital stay after face-to-face, and face-to-face + written		MD 0.96 days fewer (5.49 fewer to 3.56 more)	-	237 (2 RCTs)	⊕○○○ Very low ^{a,h}	
Duration of hospital stay after online	The mean duration of hospital stay after online was 13.33 days	MD 1.33 days lower (6.89 lower to 4.23 higher)	-	41 (1 non-randomised study)	⊕○○○ Very low ^{b,d,f}	
Breastfeeding at discharge after face-to-face + written	Study population		RR 1.21 (0.47 to 3.13)	53 (1 non-randomised study)	⊕○○○ Very low ^{b,d}	
	22 per 100	27 per 100 (10 to 70)				
Weight at discharge after face-to-face		MD 172.2 grams more (15.08 more to 329.32 more)	-	68 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
Weight at discharge after face-to-face + written	The mean weight at discharge after face-to-face + written was 2466.7 grams	MD 187.9 grams higher (14.62 higher to 361.18 higher)	-	53 (1 non-randomised study)	⊕○○○ Very low ^{b,c}	
Length at discharge after face-to-face + written	The mean length at discharge after face-to-face + written was 47.4 cm	MD 0.2 cm more (1.04 fewer to 1.44 more)	-	53 (1 non-randomised study)	⊕○○○ Very low ^{b,d}	
Head circumference at discharge after face-to-face + written	The mean head circumference at discharge after face-to-face + written was 32.9 cm	MD 0.6 cm more (0.02 fewer to 1.22 more)	-	53 (1 non-randomised study)	⊕○○○ Very low ^{b,d}	

- a. Downgraded two levels for risk of bias due to concerns around randomisation and blinding process
b. Downgraded one level for indirectness as evidence is based on a single study
c. Downgraded one level for imprecision due to small sample size
d. Downgraded two levels for imprecision due to small sample size and wide confidence intervals that cross the line of no effect

- e. Downgraded two levels for inconsistency due to considerable heterogeneity
- f. Downgraded one level for risk of bias due to concerns around blinding process
- g. Downgraded two levels for risk of bias due to lack of reporting
- h. Downgraded two levels for imprecision due to methodological variability and wide confidence intervals that cross the line of no effect

Family wellbeing - confidence after **written education**:

Jones 2009 (cross-sectional, questionnaire): 10 respondents (11%) found the leaflet reassuring. "I read the leaflet from cover to cover again and again. I found it encouraged me to persevere, even when my baby's condition took a nose dive. The parents' story made me keep going"

From the qualitative studies (Boucher 2011, Franck 2024, Tada 2020), we found that **face-to-face education is highly valued**:

Parents gained confidence in breastfeeding through tailored, hands-on instruction—nurses taught techniques like positioning, latching, and interpreting infant cues, with ongoing feedback that helped mothers feel more comfortable and competent.

Parents expressed the need for guidance to safely perform activities like nappy changes, skin-to-skin contact, and breastfeeding, as well as emotional reassurance.

Group sessions and individualised nurse support equipped parents with practical knowledge, confidence, and readiness for discharge and future caregiving responsibilities.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know		

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Standard care	Risk with additional education delivered through different methods (face-to-face, written, online)				
Whānau preferences - Acceptability/usefulness of education	Written education Booth 2014 (questionnaire): 23.7% respondents stated that they did not receive enough written information Jones 2009 (questionnaire): 4 out of 69 parents (6%) said the written education was not very useful, 2 out of 69 parents (2%) didn't answer.		-	92 (2 non-randomised studies)	-	
Whānau wellbeing - Paternal depression assessed with: EPDS after face-to-face+video Scale from: 0 to 30	The mean whānau wellbeing - Paternal depression was 3.9	MD 0.47 higher (0.33 higher to 0.61 higher)	-	144 (1 RCT)	⊕⊕○○ Low ^{a,b,c}	
Whānau wellbeing - confidence	Face-to-face and video education, maternal confidence Brown 2013 (Case study, questionnaire ranging 14-70):		-	2 (1 study)	-	

	65 right after intervention, 61 at discharge. <u>Lower</u> confidence				
Whānau wellbeing - Paternal worry assessed with: My Baby and I Questionnaire (MBI) after face-to-face + video Scale from: 3 to 15	The mean whānau wellbeing - Paternal worry was 6.3	MD 0.08 higher (0.04 lower to 0.2 higher)	-	144 (1 RCT)	⊕○○○ Very low ^{a,b,c}
Other lived experiences - Parental bonding assessed with: Parental bonding questionnaire (PBQ) after face-to-face + video Scale from: 0 to 125		MD 1.4 lower (2.77 lower to 0.04 lower)	-	294 (1 RCT)	⊕⊕○○ Low ^{a,b,c}

- a. Downgraded one level for risk of bias due to concerns around blinding process
b. Downgraded one level for indirectness as evidence is based on a single study
c. Downgraded one level for imprecision due to small sample size

From one qualitative study (Tada 2020) we found:

Tada 2020: "Of the 19 mothers interviewed, four mothers did not receive education from healthcare workers. They were not satisfied with this experience and gave suggestions to improve the education given by healthcare workers. They suggested that healthcare workers 1) provide information about the risk of not achieving exclusive breastfeeding, 2) confirm understanding of individual mothers, 3) allocate time for education or identify a healthcare worker responsible for education, 4) emphasize things that are important, and 5) educate family members."

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Certainty of evidence at the outcome level:	

Outcomes	Importance	Certainty of the evidence (GRADE)
[RCT] Whānau preferences - Satisfaction with pain control information assessed with: Questionnaire (lower=more satisfied) after face-to-face + written education Scale from: 1 to 6	CRITICAL	⊕⊕⊕○ Moderate
[RCT] Whānau preferences - Satisfaction with care assessed with: Questionnaire after face-to-face + written education Scale from: 0 to 232	CRITICAL	⊕⊕○○ Low
[RCT] Decision-making - Perceived ability to make care decisions assessed with: Survey after all educational methods Scale from: 0 to 100	CRITICAL	⊕⊕○○ Low

[RCT] Whānau wellbeing - Maternal stress assessed with: PSS:NICU scale (different versions) after face-to-face + written/video	CRITICAL	⊕○○○ Very low
[RCT] Whānau wellbeing - Paternal stress assessed with: PSS:NICU scale (different versions) after face-to-face + written/video	CRITICAL	⊕⊕⊕○ Moderate
[RCT] Whānau wellbeing - Stress assessed with: Questionnaire after face-to-face + written Scale from: 0 to 63	CRITICAL	⊕○○○ Very low
[Non-randomised] Whānau wellbeing - stress at discharge assessed with: Depression Anxiety and Stress Scale DASS-21 Scale from: 0 to 21	CRITICAL	⊕○○○ Very low
[RCT] Whānau wellbeing - Maternal depression assessed with: EPDS after face-to-face & face-to-face+video Scale from: 0 to 30	CRITICAL	⊕⊕○○ Low
[RCT] Whānau wellbeing - Paternal depression assessed with: EPDS after face-to-face+video Scale from: 0 to 30	CRITICAL	⊕⊕○○ Low
[Non-randomised] Whānau wellbeing - Depression at discharge assessed with: DASS-21 scale after face-to-face + written Scale from: 0 to 21	CRITICAL	⊕○○○ Very low
[Non-randomised] Whānau wellbeing - Parenting confidence at discharge assessed with: Pharis's Self-confidence Scale (Korean adaptation) after face-to-face + written Scale from: 38 to 190	CRITICAL	⊕○○○ Very low
[RCT] Whānau wellbeing - Parental anxiety assessed with: State-Trait Anxiety Inventory STAI after face-to-face + video	CRITICAL	⊕○○○ Very low
[Non-randomised] Whānau wellbeing - Anxiety at discharge assessed with: Depression Anxiety and Stress Scale DASS-21 after face-to-face + written Scale from: 0 to 21	CRITICAL	⊕○○○ Very low
[RCT] Whānau wellbeing - Maternal worry assessed with: My Baby and I Questionnaire (MBI) after face-to-face + video Scale from: 3 to 15	CRITICAL	⊕○○○ Very low
[RCT] Whānau wellbeing - Paternal worry assessed with: My Baby and I Questionnaire (MBI) after face-to-face + video Scale from: 3 to 15	CRITICAL	⊕○○○ Very low
[RCT] Whānau wellbeing - Hope assessed with: Miller Hope Scale (MHS) after face-to-face + written Scale from: 40 to 200	CRITICAL	⊕⊕○○ Low
[Non-randomised] Breastfeeding knowledge assessed with: Breastfeeding knowledge questionnaire (BKQ) after online education Scale from: 0 to 18	CRITICAL	⊕○○○ Very low
[RCT] Other lived experiences - Maternal self-efficacy	CRITICAL	⊕⊕⊕○

assessed with: Questionnaire after all educational methods Scale from: 0 to 100		Moderate
[RCT] Other lived experiences - Breastfeeding self-efficacy assessed with: BSES scale (different ranges) after face-to-face + written	CRITICAL	⊕⊕○○ Low
[Non-randomised] Other lived experiences - Breastfeeding self-efficacy assessed with: BSES (Chinese adaptation) after online Scale from: 30 to 150	CRITICAL	⊕○○○ Very low
[RCT] Other lived experiences - Parental bonding assessed with: Parental bonding questionnaire (PBQ) after face-to-face + video Scale from: 0 to 125	CRITICAL	⊕⊕○○ Low
[RCT] Other lived experiences - Readiness for discharge assessed with: Questionnaire after face-to-face Scale from: 20 to 154	CRITICAL	⊕⊕○○ Low
[RCT] Time to reach full enteral feeds after face-to-face	IMPORTANT	⊕○○○ Very low
[RCT] Duration of hospital stay after face-to-face, and face-to-face + written	IMPORTANT	⊕○○○ Very low
[Non-randomised] Duration of hospital stay after online	IMPORTANT	⊕○○○ Very low ^a
[Non-randomised] Breastfeeding at discharge after face-to-face + written	IMPORTANT	⊕○○○ Very low
[RCT] Weight at discharge after face-to-face	IMPORTANT	⊕○○○ Very low
[Non-randomised] Weight at discharge after face-to-face + written	IMPORTANT	⊕○○○ Very low
[Non-randomised] Length at discharge after face-to-face + written	IMPORTANT	⊕○○○ Very low
[Non-randomised] Head circumference at discharge after face-to-face + written	IMPORTANT	⊕○○○ Very low
Quality of qualitative studies was moderate/high:		

QUALITATIVE STUDIES: CRITICAL APPRAISAL SKILLS PROGRAMME (CASP) CHECKLIST

Table 5. CASP checklist for appraisal of qualitative studies

	Boucher 2011	Franck 2024	Tada 2020
<i>Section A: Are the results valid?</i>			
1. Was there a clear statement of the aims of the research?	Yes	Yes	Yes
2. Is a qualitative methodology appropriate?	Yes	Yes	Yes
3. Was the research design appropriate to address the aims of the research?	Yes	Yes	Yes
4. Was the recruitment strategy appropriate to the aims of the research?	No	Yes	Yes
5. Was the data collected in a way that addressed the research issue?	Yes	Yes	Yes
6. Has the relationship between researcher and participants been adequately considered?	No	No	Yes
<i>Section B: What are the results?</i>			
7. Have ethical issues been taken into consideration?	Yes	Yes	Yes
8. Was the data analysis sufficiently rigorous?	Yes	Yes	Yes
9. Is there a clear statement of findings?	No	No	Yes
<i>Section C: Will the results help locally?</i>			
10. How valuable is the research?	Yes	Yes	Yes
Overall quality assessment (High, Moderate, Low)	Moderate	High	High+

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Parents often value receiving information that is not only comprehensive but also tailored to their infant's specific needs and their own circumstances. This might be not as high in the priority list for staff in the neonatal ward, likely due to a focus on clinical survival, limited educational resources/training and short staffing.	Critical outcomes of this question are: - Family information preferences - Family decision-making experiences - Family wellbeing - Parental understanding of information received: self-reported and measured. - Other lived experiences of receiving information throughout their infants' NICU journey.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ● Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	High quality evidence (qualitative studies) Increased parental confidence in breastfeeding and infant care through hands-on, tailored instruction from nurses (<i>face-to-face</i>) Greater emotional reassurance and preparedness for discharge and future caregiving through group and individual education and support during the NICU stay (<i>face-to-face</i>) Moderate certainty evidence Increased maternal self-efficacy and satisfaction with pain control information (<i>combination</i>) Reduced paternal stress (<i>combination</i>) Low certainty evidence Increased satisfaction with care, hope and breastfeeding self-efficacy (<i>combination</i>) Improved decision-making (<i>combination</i>) Reduced maternal depression (<i>face-to-face & combination</i>) Increased readiness for discharge (<i>face-to-face</i>) Increased paternal depression (<i>combination</i>) Slightly reduced parental bonding (<i>combination</i>) Very low certainty evidence Increased breastfeeding self-efficacy and breastfeeding knowledge (<i>App</i>) Increased parenting confidence (<i>combination</i>) Slightly reduced maternal worry (<i>combination</i>) Increased paternal worry (<i>combination</i>) Reduced anxiety, maternal stress and stress levels at discharge (<i>combination</i>) Slightly higher weight, length, head circumference and rates of breastfeeding at discharge (<i>face-to-face & combination</i>) Lower duration of hospital stay and time to full enteral feeds (<i>face-to-face & combination</i>) Minor undesirable effects such as inconsistent delivery or insufficient written information (<i>written</i>)	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings	Additional staff time to deliver information (from nurses, lactation consultants and/or neonatologists). Potentially, allocating educators for staff to be trained. If information is to be delivered online or via App, the pertinent technology would have to be available / purchased	

○ Varies ○ Don't know		
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	We are relatively certain of what would be needed for the intervention, however not as certain about how much it would cost to each unit exactly.	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ No included studies	Rice et al. (2010), in the UK, assessed the cost-effectiveness of providing <i>enhanced staff contact</i> to mothers of low-birth-weight infants in NICU, defined as providing individualised education, support and care plans by specially trained NICU staff. Compared to standard care, the intervention was found to lower overall costs and improve health outcomes across all weight groups, driven largely by increased breastmilk intake and reduced NEC. The model estimated savings of £66–£586 per infant and quality-adjusted life-years (QALYs) of +0.01 – +0.25, with the largest cost saving (£586 per infant) and health gain (+0.25 QALYs) in the 500–999g group. These findings suggest that enhanced staffing focused on lactation support may be a cost-effective strategy, especially for infants under 1,750g. However, the authors emphasised that this was the first economic evaluation in this field and highlighted the need for further research to confirm these findings with greater confidence.	A cost-effectiveness analysis may need to be undertaken in Aotearoa New Zealand.
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably	Equity for Māori: Whānau Māori navigating neonatal care often encounter systemic barriers that limit their access to timely, culturally grounded education. Standard care may not adequately	

reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	reflect mātauranga Māori or support meaningful engagement in feeding and wellbeing decisions. When additional education is delivered in ways that honour Māori values—such as kanoahi ki te kanoahi (face-to-face), through trusted relationships, and in culturally safe formats—it can enhance understanding, build trust, and empower whānau to advocate for their pēpi. Equity-focused interventions must prioritise relational, inclusive communication and ensure Māori voices shape how information is shared and understood. Equity for Pacific Peoples: Pacific families bring strong collective values and caregiving traditions to neonatal care, yet often face gaps in communication and culturally relevant education. Standard care may overlook the importance of family involvement and the need for accessible, respectful information. Additional education—especially when delivered in community-informed formats such as visual materials, translated resources, or online platforms co-designed with Pacific health workers—can improve confidence and support informed decision-making. Equity means recognising diverse learning preferences and ensuring Pacific families are supported throughout their care journey with culturally affirming education. Equity for Other Underrepresented Groups: Families from migrant, low-income, or rural backgrounds may struggle to access consistent and understandable information about neonatal care and feeding. Language barriers, digital exclusion, and limited transport can reduce their ability to engage with standard care. Additional education that is flexible—offered online, in print, or through interpreters—and tailored to individual needs can help bridge these gaps. Equity requires not only providing information, but ensuring families are equipped to act on it, with support systems that reflect their realities and strengths.	
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Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Probably acceptable to all relevant stakeholders, as we all want to prioritise whānau wellbeing and whānau -centred care	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no	Potential issues around staffing to provide additional and more tailored information delivery	

☐ Probably yes ☐ Yes ☒ Varies ☐ Don't know		
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Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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EtD 60. How does encouraging parents to be involved in tube feeding (feeding, changing tubes and using feeding pumps if needed) and preparing supplements (fortification and similar supplements) of their infants affect breastmilk expression and establishment of breastfeeding and their confidence, participation and overall care experience, as well as the health and development of their infants?

POPULATION:	Preterm infants
INTERVENTION:	How does encouraging parents to be involved in tube feeding (feeding, changing tubes and using feeding pumps if needed) and preparing supplements (fortification and similar supplements) of their infants affect EBM expression and initiation/establishment of breastfeeding and their confidence, participation, and overall care experience, as well as the health and development of their infants?
COMPARISON:	(no comparison)
MAIN OUTCOMES:	Critical outcomes Mortality Necrotising enterocolitis Adverse effects Neurodevelopmental impairment Fully breastfed or breastmilk feeding at hospital discharge Faltering growth/body composition Time to full enteral feeds Duration of initial hospital stay Parental engagement or confidence Important but not critical Sepsis: proven or suspected Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost Less important for decision making Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical guideline recommendation. Patient perspective

BACKGROUND:	For many preterm infants, enteral tube feeding via a tube into the stomach is necessary to meet their nutritional requirements until breastfeeding is being established. Tube feeding is often delivered primarily by clinical staff, which may limit opportunities for parental involvement during a critical period for lactation development and bonding. Early and sustained parental engagement in infant feeding activities is increasingly recognised as an important component of family-centred neonatal care. Encouraging parents to participate in tube feeding, preparation of expressed breastmilk and supplements, and tube feeding equipment may support maternal confidence, sense of agency and understanding of their infant's nutritional needs. This involvement may also influence breastmilk production, timely initiation and establishment of breastfeeding, and the overall care experience for families, while potentially affecting infant health and developmental outcomes. However, the impact of structured parental involvement in these feeding tasks on breastfeeding outcomes and parental experience has not been clearly defined, warranting focused consideration within neonatal practice guidelines.
CONFLICT OF INTERESTS:	None

Assessment

Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	A narrative summary of findings is provided for two RCTs [1] [2] and an observational study [3]. There was no evidence identified for expressed breastmilk expression or the initiation/establishment of breastfeeding before discharge. Mortality: RCT: There were no events of death in either the Early Parent Participation Program or the usual care group [Critical]. Necrotising enterocolitis (NEC): RCT: There were no events of NEC in either the Early Parent Participation Program or the usual care group [Critical]. Adverse effects: RCT: There was a significant decrease in feeding intolerance in the Early Parent Participation Program compared with the usual care group (17.8 vs. 36.5%, respectively; $p = 0.011$). Neurobehavioural assessment: Observational study: There was no relationship between parental participation in tube feeding and neurobehavioral assessment of the preterm infant alerting/orienting or motor development and vigour assessed at the time infants began the transition from tube feeding to oral feedings ($\beta = 0.029$, 95% CI -0.0025 to 0.061, $p = .071$; $\beta = -0.00024$, 95% CI -0.025 to 0.025] $p = .99$, respectively) [Critical]. Breastfeeding at discharge: RCT: There was no difference in rates of predominant breastmilk	[1] France: Crossover RCT: 15 infants <33 weeks' gestation and over 7 days old. Manual milk administration by parents versus electric syringe administration. [2] India: RCT: 147 infants born 28 to 33 weeks' gestation. Intervention was an Early Parent Participation Program that included participation in orogastric tube feeding from day 1 to 2 after birth. Comparison was usual care. [3] USA: Secondary analysis of a RCT: 87 preterm infants 24-32 weeks' gestational age. Other outcomes of interest: Wellbeing signs: RCT: Wellbeing was

	feeding at discharge in the Early Parent Participation Program compared with the usual care group (66 vs. 51% respectively, $p=0.076$) [Critical]. No faltering growth/body composition: RCT: There was no difference in weight z-score at discharge in the Early Parent Participation Program compared with the usual care group (Median -1.9; IQR -2.5 to -1.3 days vs. -2.0; IQR -2.5 to -1.5 days respectively; not significant) [Critical]. Time to full enteral feeds: RCT: There was no difference in days to reach full enteral feeds in the Early Parent Participation Program compared with the usual care group (Median 8; IQR 5 to 11 days vs. 7; IQR 4 to 10.5 days respectively; not significant) [Critical]. Duration of hospital stay: RCT: There was no difference in length of hospital stay in the Early Parent Participation Program compared with the usual care group (Median 29; IQR 19 to 43 days vs. 31; IQR 19 to 44.5 days respectively; not significant) [Critical]. Participation: RCT: Both mother and father were available to participate in care for 85 infants (57.8%) [Critical]. Parental experience: RCT: Parents were content to be close to their infants. Most of the families in the Early Parent Participation Program were confident about the care activities, although they found orogastric feeding to be the most difficult skill [Critical]. Desirable effects for Māori No additional evidence available	a composite score of motor, behaviour (attention) and digestive (e.g. hand to mouth/sucking) behaviours. Wellbeing was significantly higher in the manual milk administration by parents group (mean 36.2 +/- 8.0 points) compared with electric syringe administration (mean 30.7 +/- 9.5 points; $P=0.049$). Withdrawal signs: RCT: Withdrawal was a composite score of motor, behaviour (e.g. grimace, crying) and digestive (e.g. vomiting, regurgitation) behaviours. There was no significant difference in withdrawal signs between manual milk administration by parents (Mean 37.2 ± 9.4 points) and electric syringe administration (Mean 41.9 ± 13.2 points). The item "tightness or distention of the limbs" was significantly less frequent during manual administration; while its frequency remained stable during feeding, it fluctuated more during administration with the electric syringe pump. Toleration: RCT: Video analysis indicated that 60% (9/15) of children seemed to tolerate manual milk administration by parents better than electric syringe administration. There were no clear difference in toleration in 26.7% (4/15) and 13.3% (2/15) seemed to be more tolerant to electric syringe pump administration.
Undesirable Effects How substantial are the undesirable anticipated effects?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Participation: Observational study: A secondary analysis of a RCT reported low parental participation rates in tube feedings (mean 6.7% +/- 5.4). Undesirable effects for Māori No additional evidence available	
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	One RCT is low certainty of evidence. Another RCT and the observational study are very low certainty evidence. Certainty of evidence for Māori No additional evidence available	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability Values for Māori No additional evidence available	
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison	Encouraging parents to be involved in tube feeding versus no involvement - low certainty evidence	

○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Probable decrease in feeding intolerance Uncertain effect on mortality, breastfeeding at discharge, days to full enteral feeds, NEC, duration of hospital stay, weight z-score at discharge High participation despite tube feeding task being perceived as difficult Encouraging parents to be involved in tube feeding versus no involvement - very low certainty evidence Probable increase in wellbeing signs, tolerance of procedure Uncertain effect on neurobehaviour, withdrawal signs Low participation Balance of effects for Māori No additional evidence available		
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Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Staff required to train and support parents with tube feeding.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Certainty of the staff-related costs is low.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No included studies	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Equity for Māori Pēpi Māori are disproportionately affected by preterm birth and experience lower rates of exclusive breastfeeding at discharge. Parents may be less likely to be actively involved in care practices such as tube feeding and supplement preparation due to historical mistrust of the health system, culturally inappropriate communication or lack of invitation to participate. Encouraging Māori parents to engage in feeding-related tasks may strengthen their connection to their pēpi, support breastfeeding intentions and restore traditional caregiving roles. When supported with culturally safe guidance, hands-on involvement can empower whānau, increase breastmilk expression and improve early bonding. Equity requires affirming the role of Māori parents as partners in care and ensuring services uphold tino rangatiratanga in neonatal care. Equity for Pacific families Pacific families often express a strong desire to be involved in their baby's care, but may face barriers such as language, limited health literacy and time constraints due to work and family responsibilities. Without culturally tailored support, they may not feel confident preparing feeds or using equipment like feeding pumps. Encouraging involvement in feeding and supplementation, alongside practical, language-appropriate education, may build parental	

	confidence and reinforce traditional nurturing roles. Supporting this engagement has the potential to improve breastfeeding outcomes and increase family satisfaction with neonatal care. Equity requires that Pacific families are meaningfully included and supported with culturally resonant approaches that respect their strengths and values. Equity for underrepresented groups Families from migrant, refugee, or rural backgrounds may experience exclusion from active caregiving due to systemic barriers, including inflexible visiting hours, transportation challenges or unfamiliarity with healthcare processes. These families may also face assumptions about their capacity or willingness to participate. Actively encouraging and supporting all parents to participate in feeding activities, such as tube feeds, pump use or fortifier preparation, can improve parental confidence, strengthen attachment, and enhance infant outcomes. Equity demands flexible policies, interpreters and practical supports to ensure every family has the opportunity to be fully involved in their infant's nutrition and care journey.	
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Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☐ Varies ☐ Don't know	Probably acceptable to most. Parents were content to be close to their babies. Most of the families in the Early Parent Participation Program were confident about the care activities although they found orogastric feeding to be the most difficult skill [2].	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☐ Varies ☐ Don't know	Likely to be feasible	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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Appendix I. Adolopment of Existing Guideline Recommendations

NB. Only published existing guidelines deemed high quality due to at least two domains scoring $\geq 70\%$ on appraisal with the AGREE II instrument were included. Minimal or no evidence was found for the “Summary of local evidence or context” sections of the following Evidence to Decision documents so local context has been provided by Guideline Development Group members.

Topic 1 – Parenteral Nutrition

AA 2. Which infants (by birthweight or gestational age) should receive parenteral nutrition?

Source recommendation		Back to question list	
Source guideline title and developer		Neonatal parenteral nutrition NICE Guideline, 2020, No. 154 https://www.nice.org.uk/guidance/ng154/chapter/Recommendations#indications-for-and-timing-of-neonatal-parenteral-nutrition	
Existing guidelines recommendation		For preterm babies born before 31+0 weeks, start neonatal parenteral nutrition. For preterm babies born at or after 31+0 weeks, start parenteral nutrition if sufficient progress is not made with enteral feeding in the first 72 hours after birth. For preterm babies on enteral feeds, start parenteral nutrition if: enteral feeds have to be stopped and it is unlikely they will be restarted within 48 hours. enteral feeds have been stopped for more than 24 hours and there is unlikely to be sufficient progress with enteral feeding within a further 48 hours.	
Year published		2020	
Search updated/assessment of new evidence		August 2025	
Strength of recommendation		Expert opinion	
GRADE certainty of evidence		Very low	
Were EtD and SoF available?		Yes https://www.nice.org.uk/guidance/ng154/evidence/a1-predictors-of-enteral-feeding-success-pdf-7083230941 https://www.nice.org.uk/guidance/ng154/evidence/a2-optimal-timeframe-to-start-parenteral-nutrition-pdf-7083230942	
Is the recommendation recent and credible?		Yes AGREE II score: 88%	
Assessment of suitability for adolopment			
Is the recommendation relevant to local setting (population/ intervention/comparator)?		Yes, but several Aotearoa New Zealand hospitals already use <32 weeks as the criteria for parenteral nutrition.	
Are the judgements in the source EtD acceptable without modification?		Yes	
Are any local contextual factors different (e.g. cost, equity, feasibility)?		No	
EtD Criterion	Summary of local evidence or context	Judgement	Notes
Problem	High risk of faltering growth and nutritional deficits in infants	Priority	Aligns with local incidence of early feeding intolerance and

	<31 weeks or <1,500g; timely parenteral nutrition may address early deficits.		metabolic instability in very preterm infants.
Desirable effects	Prevents early catabolism; ensures early provision of nutrition; supports early metabolic stability.	Large	Supported by clinical practice consensus and ASPEN guidance, even with limited RCT evidence.
Undesirable effects	Potential risk of metabolic disturbances, line-associated sepsis, fluid overload.	Small	Risks are manageable with monitoring; considered acceptable compared to benefits.
Certainty of evidence	Both NICE & ASPEN are based on expert consensus or low-quality evidence.	Very low	No high-certainty RCTs guide specific gestational age or birthweight thresholds.
Values and preferences	Clinicians prioritise early nutrition and stabilisation; families likely to support interventions that support survival and development.	Possibly some uncertainty	Acceptable due to clear benefit in vulnerable population.
Balance of effects	Benefits of preventing early catabolic state and nutrient deficits outweigh manageable risks.	Favours intervention	Adapted recommendation improves clarity on timing.
Resources required	Trivial costs for central access, parenteral nutrition compounding and monitoring.	Trivial	Already standard practice in tertiary neonatal units.
Certainty of resource evidence	Local costing data consistent and reliable; international comparators align.	High	Data from hospital formularies and budgeting sources.
Cost-effectiveness	More cost-effective to prevent complications of undernutrition than to treat later faltering growth or NEC.	Favours intervention	Especially relevant where enteral feeds are delayed. No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.
Equity	Standardised early policy could improve equity for Māori and Pacific babies who may otherwise receive later intervention.	Probably increased	Alignment with equity goals of Te Tiriti o Waitangi and Aotearoa New Zealand neonatal strategy.
Acceptability	Generally accepted by neonatal staff, though workload may increase slightly with earlier initiation targets.	Yes	Emphasises role of early vascular access and workflow coordination.
Feasibility	Vascular access achievable soon after birth; protocols can support early parenteral nutrition delivery.	Yes	Supported by existing parenteral nutrition infrastructure in most units.
Judgement criteria for EtD			
Decision Type		☒ Adopted as is ☐ Adapted ☐ De novo recommendation required	
Explanation of adoption		Current Aotearoa New Zealand practice is to use <32 weeks as the criterion. As there is no evidence to support the criterion of <32 weeks, the consensus was to adopt the NICE recommendations.	
Final Recommendation			
Recommendation statement (adopted)		For preterm babies born <31+0 weeks, start neonatal parenteral nutrition. For preterm babies born ≥31+0 weeks, start parenteral nutrition if sufficient progress is not made with enteral feeding in the first 72 hours after birth. For preterm babies on enteral feeds, start parenteral nutrition if: enteral feeds need to be stopped and it is unlikely they will be restarted within 48 hours.	

	enteral feeds have been stopped for more than 24 hours and there is unlikely to be sufficient progress with enteral feeding within a further 48 hours.
Strength	Conditional
Certainty of evidence	Very low
Basis for decision	While there was no specific evidence for this, there is a risk of significant deficits in nutrition and short-term and long-term adverse events if infants born before 32 weeks are not supported by parenteral nutrition from birth.
Subgroup Considerations	Infants <28 weeks may have greater benefit from early initiation due to higher nutrient deficits.
Implementation Considerations	Requires streamlined processes to ensure vascular access is secured and parenteral nutrition can be started within 6–8 hours of birth.
Monitoring and Evaluation	Track time from birth to initiation of parenteral nutrition.
Research Priorities	Early vs. delayed parenteral nutrition initiation stratified by gestation and birthweight.

AA 3. How many hours should pass before starting parenteral nutrition in extremely preterm infants?

Source recommendation		Back to question list	
Source guideline title and developer	Neonatal parenteral nutrition NICE Guideline, 2020, No. 154 https://www.nice.org.uk/guidance/ng154/chapter/Recommendations#indications-for-and-timing-of-neonatal-parenteral-nutrition		
Existing guidelines recommendation	When a preterm baby meets the indications for parenteral nutrition, start it as soon as possible, and within 8 hours at the latest.		
Year published	2020		
Search updated/assessment of new evidence	August 2025. No new evidence was identified.		
Strength	Conditional		
GRADE certainty of evidence	Very low		
Were EtD and SoF available?	https://www.nice.org.uk/guidance/ng154/evidence/a2-optimal-timeframe-to-start-parenteral-nutrition-pdf-7083230942		
Is the recommendation recent and credible	Yes - AGREE II score 88%		
Assessment of suitability for adoption			
Is the recommendation relevant to local setting (population/ intervention/comparator)?	Yes		
Are the judgements in the source EtD acceptable without modification?	Yes		
Are any local contextual factors different (e.g. cost, equity, feasibility)?	Some Aotearoa New Zealand units already aim to provide parenteral nutrition within 6 hours of birth.		
EtD Criterion	Summary of Local Evidence or Context	Judgement	Notes
Problem	Timely nutritional support is critical in extremely preterm infants who are unable to tolerate enteral feeding.	Priority	Associated with metabolic instability and catabolism in early life.
Desirable effects	Provides early energy and protein to prevent catabolic state and support organ development.	Large	Supports survival, growth and long-term neurodevelopment potential.
Undesirable effects	Potential line-related infections and metabolic disturbances with early use.	Small	Manageable with proper aseptic technique and monitoring.
Certainty of evidence	Very low certainty of evidence and consensus-based guidance from NICE	Very low	No strong RCTs on current clinical practice, but consistent expert support. Very low quality, indicating high uncertainty in the reliability of the data, with the exception of energy intake which was considered moderate quality.
Values and preferences	Clinicians value early stabilisation: families often accept early intervention to support fragile infants.	Possibly some variability	Likely acceptable given perceived benefit and low risk.
Balance of effects	Net benefit from early initiation likely outweighs small risks when managed well.	Favours intervention	Consistent with international standards.

Resources required	Early preparation and administration may require extra nursing time.	Moderate	Requires coordination across disciplines.
Certainty of resource evidence	Aotearoa New Zealand cost data and staffing estimates available; comparable to ASPEN context.	High	Routine practice in neonatal units.
Cost-effectiveness	Avoiding complications from catabolic state or delayed nutrition likely to save long-term costs.	Favours intervention	Supported by modelling and neonatal outcome data.
Equity	Clear guidance helps ensure timely and consistent care for all babies, including Māori and Pacific infants.	Probably increased	Reduces care variation by ethnicity or location.
Acceptability	Neonatal teams familiar with early parenteral nutrition protocols; families reassured by proactive care.	Yes	Likely high uptake if recommendation is clear.
Feasibility	Widespread use already exists; protocols and training can support consistent delivery.	Yes	Feasible in both tertiary and regional settings.
Judgement criteria for EtD			
Decision Type		☒ Adopted as is ☐ Adapted ☐ De novo recommendation required	
Explanation of adoption		NICE recommendations and our current practice align on starting parenteral nutrition early.	
Final Recommendation			
Recommendation statement (adopted)		When a preterm baby meets the indications for parenteral nutrition, start it as soon as possible, and within 8 hours at the latest.	
Strength		Conditional	
Certainty of evidence		Very low	
Basis for decision		Adopted from NICE 2020 guidelines. Supports early initiation of parenteral nutrition while allowing for realistic clinical application in all neonatal units.	
Subgroup Considerations		Particularly relevant to infants born <28 weeks or <1,000 g who may have a prolonged transition to full enteral feeding.	
Implementation Considerations		Ensure availability of early vascular access protocols, standard parenteral nutrition solutions, education for staff on timing targets and coordination between clinical teams.	
Monitoring and Evaluation		Audit timing of parenteral nutrition initiation and correlate with short-term metabolic outcomes and infection rates.	
Research Priorities		Research comparing parenteral nutrition initiation at <8 hours vs. 8–12 hours in extremely preterm infants	

AA 6. In preterm infants what is the minimum glucose load (mg/kg/min) administered via IV infusion needed for maintenance of metabolic homeostasis or prevention of hypoglycaemia?

Source recommendation		Back to question list	
Source guideline title and developer	NICE 2020 https://www.nice.org.uk/guidance/ng154/chapter/Recommendations#constituents-of-neonatal-parenteral-nutrition		
Year published	2020		
Search updated/assessment of new evidence	August 2025. No new evidence was identified.		
Existing guidelines recommendation	For preterm and term babies, give glucose as follows: If starting parenteral nutrition in the first 4 days after birth: give a starting range of 6 to 9 g/kg/day gradually increase (for example, over 4 days) to a maintenance range of 9 to 16 g/kg/day. If starting parenteral nutrition more than 4 days after birth give a range of 9 to 16 g/kg/day.		
Strength of recommendation	Conditional		
GRADE certainty of evidence	Low		
EtD and SoF available	Yes - https://www.nice.org.uk/guidance/ng154/evidence/d1-glucose-pdf-7083230945		
Is the recommendation recent and credible	Yes (chosen over ESPGHAN 2018 as more recent and EtD/SoF available) AGREE II score: 88%		
Assessment of suitability for adolopment			
Relevant to local setting?	Yes		
Acceptable without modification?	Yes		
Contextual factors different?	Yes		
EtD Criterion	Summary of Local Evidence or Context	Judgement	Notes
Problem	Hypoglycaemia is common in preterm infants and associated with adverse neurodevelopmental outcomes.	Priority	Early intravenous glucose is a cornerstone of parenteral support.
Desirable effects	Maintains metabolic homeostasis, prevents neuroglycopenia, stabilises blood sugar levels.	Large	Standard practice and high clinical importance.
Undesirable effects	Risk of hyperglycaemia and glycosuria at higher infusion rates.	Small	Mitigated with careful monitoring and gradual increases.
Certainty of evidence	Recommendations based on expert consensus and practice norms; limited trial data.	Low	No clear RCT data on thresholds; values extrapolated from physiology.
Values and preferences	Clinicians prioritise glucose stability; parents value interventions that protect brain development.	Possibly major variability	Well accepted across neonatal units.
Balance of effects	Benefits clearly outweigh risks when infusion targets are adhered to.	Favours intervention	Supported by long-standing clinical practice.
Resources required	Minimal; glucose solutions readily available; part of routine care.	Trivial	No special equipment or infrastructure required.
Certainty of resource evidence	Costs well known and standardised; negligible impact on total cost.	High	Standard component of neonatal nutrition.

Cost-effectiveness	No studies identified	Favours intervention	Prevention of hypoglycaemia avoids costly long-term neurodisability.
Equity	Universal implementation contributes to equitable prevention of hypoglycaemia.	Increased	Reduces variation in management and access.
Acceptability	Likely acceptable to both clinicians and families.	Yes	Routine part of neonatal care protocols.
Feasibility	Easily implemented and widely feasible in all neonatal units.	Yes	Requires no additional capacity or staff time.
Judgement criteria for EtD			
Decision Type	☐ Adopted as is ☒ Adapted ☐ De novo recommendation required		
Explanation of adaptation	Recommendation as per with NICE guidance. No local contextual changes required. Minimum glucose load added from our literature search ETD (link).		
Final recommendation			
Recommendation statement (adopted)	The minimum glucose load (mg/kg/min) via IV infusion to maintain metabolic homeostasis or prevent hypoglycaemia is at least 4 to 8 mg/kg/minute		
Strength	Conditional		
Certainty of evidence	Low		
Basis for decision	Based on widely adopted international guidance. NICE 2020 is based on a more recent literature review than ESPGHAN.		
Subgroup Considerations	Extremely preterm infants may require lower initial rates and more gradual escalation due to immature glucose metabolism.		
Implementation considerations	Protocols for standardised initiation and titration of glucose infusions should be in place; ensure glucose monitoring systems are available.		
Monitoring and evaluation	Monitor glucose concentrations at least 4–6 hourly during the first 24–48 hours and audit incidence of hypoglycaemia.		
Research priorities	High-quality trials comparing different glucose initiation strategies in the first 48 hours after birth in preterm infants.		

AA 8. Are there any indications (e.g. high triglycerides, sepsis) to wean, reduce or restrict parenteral lipid administration?

Source recommendation		Back to question list	
Source guideline title and developer	NICE 2020 https://www.nice.org.uk/guidance/ng154/chapter/Recommendations#indications-for-and-timing-of-neonatal-parenteral-nutrition		
Existing guidelines recommendation	Serum triglycerides Measure serum triglycerides: daily while increasing the parenteral nutrition lipid dosage weekly after reaching a maintenance intravenous lipid dosage. Measure serum triglycerides more frequently, but not more than once a day, if: the level is elevated the preterm or term baby is at risk of hypertriglyceridaemia, for example, if the baby is critically ill or has a lipaemic blood sample. Be aware that ongoing serum triglyceride monitoring may not be needed for stable preterm or term babies transitioning from parenteral nutrition to enteral nutrition.		
Year published	2020		
Search updated/assessment of new evidence	August 2025. No new evidence was identified.		
Strength and direction of recommendation	The NICE committee acknowledged that some neonatal units monitor triglycerides more or less frequently, and some neonatal units do not monitor triglycerides at all. No research evidence was found but based on expert opinion, the NICE committee agreed that when an infant is at risk of hypertriglyceridaemia for example is critically ill or has a lipaemic blood sample, triglycerides should be monitored more frequently to ensure the safety of the baby (but no more than once a day).		
GRADE certainty of evidence	Very low		
Were EtD and SoF available?	Yes https://www.nice.org.uk/guidance/ng154/evidence/f-monitoring-neonatal-parenteral-nutrition-pdf-254996313882		
Is the recommendation recent and credible	Yes AGREE II score: 88%		
Assessment of suitability for adolopment			
Is the recommendation relevant to local setting (population/ intervention/comparator)?		Yes	
Are the judgements in the source EtD acceptable without modification?		No	
Are any local contextual factors different (e.g. cost, equity, feasibility)?		Yes	
EtD Criterion	Summary of local evidence or context	Judgement	Notes
Problem	Hypertriglyceridaemia and lipid intolerance are occasionally observed in very preterm infants receiving parenteral lipid emulsions.	Priority	There is variability in monitoring triglycerides in clinical practice.

Desirable effects	Reduces risk of fat overload, liver dysfunction and metabolic complications.	Moderate	May be important for patient safety and long-term outcomes.
Undesirable effects	Reducing lipids limits energy provision and essential fatty acid intake. Additional blood testing is distressing to infants and parents and increases the risk of anaemia.	Moderate	May impact growth if prolonged.
Certainty of evidence	No studies were identified	Very low	No high-quality trials.
Values and preferences	Clinicians value safety but balance it with nutrient needs; families may be unaware of technical decisions.	Possibly major variability	Likely to align with clinical judgement in most units.
Balance of effects	Little evidence of benefit in preterm infants and limits early energy intake. Extra blood test needed.	Favours comparator	Enables continuation of adequate parenteral nutrition.
Resources required	Requires triglyceride monitoring; may involve switching emulsions or dose reduction.	Small	Triglyceride measurement not universally rapid in all settings.
Certainty of resource evidence	Cost and availability of lipid emulsions and lab monitoring are well known locally.	High	No significant uncertainty.
Cost-effectiveness	No studies	Unknown	
Equity	Consistent protocols can increase equity.	Probably increased	Standardised approach supports fair care access.
Acceptability	May be acceptable among clinicians if there was evidence of benefit. Extra blood tests less acceptable. More frequent blood monitoring may result in reduced parenteral satisfaction and increased infant distress and pain associated with blood taking.	Probably yes	Already practiced informally in many settings.
Feasibility	Feasible where biochemical monitoring and clinical support are available.	Yes	May require improved lab access in smaller units.
Judgement criteria for EtD			
Decision Type	☐ Adopted as is ☒ Adapted ☐ De novo recommendation required		
Explanation of adaptation	The Guideline Development Group acknowledges that some Aotearoa New Zealand neonatal units monitor triglycerides more or less frequently, and some neonatal units do not routinely monitor triglycerides at all. No research evidence was found to support a recommendation to begin monitoring triglycerides in neonatal units that do not already do this.		
Final Recommendation			
Recommendation statement (adapted)	When an infant is at risk of hypertriglyceridaemia, for example has a lipaemic blood sample, triglycerides should be monitored. The reduction of lipid emulsion during episodes of sepsis is not recommended.		
Strength	Conditional		
Certainty of evidence	Very low		
Basis for decision	No research evidence was found to support the routine measurement of triglycerides or the reduction of lipid emulsion during		

	episodes of sepsis.
Subgroup considerations	Caution is needed in extremely preterm infants and those with pre-existing metabolic instability.
Implementation considerations	No implementation required
Monitoring and evaluation	If triglycerides are monitored, this should be no more than once a day.
Research priorities	Whether routine monitoring of serum triglycerides and reduction of the lipid emulsion dose is beneficial and if so at what serum triglycerides concentration should the lipid emulsion dose be reduced.

AA 10. Is there evidence for addition of specific fatty acids?

Source recommendation		Back to question list
Source guideline title and developer	ESPGHAN 2018 https://www.espen.org/files/ESPEN-Guidelines/Pediatrics/ESPGHAN_ESPEN_ESPR_CSPEN-guidelines-on-pediatric-parenteral-nutrition-Lipids.pdf NICE 2020 https://www.nice.org.uk/guidance/ng154/chapter/Recommendations#constituents-of-neonatal-parenteral-nutrition ESPGHAN 2022 Enteral Nutrition in Preterm Infants: ESPGHAN/ESPEN/ESPR/CSPEN Guidelines 2022, Koletzko et al. https://onlinelibrary.wiley.com/doi/10.1097/MPG.0000000000003642	
Year published	2020	
Search updated/assessment of new evidence	August 2025. No new evidence was identified.	
Existing guidelines recommendation	ESPGHAN 2018 In order to prevent essential fatty acid deficiency in preterm infants a lipid emulsion dosage providing a minimum linoleic acid intake of 0.25 g/kg/day can be given. This lipid emulsion dosage ensures an adequate intake of linolenic acid with all lipid emulsions currently registered for paediatric use. ESPGHAN recommends supplementation of long-chain polyunsaturated fatty acids (LC-PUFAs), especially DHA, in parenteral and enteral nutrition, although based on limited evidence. NICE 2020 For preterm and term babies with parenteral nutrition-associated liver disease, consider giving a composite lipid emulsion rather than a pure soy lipid emulsion. ESPGHAN (Enteral) 2022 Linoleic acid 385–1540 mg/kg/day α-Linolenic acid >55 mg/kg/day DHA 30–65 mg/kg/day ARA 30–100 mg/kg/day EPA <20 mg/kg/day	
Strength of recommendation	Conditional	
GRADE certainty of evidence	Low	
EtD and SoF available	Yes NICE 2020 https://www.nice.org.uk/guidance/ng154/evidence/d4-lipid-emulsions-pdf-7083230948 ESPGHAN 2018	

	Lapillonne A, et al., ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Lipids, Clinical Nutrition (2018), https://doi.org/10.1016/j.clnu.2018.06.94 https://www.espen.org/files/ESPEN-Guidelines/Pediatrics/ESPGHAN_ESPEN_ESPR_CSPEN-guidelines-on-pediatric-parenteral-nutrition-Lipids.pdf ESPGHAN 2022 https://cdn-links.lww.com/permalink/mpg/c/mpg_1_1_2022_11_28_ingleton_228_sdc1.pdf		
Is the recommendation recent and credible	Yes (chosen over ESPGHAN 2018 as more recent and EtD/SoF available) AGREE II score: Nice 2020 - 88% ESPGHAN 2018 - 79% ESPGHAN 2022 - 67%		
Assessment of suitability for adoption			
Is the recommendation relevant to local setting (population/ intervention/comparator)?	Yes		
Are the judgements in the source EtD acceptable without modification?	No. The DINO (https://jamanetwork.com/journals/jama/fullarticle/183204 and https://pubmed.ncbi.nlm.nih.gov/25787990/), N3RO https://www.nejm.org/doi/10.1056/NEJMoa1611942?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%20www.ncbi.nlm.nih.gov) and MOBYDick (https://jamanetwork.com/journals/jama/fullarticle/2768134) trials conducted in Australia showed that for preterm infants, enteral DHA supplementation did not demonstrate consistent clinical benefits and may lead to harm highlighting a need for more rigorous, long-term research before definitive DHA supplementation recommendations for can be made.		
Are any local contextual factors different (e.g. cost, equity, feasibility)?	Yes. An enteral DHA supplement is not currently available.		
EtD Criterion	Summary of local evidence or context	Judgement	Notes
Problem	Suboptimal clinical and neurodevelopmental outcomes and inflammation in preterm infants may be linked to low levels of LC-PUFAs.	Priority	Early DHA provision may be important
Desirable effects	Potential benefit of LC-PUFAs on retinopathy of prematurity, vision and brain development.	Moderate	Potentially beneficial, especially in very preterm infants.
Undesirable effects	Decreased executive function and increased conduct problems in girls who received high dose DHA supplementation (DINO trial). BPD or death increased in the DHA supplemental group (N3RO and MOBYDick trials)	Moderate	The DINO, N3RO and MOBYDick trials showed that DHA enteral supplementation for preterm infants had no clinical benefits and may lead to potential harm.
Certainty of evidence	Very low certainty for LC-PUFAs, based on inconsistent and limited trials.	Very low	Based on observational data, small studies and expert consensus.
Values and preferences	Clinicians value neurodevelopmental outcomes but are cautious about adding components without strong evidence.	Possibly major variability	No known conflict between clinicians or families about desirability.
Balance of	Currently uncertain; possible benefit of LC-PUFAs.	Uncertain	Evidence for LC-PUFAs promising but uncertain.

effects			
Resources required	May increase cost of parenteral lipid emulsions or enteral supplements.	Moderate	Costs relate to choice of lipid emulsions
Certainty of resource evidence	Limited; pricing of LC-PUFA-enriched products is available, but outcome-based costing is lacking.	Low	Uncertainty due to lack of formal economic evaluations.
Cost-effectiveness	Not established for either intervention.	Uncertain	Further modelling studies required.
Equity	Routine supplementation could exacerbate inequity unless universally available.	Probably reduced	Access to enriched products varies between centres.
Acceptability	Likely acceptable if recommended in guidelines but requires careful communication with families.	Yes	Parental support likely if explained clearly and benefits made evident.
Feasibility	Feasible with commercial LC-PUFA lipid emulsions.	Yes	Commercial LC-PUFA emulsions are available.
Judgement criteria for EtD			
Decision Type	☐ Adopted as is ☒ Adapted ☐ De novo recommendation required		
Explanation of adaptation	Adapted to reflect current prescribing practices, updated evidence from local RCTs and current lipid emulsions.		
Final Recommendation			
Recommendation statement (adapted)	To prevent essential fatty acids deficiency a lipid emulsion dose providing a minimum linoleic acid intake of 0.25 g/kg/day should be given (~1.5 g/kg/day SMOFLipid). Parenteral LC-PUFA supplementation is recommended where LC-PUFA containing lipid emulsion products are available and cost-effective, e.g. SMOFLipid. Routine enteral long chain polyunsaturated fatty acid supplementation is not recommended.		
Strength	Conditional		
Certainty of evidence	Very low		
Basis for decision	Based on ESPGHAN and local high quality RCTs. The N3RO and MOBYDICK trials reinforce that DHA-centric enteral supplementation for preterm infants does not demonstrate clinical benefits, may lead to potential harm and should be avoided.		
Subgroup Considerations	Extremely preterm infants at risk of retinopathy of prematurity may benefit more from LC-PUFAs.		
Implementation Considerations	~1.5 g/kg/day SMOFLipid ensures an adequate intake of linolenic acid. Standardisation of parenteral lipid emulsions across units would be beneficial.		
Monitoring and Evaluation	Track clinical use and any adverse effects related to LC-PUFA products.		
Research Priorities	High-quality trials of LC-PUFA supplementation in very preterm infants.		

AA 13. What is the recommended parenteral energy and macronutrient intake by postnatal age?

Source recommendation Back to question list	
Source guideline title and developer	NICE 2020 (chosen over ESPGHAN 2018 as more recent and EtD/SoF available) https://www.nice.org.uk/guidance/ng154/chapter/Recommendations#indications-for-and-timing-of-neonatal-parenteral-nutrition
Existing guidelines recommendation	
Energy https://www.nice.org.uk/guidance/ng154/evidence/c-energy-needs-pdf-7083230944	Energy NICE (Consistent with ESPGHAN): If starting parenteral nutrition in the first 4 days after birth: give a starting range of 40 to 60 kcal/kg/day gradually increase (for example, over 4 days) to a maintenance range of 75 to 120 kcal/kg/day. If starting parenteral nutrition more than 4 days after birth give a range of 75 to 120 kcal/kg/day.
Carbohydrate https://www.nice.org.uk/guidance/ng154/evidence/d1-glucose-pdf-7083230945	Carbohydrate If starting parenteral nutrition in the first 4 days after birth: give a starting range of 6 to 9 g/kg/day glucose gradually increase (for example, over 4 days) to a maintenance range of 9 to 16 g/kg/day. If starting parenteral nutrition more than 4 days after birth give a range of 9 to 16 g/kg/day.
Protein https://www.nice.org.uk/guidance/ng154/evidence/d2-amino-acids-pdf-7083230946	Protein If starting parenteral nutrition in the first 4 days after birth: give a starting range of 1.5 to 2 g/kg/day amino acid and gradually increase (for example, over 4 days) to a maintenance range of 3 to 4 g/kg/day. If starting parenteral nutrition more than 4 days after birth: give a range of 3 to 4 g/kg/day.
Protein:Energy ratio https://www.nice.org.uk/guidance/ng154/evidence/d7-ratio-of-nonnitrogen-energy-to-nitrogen-pdf-254996313877	Protein:Energy ratio 23 to 34 kcal of total energy per g amino acid
Lipid https://www.nice.org.uk/guidance/ng154/evidence/d3-lipids-pdf-7083230947	Lipid If starting parenteral nutrition in the first 4 days after birth give a starting range of 1 to 2 g/kg/day and gradually increase (for example, in daily increments of 0.5 to 1 g/kg/day) to a maintenance range of 3 to 4 g/kg/day. If starting parenteral nutrition more than 4 days after birth give a range of 3 to 4 g/kg/day.
Year published	2020 (NICE)
Search updated/assessment of new evidence	August 2025
GRADE certainty of evidence	Very low to high quality

EtD and SoF available		Yes (chosen over ESPGHAN 2018 as more recent and EtD/SoF available)	
Is the recommendation recent and credible		Yes AGREE II score 88%	
Assessment of suitability for adolopment			
Relevant to local setting?		Yes	
Acceptable without modification?		Yes	
Contextual factors different?		No	
EtD Criterion	Summary of Local Evidence or Context	Judgement	Notes
Problem	Suboptimal energy delivery in early neonatal care is associated with faltering growth and adverse neurodevelopment.	Priority	Standardised targets needed to avoid under- or overfeeding.
Desirable effects	Provides fuel for growth, organ function and metabolism.	Large	Essential for survival and development of very preterm infants.
Undesirable effects	Excessive energy can increase carbon dioxide production and risk hepatic steatosis.	Small	Dose titration and monitoring help mitigate risks.
Certainty of evidence	Guidelines based on physiology and clinical practice consensus; no RCTs.	Very low	Derived from indirect evidence and expert opinion.
Values and preferences	Clinicians and families value growth, survival, and development.	Possibly major variability	Widely accepted target ranges.
Balance of effects	Clear benefits with minimal harms when energy provision is appropriately titrated.	Favours intervention	No major safety concerns with recommended ranges.
Resources required	Requires compounding of parenteral nutrition with energy targets; standard practice.	Low	Readily feasible in neonatal units.
Certainty of resource evidence	Reliable cost and feasibility data from routine practice.	High	Consistent with established protocols.
Cost-effectiveness	No available studies	Favours intervention	Adequate early nutrition reduces long-term cost from complications and faltering growth.
Equity	Standardising energy delivery helps reduce variation in practice.	Probably increased	Supports standard care across units.
Acceptability	Acceptable to clinicians; supports clinical workflow and growth monitoring.	Yes	Forms part of nutrition protocols.
Feasibility	Easily implemented through standard intravenous nutrition formulations.	Yes	No additional resources required.
Judgement criteria for EtD			
Decision Type	☐ Adopted as is ☒ Adapted ☐ De novo recommendation required		
Explanation of adaptation	Wording adapted to reflect local parenteral nutrition practices, i.e. less gradual grading up over several days of protein and lipid and		

	to ensure alignment with recommended protein:energy ratio.
Final Recommendation	
Recommendation statement (adapted)	Initiate parenteral nutrition on day 1 and adjust for tolerance and clinical condition. Energy Give a starting range of 40 to 60 kcal/kg/day Gradually increase to a maintenance range of 75 to 120 kcal/kg/day If starting parenteral nutrition more than 4 days after birth give 75 to 120 kcal/kg/day. Carbohydrate Give a starting range of 6 to 9 g/kg/day (equivalent to ~4 to 6 mg/kg/min) glucose Gradually increase to a maintenance range of 9 to 16 g/kg/day (6 to 11 mg/kg/min) If starting parenteral nutrition more than 4 days after birth give 9 to 16 g/kg/day (6–11 mg/kg/min). Protein Give a starting range of 1.5 to 2 g/kg/day amino acid Increase to a maintenance range of 3 to 4 g/kg/day. If starting parenteral nutrition more than 4 days after birth give 3 to 4 g/kg/day. Protein:Energy ratio Ensure protein:energy ratio is 23 to 34 kcal of total energy per g amino acid Lipid Give a starting range of 1 to 2 g/kg/day and increase to 3 to 4 g/kg/day If starting parenteral nutrition more than 4 days after birth give a range of 3 to 4 g/kg/day.
Strength	Conditional
Certainty of evidence	Certainty: Very low
Basis for decision	Extremely preterm or growth-restricted infants may require closer monitoring and tailored progression.
Subgroup Considerations	Protocols for energy targets should be standardised.
Implementation Considerations	Ensure standard parenteral nutrition solutions that meet these recommendations are available.
Monitoring and Evaluation	Audit energy and macronutrient delivery vs. recommendations
Research Priorities	Early vs. delayed energy escalation Determine optimal energy and macronutrient intake for survival, growth and long-term development

AA 16. What is the recommended parenteral intake of: sodium, potassium, chloride, acetate, calcium, phosphorus, magnesium, iron, zinc, selenium, chromium, copper, manganese, molybdenum, fluoride, iodine and vitamins

Source recommendation Back to question list	
Source guideline title and developer	ESPGHAN 2018 Sodium, potassium, chloride https://doi.org/10.1016/j.clnu.2018.06.948 Jochum F, Moltu SJ, Senterre T, Nomayo A, Goulet O, Iacobelli S, ESPGHAN/ESPEN/ESPR/CSPEN Working Group on Pediatric Parenteral Nutrition. ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: fluid and electrolytes. Clin Nutr 2018;37:2344e53. Calcium, phosphate, magnesium https://www.sciencedirect.com/science/article/pii/S0261561418311695?via%3Dihub Mihatsch W, Fewtrell M, Goulet O, Molgaard C, Picaud JC, Senterre T, ESPGHAN/ESPEN/ESPR/CSPEN Working Group on Pediatric Parenteral Nutrition. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: calcium, phosphorus and magnesium. Clin Nutr 2018;37: 2360e5. Trace elements https://www.sciencedirect.com/science/article/pii/S0261561418311683?via%3Dihub Domellöf M, Sztanyi P, Simchowitz V, Franz A, Mimouni F, ESPGHAN/ESPEN/ESPR/CSPEN Working Group on Pediatric Parenteral Nutrition. ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: iron and trace minerals. Clin Nutr 2018;37:2354e9. Vitamins https://www.clinicalnutritionjournal.com/article/S0261-5614(18)31170-1/fulltext Bronsky J, Campoy C, Braegger C; ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Vitamins. Clin Nutr. 2018 Dec;37(6 Pt B):2366-2378. doi: 10.1016/j.clnu.2018.06.951
Existing guidelines recommendation	Sodium: 2–7 mmol/kg/day (<1,500 g) 2–5 mmol/kg/day (>1,500 g) Potassium: 2–3 mmol/kg/day Chloride: 2–5 mmol/kg/day Calcium: 1.6–3.5 mmol/kg/day Phosphorus: 1.6–3.5 mmol/kg/day Magnesium: 0.2–0.3 mmol/kg/day Iron: 200-500 µg/kg/day Zinc: 400-500 µg/kg/day Copper: 40 µg/kg/day Iodine: 1-10 µg/kg/day Selenium: 7 µg/kg/day Manganese: ≤1 µg/kg/day Molybdenum: 1 µg/kg/day Chromium: nil Biotin: 5-8 µg Vitamin A: 227-455 µg (700-1500 IU) Vitamin D: 2-10 µg (80-400 IU)

	Vitamin E: 2.8-3.5 mg Vitamin K: 10 µg Vitamin C: 15-25 mg Thiamin: 350-500 µg Riboflavin: 150-200 µg Pyridoxine: 150-200 µg Vitamin B12: 0.3 µg Niacin: 4-6.8 mg Folic acid: 56 µg Pantothenic acid: 2,500 µg		
Year published	2018		
Search updated/assessment of new evidence	August 2025. No new evidence was identified.		
Strength and direction of recommendation	Provide electrolytes and micronutrients within recommended ranges based on weight and gestational age.		
GRADE certainty of evidence	Moderate (varies by nutrient)		
Were EtD and SoF available?	No		
Is the recommendation recent and credible AGREE II score:	Yes AGREE II score: 79%		
Assessment of suitability for adoption			
Is the recommendation relevant to local setting (population/ intervention/comparator)?	Yes		
Are the judgements in the source EtD acceptable without modification?	Yes		
Are any local contextual factors different (e.g. cost, equity, feasibility)?	Access to individual trace elements may be limited in some units, requiring compounded solutions or adjustments. Aotearoa New Zealand soil is deficient in iodine, selenium and zinc.		
EtD Criterion	Summary of local evidence or context	Judgement	Notes
Problem	Preterm infants have low stores of electrolytes and trace elements and are at risk of deficiencies when on parenteral nutrition.	Yes	
Desirable effects	Supports metabolic stability, growth, neurodevelopment and bone health.	Favourable	
Undesirable effects	Risk of toxicity if not appropriately dosed or monitored, particularly in cholestasis.	Manageable	Particular concern with manganese and copper.
Certainty of evidence	Evidence is based on estimated requirements, expert consensus and observational data from neonatal units.	Low	
Values and preferences	Neonatal clinicians value accurate provision and monitoring of micronutrients.	Possibly some uncertainty	
Balance of effects	Benefits of adequate nutrition clearly outweigh risks.	Favourable	

Resources required	Micronutrient solutions are available but may require compounding and incur additional cost.	Moderate	
Certainty of resource evidence	Resource estimates vary between settings.	Low	
Cost-effectiveness	No available studies	Likely	Cost-effective if deficiencies and complications are prevented.
Equity	Regional centres may have reduced access to specific trace element products.	Possibly reduced	Equity gaps may exist between tertiary and regional centres.
Acceptability	Provision is standard practice and supported by clinicians.	Yes	
Feasibility	Feasible with pharmacy support.	Yes	
Judgement criteria for EtD			
Decision Type	☒ Adopted as is ☐ Adapted ☐ De novo recommendation required		
Explanation of adaptation	Recommendation consistent with ESPGHAN and NICE guidance. Adopt as is with minor local contextual comment.		
Final Recommendation			

Provide parenteral electrolytes, minerals trace elements and vitamins in accordance with ESPGHAN 2018 recommendations for preterm infants. As Aotearoa New Zealand soil is deficient in iodine, selenium and zinc, use mid to upper half of recommended intake:

Nutrient	Recommended intake/kg/day	Vitamin	Recommended intake/kg/day
Sodium	2–7 mmol (<1500 g) 2–5 mmol (>1500 g)	Vitamin A	227–455 µg (700–1500 IU)
Potassium	2–3 mmol	Vitamin D	2–10 µg (80–400 IU)
Chloride	2–5 mmol	Vitamin E	2.8–3.5 mg
Calcium	1.6–3.5 mmol	Vitamin K	10 µg
Phosphorus	1.6–3.5 mmol	Vitamin C	15–25 mg
Magnesium	0.2–0.3 mmol	Thiamin	350–500 µg
Iron	200–500 µg	Riboflavin	150–200 µg
Zinc	400–500 µg	Pyridoxine	150–200 µg
Copper	40 µg/	Vitamin B12	0.3 µg
Iodine	1–10 µg	Niacin	4–6.8 mg
Selenium	7 µg	Folic acid	56 µg
Manganese	≤1 µg	Pantothenic acid	2500 µg
Molybdenum	1 µg		
Chromium	nil		

Recommendation statement (adapted)	
Strength	Conditional
Certainty of evidence	Low
Basis for decision	Consensus from international guidelines and knowledge of local soil deficits.
Subgroup Considerations	Adjustments may be needed in cases of cholestasis or renal impairment.
Implementation Considerations	Routine standard solutions and monitoring protocols can facilitate standardisation. Provide guidance on refeeding syndrome testing and phosphate supplementation.
Monitoring and Evaluation	Routine monitoring of biochemical markers and growth parameters is necessary. Monitor clinical parameters of refeeding syndrome, particularly during the first 5-7 days, especially in infants with birthweight <1,500 g or <10th centile.
Research Priorities	RCTs to determine optimal dosing for micronutrients in extremely preterm and growth-restricted infants.

Topic 2 – Enteral Nutrition

AA 17. When to start enteral feeding after birth, recommended type (breastmilk, formula etc), route, method, starting feed volume and frequency of enteral feeding

Source recommendation		Back to question list	
Source guideline title and developer		ESPGHAN 2022 Enteral Nutrition in Preterm Infants: ESPGHAN/ESPEN/ESPR/CSPEN Guidelines 2022, Koletzko et al. https://onlinelibrary.wiley.com/doi/10.1097/MPG.0000000000003642	
Existing guidelines recommendation		Initiate minimal enteral feeding (trophic feeding) within the first 24 hours of life in stable preterm infants. Use mother's own milk where possible, followed by donor breastmilk, and preterm formula if no breastmilk is available. Use gastric route and intermittent bolus feeding. Start with 10–20 mL/kg/day and increase daily by 15–25 mL/kg/day depending on tolerance.	
Year published		2022	
Search updated/assessment of new evidence		August 2025. No new evidence was identified.	
Strength and direction of recommendation		Strong recommendation for early initiation of breastmilk feeds using gastric bolus method.	
GRADE certainty of evidence		Moderate	
Were EtD and SoF available?		Yes https://cdn-links.lww.com/permalink/mpg/c/mpg_1_1_2022_11_28_ingleton_228_sdc1.pdf	
Is the recommendation recent and credible		Yes AGREE II score: 67%	
Assessment of suitability for adoption			
Is the recommendation relevant to local setting (population/ intervention/comparator)?		Yes – aligns with national priorities for preterm infant nutrition and promotion of breastmilk use.	
Are the judgements in the source EtD acceptable without modification?		Generally, yes but the speed of feed advancement is slower than is current practice in Aotearoa New Zealand units.	
Are any local contextual factors different (e.g. cost, equity, feasibility)?		Yes – access to donor milk and lactation support services varies between regions. Some units may face staffing or training limitations that could impact implementation.	
EtD Criterion	Summary of local evidence or context	Judgement	Notes
Problem	Delayed enteral feeding remains a challenge in some neonatal units due to variability in protocols and clinical caution.	Yes	
Desirable effects	Aotearoa New Zealand neonatal units increasingly support early feeding with mother's milk and donor milk availability is expanding but variable in access.	Favourable	Early feeding reduces reliance on parenteral nutrition.
Undesirable effects	Some clinicians remain concerned about feeding intolerance and necrotising enterocolitis, particularly in extremely preterm or growth-restricted infants.	Manageable	Careful advancement mitigates risks.

Certainty of evidence	Evidence from local audits aligns with international trials; early feeding is safe when breastmilk is used and volume advancement is standardised.	Moderate	
Values and preferences	Families strongly value early use of expressed breastmilk. Clinical teams are motivated by reduced infection risk and shorter hospital stays.	Possibly some variation	
Balance of effects	Neonatal teams generally agree that benefits outweigh risks when standardised protocols are followed.	Favourable	
Resources required	Lactation consultant services and access to donor milk varies regionally.	Small	
Certainty of resource evidence	Moderate certainty	Moderate	
Cost-effectiveness	No available studies. Reductions in central line days, infections and parenteral nutrition duration with earlier full enteral feeding offer cost savings.	Favourable	
Equity	Māori and Pacific infants may have reduced access to lactation support and donor milk.	Concern	Regional variation in resource access.
Acceptability	Use of breastmilk and early feeding is highly acceptable to parents when communicated well and with cultural values at the center of the conversation.	High	
Feasibility	Implementation is feasible in tertiary centres. Regional units require support with protocols, training and donor milk access.	High	
Judgement criteria for EtD			
Decision Type	☐ Adopted as is ☒ Adapted ☐ De novo recommendation required		
Explanation of adaptation	Speed of feed advancement adapted to match recent evidence and our own systematic review (see link XXX). Wording changed to remove reference to “stable” infants and “trophic /minimal” enteral feeding.		
Final Recommendation			
Recommendation statement (adapted)	Initiate enteral feeding within the first 24 hours after birth. Use mother's own milk where possible, followed by donor breastmilk and preterm formula if no breastmilk is available. Use gastric route and intermittent bolus feeding. Start with 10–20 mL/kg/day and increase by 24 to 30 mL/kg/day depending on tolerance.		
Strength	Conditional		
Certainty of evidence	Moderate		
Basis for decision	Based on widely adopted international guidance with modifications for current clinical practice in Aotearoa New Zealand.		
Subgroup Considerations	Extremely preterm infants may require lower initial rates and more gradual escalation due to an immature gastrointestinal tract		
Implementation Considerations	Protocols for standardised initiation and feed advancement are needed.		
Monitoring and Evaluation	Monitor compliance with feeding protocols and time to full enteral feeds.		
Research Priorities	High-quality trials comparing different feed initiation strategies in the first 48 hours after birth in preterm infants.		

AA 34. What is the recommended enteral nutritional intake by postnatal age of energy, protein, carbohydrates, lipids, sodium, potassium and chloride, calcium, phosphorus and magnesium and trace elements: e.g. iron, selenium, iodine, chromium, copper, manganese, molybdenum, fluoride

Source recommendation Back to question list	
Source guideline title and developer	ESPGHAN 2022 Enteral Nutrition in Preterm Infants: ESPGHAN/ESPEN/ESPR/CSPEN Guidelines 2022, Koletzko et al. https://onlinelibrary.wiley.com/doi/10.1097/MPG.0000000000003642
Existing guidelines recommendation	Energy: 115–140 (–160) kcal/kg/day Protein: 3.5–4.0 (–4.5) g/kg/day Carbohydrates: 11–15 (–17) g/kg/day Lipids: 4.8–8.1 g/kg/day Sodium 3.0–5.0 (–8.0) mmol/kg/day Chloride 3.0–5.0 (–8.0) mmol/kg/day Potassium 2.3–4.6 mmol/kg/day Calcium 3.0–5.0 mmol/kg/day Phosphorus 2.2–3.7 mmol/kg/day Magnesium 0.4–0.5 mmol/kg/day Iron 2.0–3.0 (–6.0) mg/kg/day Zinc 2.0–3.0 mg/kg/day Copper 120–230 µg/kg/day Selenium 7–10 µg/kg/day Manganese 1–15 µg/kg/day Iodine 11–55 µg/kg/day Chromium 0.03–2.25 µg/kg/day Molybdenum 0.3–5.0 µg/kg/day Thiamine (B1) 140–290 µg/kg/day Pantothenic acid 0.6–2.2 mg/kg/day Biotin 3.5–15 µg/kg/day Niacin 1100–5700 µg/kg/day Ascorbic acid (vitamin C), 17–43 mg/kg/day Riboflavin (B2) 200–430 µg/kg/day Pyridoxine 70–290 µg/kg/day Folic acid 23–100 µg/kg/day Cobalamin (B12) 0.1–0.6 µg/kg/day Vitamin A 1333–3300 IU/kg/day (400–1000 µg retinol ester/kg/day) Vitamin D 400–700 IU/kg/day (<1000) Vitamin E 2.2–11 mg/kg/day Vitamin K 4.4–28 µg/kg/day
Year published	2022
Search updated/assessment of new evidence	August 2025. No new evidence was identified.

Strength and direction of recommendation		Strong	
GRADE certainty of evidence		Low to moderate depending on nutrient	
Were EtD and SoF available?		Yes https://cdn-links.lww.com/permalink/mpg/c/mpg_1_1_2022_11_28_embleton_228_sdc1.pdf	
Is the recommendation recent and credible		Yes AGREE II score: 67%	
Assessment of suitability for adoption			
Is the recommendation relevant to local setting (population/ intervention/comparator)?		Yes	
Are the judgements in the source EtD acceptable without modification?		Yes	
Are any local contextual factors different (e.g. cost, equity, feasibility)?		Yes	
EtD Criterion	Summary of local evidence or context	Judgement	Notes
Problem	Micronutrient deficiencies in preterm infants are common and may impair growth, neurodevelopment and immune function.	Yes	Aotearoa New Zealand soil is low in iodine and selenium.
Desirable effects	Preventing deficiencies supports optimal growth, development and metabolic stability.	Small	
Undesirable effects	Over-supplementation may cause toxicity but can be minimised with monitoring.	Manageable	High serum copper or manganese may occur with excess intake especially in cholestasis.
Certainty of evidence	Based on physiological needs and expert opinion. Few RCTs.	Low to moderate	Most evidence from observational studies or expert panels, not interventional trials.
Values and preferences	Parents and clinicians value strategies that support growth and development safely.	Possibly some variation	Strong preference among clinicians for guidance on dosing ranges for specific trace elements.
Balance of effects	Favourable when standardised and monitored.	Favourable	Net benefit seen with standardised dosing and monitoring protocols across neonatal units.
Resources required	May require specific micronutrient preparations and local compounding.	Trivial	Logistics for acquiring trace elements and ensuring formulations vary by region.
Certainty of resource evidence	No available evidence	Low	Few cost analyses available; most data extrapolated from NICU expenditure reports.
Cost-effectiveness	Cost-effective if complications from nutrient deficiencies are avoided.	Favourable	Trace elements are low-cost; prevent costly complications like anaemia, bone disease.
Equity	Access to trace elements varies regionally in Aotearoa New Zealand.	Concern	Rural and smaller hospitals may lack consistent access to compounded preparations or dietitian input.
Acceptability	Acceptable if dosing is clear and supplies are reliable.	High	Protocols for routine supplementation are

			well-accepted if clear, with audit support.
Feasibility	Feasible with neonatal dietetic support and supply chain availability.	Variable	Practical in tertiary units; may require outreach and upskilling for regional teams.
Judgement criteria for EtD			
Decision Type	☒ Adopt as is ☐ Adapted ☐ De novo recommendation required		
Explanation of adaptation	Adopted as is from ESPGHAN 2022 guidelines (excluding fluids, some vitamins and zinc, which are addressed elsewhere in our guideline). Minor local contextual comment added.		
Final Recommendation			
Recommendation statement (adopted)	Provide enteral nutrient intakes for preterm infants according to ESPGHAN 2022 guidance. Use individualised plans considering gestational age, tolerance and clinical status. Monitor growth and biochemical markers routinely. As Aotearoa New Zealand soil is deficient in iodine, selenium and zinc, use mid to upper half of the recommended intake. Energy: 115–140 (–160) kcal/kg/day Protein: 3.5–4.0 (–4.5) g/kg/day Carbohydrates: 11–15 (–17) g/kg/day Lipids: 4.8–8.1 g/kg/day Sodium 3.0–5.0 (–8.0) mmol/kg/day Chloride 3.0–5.0 (–8.0) mmol/kg/day Potassium 2.3–4.6 mmol/kg/day Calcium 3.0–5.0 mmol/kg/day Phosphorus 2.2–3.7 mmol/kg/day Magnesium 0.4–0.5 mmol/kg/day Iron 2.0–3.0 (–6.0) mg/kg/day Copper 120–230 µg/kg/day Selenium 7–10 µg/kg/day Manganese 1–15 µg/kg/day Iodine 11–55 µg/kg/day Chromium 0.03–2.25 µg/kg/day Molybdenum 0.3–5.0 µg/kg/day Thiamine (B1) 140–290 µg/kg/day Pantothenic acid 0.6–2.2 mg/kg/day Biotin 3.5–15 µg/kg/day Niacin 1100–5700 µg/kg/day Ascorbic acid (vitamin C), 17–43 mg/kg/day Riboflavin (B2) 200–430 µg/kg/day Pyridoxine 70–290 µg/kg/day Folic acid 23–100 µg/kg/day		

	Cobalamin (B12) 0.1–0.6 µg/kg/day Vitamin A 1333–3300 IU/kg/day (400–1000 µg retinol ester/kg/day) Vitamin D 400–700 IU/kg/day (<1000) Vitamin E 2.2–11 mg/kg/day Vitamin K 4.4–28 µg/kg/day
Strength	Conditional
Certainty of evidence	Low to moderate
Basis for decision	European consensus based on evidence available, physiological needs and prevention of known clinical complications
Subgroup Considerations	Infants <28 weeks or with comorbidities may need higher nutrition intakes.
Implementation Considerations	Availability of specific micronutrients and trained staff to support implementation may vary.
Monitoring and Evaluation	Audit nutritional intakes, biochemical and anthropometric outcomes regularly.
Research Priorities	More data needed on long-term outcomes of specific micronutrient intakes and optimal timing, specifically for iodine, selenium and zinc.

AA 48. Monitoring parameters and equipment/tools: What equipment and monitoring tools i.e. growth charts, are recommended for accurately measuring and monitoring the growth of neonates?

AA.49 What specific growth parameters (e.g. weight, length, head circumference, BMI) should be included in growth monitoring, and how frequently should they be monitored?

Source recommendation		Back to question list	
Source guideline title and developer		Enteral Nutrition in Preterm Infants: ESPGHAN Guidelines 2022, Koletzko et al.	
Existing guidelines recommendation		Length should be measured using a dedicated neonatometer with two fixed perpendicular boards and read to the nearest millimetre. Weight should be measured on calibrated digital electronic scales to the nearest 5 grams. Head circumference should be measured using non-stretchable tape in a standardised fashion. For growth monitoring, the Fenton 2013 or 2025 growth chart is recommended from birth to 50 weeks postmenstrual age. WHO growth standards are recommended after 50 weeks postmenstrual age.	
Year published		2022	
Search updated/assessment of new evidence		No	
Strength of recommendation		Conditional	
Certainty of evidence		Low	
Were EtD and SoF available?		No	
Is the recommendation recent and credible		Yes AGREE II score 67%	
Assessment of suitability for adolopment			
Is the recommendation relevant to local setting (population/ intervention/comparator)?		Yes	
Are the judgements in the source EtD acceptable without modification?		No	
Are any local contextual factors different (e.g. cost, equity, feasibility)?		Yes – a Fenton 2025 growth chart is now available and there needs to be a specification for the frequency of growth monitoring.	
EtD Criterion	Summary of local evidence or context	Judgement	Notes
Problem	Inaccurate or infrequent growth measurements lead to misclassification and missed identification of faltering growth.	Yes	Inconsistent equipment and technique across units.
Desirable effects	Standardised equipment and growth charts improve accuracy and early detection of growth deviations.	Favourable	Supports individualised nutrition planning.
Undesirable effects	Minimal, apart from potential cost of equipment and training. Too much emphasis on weight alone.	Minimal	Benefits outweigh any minor limitations.
Certainty of evidence	Moderate; based on consensus and practice recommendations.	Moderate	High agreement among clinical experts.
Values and	Clinicians and families value accurate growth monitoring as a core indicator of	Aligned	Promotes quality and safety.

preferences	wellbeing.		
Balance of effects	Strongly in favour of using standard tools and growth charts.	Favourable	
Resources required	Needs calibrated scales, neonatometers, and non-stretch tape; widely available but not always used.	Moderate	Additional staff training may be required.
Certainty of resource evidence	Costs of equipment are known. Neonatometer cost is approximately NZ\$540 for preterm size and NZ\$720 for newborn (term) size plus shipping (https://www.ellardinstrumentation.com/lengthboards-stadiometers/).	Moderate	
Cost-effectiveness	No evidence available but avoids costs associated with faltering growth and unnecessary interventions.	Favourable	
Equity	Variability in tool availability and training across neonatal units, especially smaller centres.	Reduced equity	
Acceptability	High – clinicians agree on need for standardised and reliable measurement tools.	High	
Feasibility	Feasible in most units with modest investment in training and equipment.	Yes	
Judgement criteria for EtD			
Decision Type	☐ Adopted as is ☒ Adapted ☐ De novo recommendation required		
Explanation of adaptation	ESPGHAN 2022 recommendations directly apply to our neonatal setting. Recommendation on frequency of monitoring added and updated to include Fenton 2025 growth chart. The additional question about when to stop correcting for gestational age can be answered by the NICE guideline (National Institute for Health and Care Excellence. Developmental follow-up of children and young people born preterm (NICE Guideline NG72). London: NICE; 2017).		
Final Recommendation			
Recommendation statement (adapted)	Measure weight, length and head circumference at least weekly. Use calibrated digital scales (to nearest 5 g), a neonatometer with two perpendicular boards (to nearest mm) and non-stretch tape for head circumference. Apply Fenton 2025 growth charts from birth to 50 weeks postmenstrual age, then switch to WHO standards. Correct for gestational age up to 2 years.		
Strength	Strong		
Certainty of evidence	Moderate		
Basis for decision	Accurate growth monitoring is essential for managing preterm nutrition and wellbeing.		
Subgroup Considerations	Particularly important in very preterm or growth-restricted infants where early deviations have long-term consequences.		
Implementation Considerations	Units should ensure access to standard equipment and train staff in correct technique and use of growth charts.		
Monitoring and Evaluation	Audit compliance with measurement protocols and consistency in chart use.		
Research Priorities	Further research needed on the accuracy of growth tools in extreme prematurity and long-term outcomes based on early monitoring trends.		

AA 50. What are acceptable growth goals for appropriate for gestational age (AGA) and small for gestational age (SGA) infants?

Source recommendation		Back to question list	
Source guideline title and developer		Enteral Nutrition in Preterm Infants: ESPGHAN/ Guidelines 2022, Koletzko et al.	
Existing guidelines recommendation		Regular monitoring of weight, length and HC growth is strongly recommended. Ideally, weight should be measured at least once or twice daily during the first 1–2 weeks, followed by measurements 2–3 times weekly in the stable growing phase. Length and HC should be measured once weekly unless clinical conditions (e.g. hydrocephalus) indicate more frequent monitoring. (Good Practice Point/ expert consensus) After a typical acceptable initial weight loss of 7%–10%, reaching a nadir at days 3–4, nutritional strategies should aim to regain birthweight by 7–10 days of age, followed by growth along a target centile and a gradual transition to the corresponding birth percentile on the WHO postnatal growth chart within the first weeks or months post term. (Good Practice Point/ expert consensus) Nutritional management and growth assessment for infants born in-utero growth restriction and/or SGA should be the same as those born AGA, although initial weight loss is often less and acceptable up to 4%–7% of birthweight. (GOR B recommended) Postnatal growth trajectories (weight, length, and HC) of each infant must be followed and evaluated to ensure nutrition is adequate; ideally using a growth chart based on a large robust dataset. (Good Practice Point/ expert consensus)	
Year published		2022	
Search updated/assessment of new evidence		No	
Strength and direction of recommendation		Recommended	
Certainty of evidence		Moderate	
Were EtD and SoF available?		No	
Is the recommendation recent and credible		Yes AGREE II score: 67%	
Assessment of suitability for adoption			
Is the recommendation relevant to local setting (population/ intervention/comparator)?		Yes	
Are the judgements in the source EtD acceptable without modification?		Yes	
Are any local contextual factors different (e.g. cost, equity, feasibility)?		Yes	
EtD Criterion	Summary of local evidence or context	Judgement	Notes
Problem	Faltering growth is common in preterm SGA infants, but rapid catch-up may lead to long-term metabolic issues.	Yes	Avoid overshooting optimal growth targets.
Desirable effects	Sustainable growth improves neurodevelopment while lowering obesity risk.	Favourable	Balanced growth approach is preferred.

Undesirable effects	Excess weight gain from overfeeding is linked to insulin resistance and metabolic syndrome.	Manageable	Individualised plans help avoid this.
Certainty of evidence	Moderate, mainly based on observational studies and long-term follow-up data.	Moderate	
Values and preferences	Parents prioritise visible growth. Clinicians prefer safe, steady improvement.	Possibly some variability	Clear communication is important.
Balance of effects	Favourable with guided targets avoiding extremes of under- or overgrowth.	Favourable	
Resources required	Close growth monitoring, including weight velocity and possibly body composition.	Moderate	Access varies between units.
Certainty of resource evidence	Low	Resource implications not well quantified.	
Cost-effectiveness	No research available.	Favourable	Cost-effective if long-term chronic disease risks are reduced.
Equity	Growth faltering more likely in populations lacking availability of nutrition support with variable access across the motu (country).	Concern	
Acceptability	Well accepted with appropriate parent education and team consensus.	High	
Feasibility	Feasible with dietetic support and consistent growth tracking protocols.	Yes	
Judgement criteria for EtD			
Decision Type	☒ Adopted as is ☐ Adapted ☐ De novo recommendation required		
Explanation of adaptation	ESPGHAN 2022 guidance on growth goals is adopted with minor modifications. Small changes to wording to define “close to” birth centile as “within 0.8 z-score of birth centile”.		
Final Recommendation			
Recommendation statement (adopted)	Nutritional management and growth assessment for infants born with in-utero growth restriction and/or SGA should be the same as those born AGA, although initial weight loss is often less and acceptable up to 4%–7% of birthweight.		
Strength	Strong		
Certainty of evidence	Moderate		
Basis for decision	Supports safe and sustained growth patterns with better long-term health outcomes.		
Subgroup Considerations	Extremely preterm and SGA infants may require nuanced plans based on clinical complexity.		
Implementation considerations	Requires multidisciplinary input and education to avoid overtreatment.		
Monitoring and Evaluation	Track longitudinal growth and ensure proportionality of weight and length gain.		
Research Priorities	More evidence needed on long-term outcomes of different SGA growth trajectories and best nutrition practices.		

AA 52. Biochemical monitoring to monitor parenteral nutritional adequacy and tolerance. If, why and when should these be measured/monitored and for how long? What are the reference ranges for the neonatal population?

Sodium	Triglycerides	Ammonia
Calcium	Blood urea nitrogen	Alkaline phosphatase
Phosphate	Bicarbonate	Parathyroid hormone
Magnesium	Creatinine	Liver function tests
Potassium	Haemoglobin	Trace elements
Blood gases	Ferritin	Fat-soluble vitamins
Blood glucose	Full blood count (including reticulocytes)	Urinary sodium and phosphate
Blood pH	Albumin and protein	Urinary glucose

Source recommendation		Back to question list
Source guideline title and developer	ESPGHAN 2018 Puntis J, Hojsak I, Ksiazek J, ESPGHAN/ESPEN/ESPR/CSPEN Working Group on Pediatric Parenteral Nutrition. ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: organisational aspects. Clin Nutr 2018;37:2392e400. https://doi.org/10.1016/j.clnu.2018.06.953 and Australasian Paediatric Nutrition guidelines https://link.springer.com/article/10.1186/s12887-020-1958-9	

Existing guidelines recommendation		Laboratory monitoring of parenteral nutrition						
Investigation	Sample	Before starting parenteral nutrition	During parenteral nutrition before clinical and metabolic stabilisation			During parenteral nutrition, during clinical and metabolic stabilisation		
			Once/ 1-2 days	At least once a week	as required	Once/1-2 weeks	Once a month	As required
Sodium	Serum	X	X			X		
Potassium	Serum	X	X			X		
Chloride	Serum	X	X					X

Calcium	Serum	X	X			X		
Phosphorus	Serum	X	X			X		
Magnesium	Serum	X			X	X		
Zinc	Serum				X			X
Blood gases	Capillary	X		X		X		
Glucose	Capillary, whole blood	X	X			X		
Total protein	Serum	X		X		X		
Albumins	Serum	X		X			X	
BUN	Serum	X		X			X	
Creatinine	Serum	X		X			X	
Triglycerides	Serum	X			X			X
Cholesterol	Serum	X			X			X
Bilirubin	Serum	X			X		X	
AST	Serum	X			X		X	
ALT	Serum	X			X		X	
GGTP	Serum	X			X			X
AP	Serum	X			X			X
CBC	WB	X		X		X		
INR	Serum	X			X		X	
CRP	Serum	X			X			X
Vit. B12	Serum				X			X
Fe	Serum				X			X
Ferritin	Serum				X			X
PTH	Serum							X
25OHD3	Serum				X			X
Trace elements: Se, Zn, Cu				X				X
Urine electrolytes	Urine				X			

Biochemical reference ranges and parameters	
Parameter	Neonatal reference range
Sodium	135–145 mmol/L
Potassium	3.5–6.0 mmol/L
Calcium (total/ionised)	2.0–2.7 mmol/L / 1.1–1.3 mmol/L
Phosphate	1.8–3.0 mmol/L
Magnesium	0.65–1.0 mmol/L
Blood glucose	2.6–6.5 mmol/L
Blood gases	pH 7.35–7.45, PaCO ₂ 4.7–6.0 kPa, HCO ₃ 22–26 mmol/L

Blood pH	7.35–7.45
Urinary glucose	Negative
Triglycerides	<2.8 mmol/L (cut-off for reducing lipid infusion)
Blood urea nitrogen (BUN)	1.4–5.0 mmol/L
Bicarbonate	20–26 mmol/L
Creatinine	20–70 µmol/L (varies with GA, higher at birth)
Haemoglobin	140–200 g/L (preterm)
Ferritin	25–200 µg/L
Full Blood Count (FBC)	WBC 5–25 x10 ⁹ /L, Hb 140–200 g/L, Plt >150 x10 ⁹ /L
Reticulocytes	2–6% (higher postnatally if recovering from anaemia)
Albumin / Prealbumin	Albumin: 25–40 g/L; Prealbumin: 100–300 mg/L
Ammonia	<100 µmol/L
Alkaline Phosphatase (ALP)	100–500 U/L (up to 1000 U/L in growth phase)
Parathyroid Hormone (PTH)	1.6–6.9 pmol/L
Liver function tests (LFTs)	ALT <45 U/L, AST <100 U/L, GGT <200 U/L
Conjugated bilirubin	<17 µmol/L
Fat-soluble vitamins (A, D, E, K)	A: 0.7–1.5 µmol/L; D: >50 nmol/L; E: 11–46 µmol/L; K: 0.2–3.2 nmol/L
Trace elements	(e.g. Cu, Zn, Se, Mn) – lab-dependent norms
Transaminases	ALT/AST as part of LFT
Urinary sodium/phosphate	Urinary Na >20 mmol/L suggests adequate intake

Year published	2018
Strength of recommendation	Conditional recommendation
GRADE certainty of evidence	Low to moderate
Were EtD and SoF available?	No
Is the recommendation recent and credible	Yes AGREE II score: 79%
Assessment of suitability for adoption	
Is the recommendation relevant to local setting (population/intervention/comparator)?	Yes
Are the judgements in the source EtD acceptable without modification?	Yes - with some exceptions and adaptations to make the monitoring more preterm rather than paediatric focussed: Phosphate – No We recommend routine monitoring of serum phosphate in preterm infants to reduce the risk of severe hypophosphataemia and refeeding syndrome. Since the publication of the ESPGHAN 2018 Parenteral Nutrition guidelines, there is a growing body of evidence linking hypophosphataemia and refeeding syndrome with clinically important morbidity and increased mortality in preterm infants. Preterm infants—particularly those with birth weight <1500 g or <10th centile for gestational age—are at heightened risk due to limited phosphate stores and rapid anabolic demands during early nutritional rehabilitation. Hypophosphataemia, especially if severe (<0.9 mmol/L) may contribute to metabolic instability, impaired respiratory, cardiac function and adverse neurodevelopmental outcomes.

		In light of emerging evidence, we believe that explicit guidance on phosphate monitoring for high-risk groups should be added to the ESPGHAN 2018 monitoring recommendations to improve safety during early parenteral and enteral nutrition and to reduce preventable complications associated with refeeding. Urea In a Cochrane review comparing higher versus lower amino acid intake in parenteral nutrition, six studies reported urea concentrations. The criteria for abnormal urea differed between the studies and varied from >10 mmol/L to 21 mmol/L. Given the importance of early amino-acid administration in preterm infants, limiting amino acid intake based on serum urea alone is not warranted. Urea levels up to 14 mmol/L may be considered acceptable in infants on parenteral nutrition provided there are no other parameters to suggest protein intolerance (eg hyperammonaemia >122 µmol/L). Triglycerides (link to Question AA 1.6c Are there any indications (e.g. high triglycerides, sepsis) to wean, reduce or restrict parenteral lipid administration?) ESPGHAN 2018 guidelines recommend monitoring of triglycerides in preterm infants and suggest a triglyceride level of 2.8 mmol/L as the upper limit. The monitoring of plasma triglyceride concentrations is not routine in Aotearoa New Zealand neonatal units. A retrospective review from an Australian NICU in which routine triglyceride monitoring was in place showed a hypertriglyceridaemia incidence of 33% in 23–25 weeks and 16% in 26–28 weeks. Severe hypertriglyceridaemia (>4.5 mmol/L) was noted in 10% in 23–25 weeks and 5% in 26–28 weeks. Hypertriglyceridaemia was not associated with mortality or morbidity when adjusted for gestation and birthweight. (Sinclair R, Lui K, Bolisetty S. Hypertriglyceridaemia in extremely preterm infants receiving parenteral lipid emulsions. Presented at 21st Annual Congress of Perinatal Society of Australia and New Zealand; Canberra; 2017 April 2–5.)	
Are any local contextual factors different (e.g. cost, equity, feasibility)?		Access to extended trace element and vitamin testing may be limited in regional centres and requires coordination with tertiary laboratories.	
EtD Criterion	Summary of local evidence or context	Judgement	Notes
Problem	Biochemical derangements may go undetected without structured monitoring during parenteral nutrition.	Yes	
Desirable effects	Early identification and correction of abnormalities improves safety and outcomes.	Favourable	
Undesirable effects	Frequent sampling may cause iatrogenic anaemia and distress for infants and caregivers.	Manageable	Use micro-sampling and rational testing.
Certainty of evidence	Expert consensus and observational data support structured monitoring.	Moderate	
Values and preferences	Clinicians prioritise safety and proactive detection; families expect comprehensive monitoring balanced against invasiveness.	Possibly some variability	
Balance of effects	Favourable benefit–risk ratio for routine structured monitoring.	Favourable	
Resources required	Costs of laboratory tests, staffing, equipment, and access to specialist assays.	Moderate	
Certainty of resource evidence	Based on expert opinion and clinical practice guidelines; direct trial evidence is limited.	Cost evaluations are limited.	
Cost-effectiveness	No studies identified	Likely	
Equity	Rural/low-resource settings may face barriers to full implementation.	Concern	
Acceptability	Monitoring is routine and supported in most NICUs.	High	

Feasibility	Feasible with standard protocols and lab access.	Yes	
Judgement criteria for EtD			
Decision Type	☐ Adopted as is ☒ Adapted ☐ De novo recommendation required		
Explanation of adaptation	The recommendation has been adapted from ESPGHAN 2018 guidance to reflect current evidence or lack thereof, local clinical practice access considerations and to make the monitoring more preterm rather than paediatric focussed. Serum phosphate monitoring recommendations have been added to the ESPGHAN 2018 monitoring recommendations, cholesterol monitoring was removed, urinary sodium increased from >20 to >30 mmol/L and some missing reference ranges were added (LabPlus). ESPGHAN 2018 biochemical reference ranges and parameters are included for reference, but the use of local hospital or LabPlus reference ranges is encouraged.		
Final Recommendation			
Recommendation statement (adapted)	See table below		
Final Recommendation	Adapted tables above. Recommended monitoring for refeeding syndrome For babies with a birthweight <1500 g or <10th centile, monitor serum phosphate and calcium on days 3, 5 and 7 and then alternate days until commenced on fortified breastmilk or preterm formula. Urea Limiting amino acid intake based on serum urea alone is not warranted. Urea levels up to 14 mmol/L may be considered acceptable in infants on parenteral nutrition provided there are no other parameters to suggest protein intolerance (eg hyperammonaemia >122 µmol/L). Triglycerides (<i>link to Question AA 1.6c Are there any indications (e.g. high triglycerides, sepsis) to wean, reduce or restrict parenteral lipid administration?</i>) The routine monitoring of plasma triglyceride concentrations is not recommended.		
Strength	Conditional		
Certainty of evidence	Low to moderate		
Basis for decision	Monitoring supports early intervention and improves parenteral nutrition safety. Although largely based on expert consensus, it reflects established neonatal practice.		
Subgroup Considerations	Extremely preterm or metabolically unstable infants require more intensive and frequent testing; stable or convalescing infants may require reduced frequency.		
Implementation Considerations	Protocols should specify monitoring intervals and available tests. Regional centres may need referral pathways or courier services for specialist assays.		
Monitoring and Evaluation	Audit testing compliance, turnaround time, complication rates and frequency of critical abnormal results to guide practice improvement.		
Research Priorities	Define optimal monitoring frequency; validate predictive biochemical markers of nutrient adequacy and toxicity; evaluate less invasive testing strategies.		

Biochemical monitoring for babies on parenteral nutrition

Investigation	Neonatal reference range	Before clinical and metabolic stabilisation		Once clinically and metabolically stable		
		Every 1–2 days	As required*	Every 1–2 weeks	After one month on PN, then monthly	As required*
Glucose	2.6–6.5 mmol/L	X		X		
Blood gases (capillary)	pH 7.35–7.45, PCO ₂ 4.7–6.0 kPa, HCO ₃ 22–26 mmol/L	X		X		
Sodium	134–148 mmol/L	X		X		
Potassium	4.5–6.0 mmol/L	X		X		
Chloride	90–114 mmol/L	X				X
Calcium	Total 1.8–2.1 mmol/L, Ionised 1.15–1.45 mmol/L	X			X	
Phosphorus	1.8–3.0 mmol/L (<i>see footnote for frequency</i>)	X			X	
Magnesium	0.7–1.0 mmol/L		X			X
Zinc	9–17 µmol/L		X			X
Total protein	45–75 g/L		X			X
Albumin	25–40 g/L		X			X
Urea	1.0–4.0 mmol/L		X			X
Creatinine	<95 µmol/L		X			X
Triglycerides	<3 mmol/L		X			X
Bilirubin (conjugated)	<20 µmol/L		X		X	
AST	<80 U/L		X		X	
ALT	<45 U/L		X		X	
GGT	<150 U/L		X		X	
ALP	80–600 U/L (up to 1000 U/L in growth phase)		X		X	
PTH	1.7–7.3 pmol/L		X		X	
Vitamin A	0.7–1.5 µmol/L (200–800 µg/L)		X		X	
Vitamin B ₁₂	170–800 pmol/L		X		X	
Vitamin D	>50 nmol/L		X		X	
Vitamin E	11–46 µmol/L Starship, 5 – 50 µmol/L Waikato 23–70 µmol/L Christchurch		X		X	
INR	Lab-dependent norm		X		X	
Trace elements: Se, Zn, Cu	Lab-dependent norms					X
C-reactive protein	0–5 mg/L		X			X
Iron	10–31 µmol/L		X			X
Ferritin	15–400 µg/L		X			X
Urine electrolytes	Urinary Na >30 mmol/L adequate for growth					X

AST aspartate aminotransferase, ALT alanine aminotransferase, GGT gamma-glutamyl transferase, ALP alkaline phosphatase, INR International normalised ratio (an elevated INR may indicate vitamin K deficiency), PTH parathyroid hormone, PN parenteral nutrition *no routine monitoring is recommended. Individualised monitoring may be needed based on the clinical situation.

Monitoring for refeeding syndrome: For babies with a birthweight <1,500 g or <10th centile, monitor serum phosphate and calcium on days 3, 5 and 7 and then on alternate days until commenced on fortified breastmilk or preterm formula.

Urea: Limiting amino acid intake based on serum urea alone is not warranted. Urea levels up to 14 mmol/L may be considered acceptable in infants on parenteral nutrition provided there are no other parameters to suggest protein intolerance (e.g. hyperammonaemia >122 µmol/L).

Triglycerides: The routine monitoring of plasma triglyceride concentrations is not recommended.

AA 53. Recommendations for biochemical monitoring of enteral nutritional adequacy for vitamin D, zinc, full blood count, ferritin, sodium, potassium, phosphate, blood glucose, blood urea nitrogen, prealbumin and albumin, conjugated bilirubin, bone mineral status (alkaline phosphatase, calcium, phosphate, vitamin D, parathyroid hormone). Who should be monitored and when (gestational age, birthweight, steroids, short gut syndrome)

Source recommendation Back to question list	
Source guideline title and developer	ESPGHAN 2022 Enteral Nutrition in Preterm Infants (2022) A Position Paper from the ESPGHAN Committee on Nutrition and Invited Experts https://pubmed.ncbi.nlm.nih.gov/36705703/
Existing guidelines recommendation	Zinc Measurement of serum zinc should be considered in preterm infants with growth and low alkaline phosphatase level, especially if they have excessive GI fluid losses. Ferritin Since individual iron status in VLBW infants is highly variable, depending on the number of received blood transfusions and blood losses from phlebotomy, it is recommended to follow these infants with repeated measurements of serum ferritin. Blood urea nitrogen We conditionally recommend monitoring plasma urea concentrations at regular intervals in case standard fortification is insufficient to support desired growth and more protein is added. There are no data that allow conclusive determination of optimal levels, and every baby is unique and clinicians have to individualise and exercise judgment. Bone mineral status: Phosphorus and calcium Regular monitoring of phosphorus and calcium status is recommended.
Year published	2022
Strength of recommendation	Low certainty
GRADE certainty of evidence <i>Conclusions and recommendations were assessed using both the Level of Evidence (LOE) and the Grade of Recommendation (GOR) frameworks, with all achieving greater than 90% expert consensus.</i>	Ferritin and zinc: LOE 4, GOR GPP. Level of evidence is very limited/low level. Grade of recommendation and Good Practice Point indicated no formal evidence, but board expert consensus indicated the recommendation reflects common sense, safe and effective clinical practice. Blood urea and bone mineral status phosphorus and calcium: GOR C, Grade of recommendation is weak/conditional.
Were EtD and SoF available?	No
Is the recommendation recent and credible (e.g. AGREE II >60%)?	Yes AGREE II: 65%
Source recommendation	
Source guideline title and developer	French 2022 Vitamin D and calcium intakes in general paediatric populations: A French expert consensus paper

		https://pubmed.ncbi.nlm.nih.gov/35305879/	
Recommendation		Vitamin D We recommend measurement of 25(OH)D in children born before 32 weeks of gestation or weighing less than 1,500 g at 1 month of age.	
Year published		2022	
Strength of recommendation		Moderate recommendation.	
GRADE certainty of evidence		Grading system applied: American Academy of Paediatrics Graded C – Single or few observation studies or multiple studies with inconsistent findings or major limitations.	
Were EtD and SoF available?		No	
Is the recommendation recent and credible (e.g. AGREE II >60%)?		Yes 90%	
Assessment of suitability for adolopment			
Is the recommendation relevant to local setting (population/ intervention/comparator)?		Yes	
Are the judgements in the source EtD acceptable without modification?		Yes	
Are any local contextual factors different (e.g. cost, equity, feasibility)?		Yes ability to undertake biochemical monitoring may be restricted in some centres by limited resources.	
EtD Criterion	Summary of local evidence or context	Judgement	Notes
Problem	Infants receiving enteral nutrition are vulnerable to nutritional inadequacy which could impair long-term outcomes. Biochemical monitoring guides clinical decisions to improve outcomes.	Yes	Supports high risk populations, that would benefit from improved enteral nutrition.
Desirable effects	Enables management of enteral nutrition adapted to specific infants' requirements.	Favourable	Supports individual infants to thrive based on their unique needs.
Undesirable effects	Repeated blood sampling increases infant discomfort and anaemia risk. Additionally, the workload of staff and expenses increase.	Manageable	Manageable with minimal sampling strategies and coordination in clinical tests.
Certainty of evidence	ESPGHAN 2022: All recommendations achieved greater than 90% expert consensus. Low level certainty. French 2022 Moderate certainty.	Low to Moderate.	
Values and preferences	Clinicians and families value early detection of nutritional issues.	Potential variability	
Balance of effects	Benefits of early detection and prevention outweigh risks of over testing when guided	Favourable	Aligns with international standards.

	by standardise protocols and awareness of the risks.		
Resources required	Requires access to biochemical testing and adequality trained staff.	Moderate	The testing frequency may vary between infants, so ensuring staff that can adapt to these changes.
Certainty of resource evidence	Cost data is available.	Yes	
Cost-effectiveness	Early monitoring may prevent future health complications which lead to longer NICU stays and re-admissions.	Likely	Supported by modelling of improved growth and reduced complication cost.
Equity	Standardised monitoring protocols would contribute to equitable care across gestation ages and ethnic groups, including pēpi Māori and Pacific infants.	Favourable	Reduction in outcome disparities due to inconsistent nutritional surveillance across hospitals.
Acceptability	Clinically and ethically acceptable, families are likely to support as part of routine care.	High	If appropriate staff are available, then it will be no disturbance to infant’s usual care.
Feasibility	For the biochemical markers identified and recommended for monitoring.	Yes	It is not feasible to monitor the other biochemical markers that do not have sufficient evidence behind them. Low resource settings need to be considered for how feasible biochemical monitoring is to implement in these centres.
Judgement criteria for EtD			
Decision Type	☐ Adopted as is ☒ Adapted ☐ De novo recommendation required		
Explanation of adaptation	The ESPGHAN 2022 and French 2022 recommendation wording has been modified to align with the rest of our guidelines and with Aotearoa New Zealand current practice for preterm infants.		
Final Recommendation			
Recommendation statement (adapted)	Biochemical monitoring of enteral nutrition: Zinc: Consider measuring serum zinc in infants with faltering growth and low serum alkaline phosphatase, especially if they have excessive gastrointestinal fluid losses. Urea: Plasma urea concentration can be used to indicate whether standard breastmilk fortification is sufficient to support appropriate growth. More protein may be needed if serum urea is <2.0 mmol/L Bone mineral status: Phosphorus, calcium, ALP and parathyroid hormone status should be monitored regularly Vitamin D: Serum Vitamin D (25-hydroxyvitamin D) should be measured at one month of age in infants born before 32 weeks’ gestation or birthweight <1,500 g. If low, adjust dose and monitor every 10 – 14 days until well into the reference range.		
Strength	Conditional		
Certainty of evidence	Low to moderate		
Basis for decision	Monitoring enables early intervention and enhances the safety of enteral nutrition. Although primarily supported by expert consensus, this recommendation aligns with established neonatal practice.		
Subgroup Considerations	Extremely preterm or severely unwell infants may require case specific changes to the testing they receive, such as reduced frequency of testing.		
Implementation Considerations	Protocols should define recommended monitoring intervals and the available investigations, with established referral or courier pathways to ensure regional access to specialised assays.		

Monitoring and Evaluation	Review compliance with testing protocols, turnaround times, complication rates, and the incidence of critical abnormal results to support quality improvement initiatives.
Research Priorities	Establish evidence-based monitoring levels, identify and validate biochemical markers of nutrient sufficiency and toxicity, and explore less invasive testing methodologies.

EtD = Evidence to Decision framework, SoF = Summary of Findings table, NEC = necrotising enterocolitis, LC-PUFA = Long chain polyunsaturated fatty acids, LOE = *Level of Evidence*, GOR = *Grade of Recommendation*, GPP = *Good Practice Point*.

Appendix J. Research Gaps Prioritised by the Guideline Development Group

Topic 1 – Parenteral Nutrition

1. In preterm infants, studies to determine optimal energy and macronutrient intake for survival, growth and long-term development, including early vs. delayed energy escalation.
2. In moderate-to-late preterm infants, what impact do early nutritional decisions have on exclusive breastmilk feeding at discharge across ethnic groups?
3. In extremely and very preterm infants, studies comparing lower versus higher intravenous fluid volumes in the first week after birth with the following outcomes:
 - Clinical outcomes and neurodevelopment.
 - Feeding outcomes, body composition.
 - Health economic evaluations in Aotearoa New Zealand settings.
4. In preterm infants, studies comparing different cessation thresholds of enteral nutrition volume for stopping parenteral nutrition, including outcomes beyond discharge, including the impact of parenteral nutrition cessation volume on Māori, Pacific and underrepresented groups and cost-effectiveness analyses considering sepsis-related costs and long-term growth and neurodevelopment.
5. In extremely preterm and growth-restricted infants, RCTs to determine optimal dosing for micronutrients with both short term and long term outcomes.
6. In preterm infants, RCTs of individual and combined vitamins in preterm infants (stratified by gestational age), with clinical and long-term neurodevelopmental outcomes, with appropriate pēpi Māori, Pacific families and underrepresented groups representation.

Topic 2 – Enteral Nutrition

1. Investigation of strategies to optimise lactation and reduce early formula use.
2. In moderate-to-late preterm babies, research on whether donor milk vs. infant formula is better for short and long term outcomes.
3. Research to determine the effects of donor breastmilk on clinical outcomes to identify potential benefits (e.g. nutrition/NEC) and risks (e.g. pathogens) for the preterm infant.
4. Research to determine the cost-effectiveness of donor milk vs. infant formula for preterm infants in the Aotearoa New Zealand context and by gestational age group.
5. In preterm infants, RCTs comparing how different feeding initiation strategies in the first 48 hours after birth influence clinical and breastfeeding outcomes.
6. Research to determine the nutritional composition of donor breastmilk compared with preterm mothers' own breastmilk in Aotearoa New Zealand.
7. Research to determine the safety and cost effectiveness of double-screened peer-to-peer unpasteurised donor milk compared with pasteurised donor milk for preterm infants.

Topic 3 – Breastmilk and Breastfeeding

1. In preterm infants, high-quality prospective studies examining the impact of first feed type on long-term breastfeeding outcomes. Implementation studies evaluating structured first-feed protocols on equity and breastfeeding continuation. Qualitative research on maternal experiences and decision-making related to early feeding, with an equity lens.
2. In preterm infants, randomised trials comparing bundled lactation support interventions (timing + frequency + method) including data on whānau Māori experience and effectiveness of culturally adapted lactation support, impact on clinical outcomes like NEC, sepsis and time to full enteral feeds, evaluation of maternal wellbeing and acceptability of different expression regimens, and whānau Māori experiences of the enablers for early, frequent double pumping to be supported.
3. Research into the cost-effectiveness of lactation consultant services in reducing length of stay and improving breastfeeding rates for preterm infants. Explore different models of lactation support delivery (e.g. videos, apps, pamphlets) and barriers to access, uptake and impact on long-term breastfeeding continuation and infant outcomes by ethnicity.

4. Mana-enhancing tikanga practices: Further research into which aspect is the most effective in supporting wāhine Māori to achieve exclusive breastfeeding. Prioritise NICU-specific, Māori-led implementation studies, trials evaluating breastfeeding outcomes in preterm infants, equity-focused research, and work assessing which components of tikanga-aligned breastfeeding support are most effective.

Topic 4 – Monitoring Nutrition and Growth

1. Research on the accuracy of growth measurement tools for extremely preterm infants and whether early growth monitoring and intervention improves long-term outcomes.
2. Research in small for gestational age infants to determine the long-term outcomes of different growth trajectories and the best nutrition practices to improve outcomes for these infants.
3. What faltering growth criteria are associated with adverse outcomes in preterm infants? Does screening for growth faltering in preterm infants reduce morbidity or adverse outcomes?
4. Define optimal biochemical monitoring frequency for parenteral nutrition: validate predictive biochemical markers of nutrient adequacy and toxicity; research to develop and evaluate less invasive testing strategies.

Topic 5 – Whānau Education and Involvement

1. Evaluate specific communication models, test scalable culturally informed interventions, and measure outcomes identified as important by whānau Māori. Studies examining system changes that sustainably support culturally safe neonatal care are also needed.
2. High-quality RCTs that examine early education packages stratified by gestational age and with the inclusion of whānau Māori and Pacific peoples. Studies on delivery methods (in-person, digital, peer-led) and culturally specific approaches. Cost-effectiveness evaluation. Whānau Māori perspectives on what is helpful is essential.
3. High-quality kaupapa Māori research to evaluate the clinical and whānau outcomes of tikanga-based kai practices in NICU, including impacts on breastfeeding and other outcomes, cost implications, equity gains and co-led by Māori.
4. Research directly involving Pacific families of preterm infants, using Pacific research methodologies. Priorities include identifying preferred communication models in NICU/SCBU, evaluating culturally grounded interventions, supporting common values between Pacific Peoples whilst understanding subgroup differences across Pacific Peoples nations, and assessing impacts on feeding, engagement, and clinical outcomes.

Appendix K. Responses to Consultation

The draft Pēpi Whānau Wawe Nutrition Guideline – A National Nutrition Guideline for Preterm Babies was circulated for external review to two international expert external reviewers and to a wide range of professional and community groups. These include the New Zealand Neonatal Network, Royal Australian and New Zealand College of Obstetricians and Gynaecologists, The Royal Australasian College of Physicians (Child Health Subcommittee), Paediatric Society of New Zealand, New Zealand College of Midwives, New Zealand Nurses Organisation, Nurse Practitioners New Zealand, Ngā Maia Māori Midwives Aotearoa, Pasifika Midwives Aotearoa, Midwifery Leaders group, New Zealand Breastfeeding Association, Perinatal Society of Australia and New Zealand, Perinatal Society New Zealand, Health New Zealand and representatives from the Little Miracles Trust and the Carosika Collective. The consultation ran from 25 April to 5 June 2026. The feedback and responses have been summarised below.

Feedback topics	Summary of Comments	Responses	Actions Taken
Overall quality of the guideline	International reviewers and professional organisations consistently described the guideline as comprehensive, evidence-based, methodologically rigorous and clinically relevant. The question-and-answer format, GRADE methodology, implementation sections and focus on equity were particularly praised.	Feedback confirmed that the overall approach, methodology and structure were appropriate.	No major structural changes required. Minor refinements made to improve readability and accessibility.
Breastfeeding, lactation support and mother's own milk	Extensive feedback requested stronger emphasis on breastfeeding, mother's own milk as the preferred nutrition source, specialist neonatal lactation support, overnight expressing, prolonged skin-to-skin care, maternal wellbeing, breastfeeding-centred models of care and identification practical barriers to expressing milk.	Broad agreement that breastfeeding support could be strengthened without changing the underlying recommendations.	Wording strengthened throughout the guideline and implementation sections. Additional implementation guidance included overnight expressing, prolonged skin-to-skin care, maternal barriers to expressing, workforce requirements and specialist neonatal lactation support.
Donor breastmilk	Many stakeholders requested stronger advocacy for equitable access to donor breastmilk across New Zealand and clearer positioning of donor milk as the preferred alternative when mother's own milk is unavailable. Several suggested emphasising donor milk as a bridge to breastfeeding.	Agreed that equity of access should be emphasised while remaining consistent with available evidence.	Recommendation strengthened to support equitable access to donor breastmilk across NICUs and SCBUs. Additional implementation wording added describing donor milk as supporting breastfeeding and improved health outcomes.

Feedback topics	Summary of Comments	Responses	Actions Taken
Role of neonatal dietitians	Several organisations recommended replacing the wording “access to neonatal dietitians” with stronger language specifying embedded neonatal dietitians with recognised neonatal competencies. Respondents also requested greater emphasis on the neonatal dietitian's role in individualising nutrition care for complex infants.	Agreed that “embedded” better reflects safe service provision and reduces inequity.	Recommendation revised to state that neonatal dietitians with ANDiN neonatal nutrition competencies should be embedded within the multidisciplinary neonatal team. Additional implementation guidance describing the neonatal dietitian's role in individualising care was included.
Parenteral nutrition recommendations	Reviewers requested clarification regarding cessation of parenteral nutrition, vitamin recommendations, transition to enteral nutrition and wording that implied cessation at 120 mL/kg/day.	Clarification required rather than changes to recommendations.	Recommendation wording refined to clarify that 120 mL/kg/day represents the minimum enteral volume before considering cessation rather than a mandatory stopping point.
Enteral nutrition recommendations	Feedback addressed feed advancement, fortification thresholds, donor milk, osmolality, continuous versus bolus feeding, protein targets, transition feeding and full feed volumes. Most comments requested clarification or questioned the evidence supporting recommendations.	Recommendations were reviewed against the systematic reviews and Guideline Development Group consensus.	Several explanatory statements were added. Core recommendations remained unchanged where supported by evidence or national consensus.
Vitamin and micronutrient supplementation	Requests were made to clarify vitamin A, D, E and K recommendations, zinc supplementation, vitamin reference ranges, supplementation timing and monitoring.	Clarification was appropriate in several areas.	Explanatory wording added regarding supplementation, fortified feeds, vitamin reference ranges and monitoring. Minor editorial corrections made.
Biochemical monitoring	Respondents suggested inclusion of urinary sodium monitoring, simplification of biochemical monitoring and prioritisation of essential versus extended monitoring.	Considered alongside existing neonatal practice.	Urinary sodium monitoring added. Core monitoring recommendations retained as minimum standards.
Growth monitoring	Comments related to Fenton growth charts, transition to WHO charts, post-discharge growth assessment and management of faltering growth.	Existing recommendations reflected current evidence and consensus.	Minor clarifications made. Most recommendations remained unchanged.

Feedback topics	Summary of Comments	Responses	Actions Taken
Implementation and workforce	Stakeholders consistently identified implementation as the greatest challenge. Key themes included workforce capacity, specialist neonatal dietitians, lactation consultant services, donor milk availability, staff education, whānau education, implementation tools and minimum service standards.	Strong agreement that implementation support required expansion.	Implementation considerations substantially expanded. Additional toolkit resources, educational material and implementation guidance added.
Whānau-centred care, equity and cultural safety	Feedback strongly supported the emphasis on Te Tiriti o Waitangi, whānau-centred care and equity while suggesting further strengthening of manaakitanga, whanaungatanga, breastfeeding support, Māori and Pacific wording and support for families on postnatal wards.	Agreed that implementation guidance could better support equitable care.	Additional implementation recommendations included around whānau participation, culturally appropriate facilities, kai, breastfeeding support and family involvement.
Moderate-to-late preterm infants	Respondents requested clearer definitions, clarification of feeding terminology, greater guidance for babies cared for on postnatal wards and additional implementation support for non-NICU settings.	Clarifications were appropriate. Guidance for babies cared for on postnatal wards and additional implementation support for non-NICU settings were considered beyond the scope of this guideline.	Definitions, terminology and implementation guidance expanded where appropriate.
Implementation tools and educational resources	Numerous stakeholders requested practical implementation tools including flowcharts, anthropometry guidance, feed volume tables, supplementation guides, gastric aspirate algorithms, competency documents, BadgerNet integration, growth chart guidance and education packages.	Many suggestions aligned with planned implementation activities.	A resource toolkit will be available with the guideline.
Editorial and formatting improvements	Respondents identified editorial issues including terminology, hyperlinks, document consistency, recommendation wording, gestational age definitions and formatting.	Agreed.	Editorial corrections made throughout the guideline.
Feedback outside the scope of the guideline	Suggestions included outpatient management, responsiveness to feeding cues, specific supplementation protocols and issues covered by other national guidance.	These were considered but fell outside the agreed scope of the guideline or were addressed in other national projects.	No changes made or issues identified for future guideline updates and research priorities.