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

	parenteral nutrition is titrated down and delays the achievement of recommended nutrient intakes which may have ongoing implications for growth.
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	The title of this question was changed from "*Should fortified expressed breastmilk be commenced before full enteral feeds are established vs. once enteral feeds have been established in preterm* infants " 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.

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[g]	-	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[g]	-	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
○ 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.	

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.	

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.	

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
○	●	○	○	○

References

1. Hilditch, C.; Keir, A.; Collins, C.T.; Middleton, P.; Gomersall, J. Early versus delayed introduction of human milk fortification in enterally fed preterm infants: A systematic review and meta-analysis. *J. Paediatr. Child Health* **2022**, *58*, 30-38, doi:10.1111/jpc.15810.
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