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

	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.
CONFLICT OF INTERESTS:	The following 2019 Cochrane systematic review (Walsh *et al*) 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).

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.

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	⨁⨁◯◯

		Low
Faltering growth/body composition: RCT assessed with: Length gain mm/week	CRITICAL	⨁◯◯◯ Very low
Faltering growth/body composition: RCT assessed with: Head circumference gain mm/week	CRITICAL	⨁⨁◯◯ Lo
Faltering growth/body composition: RCT assessed with: Weight gain from enrollment to 120 days corrected age; g/day	CRITICAL	⨁◯◯◯ Very low
Faltering growth/body composition: RCT assessed with: Rate of length gain from enrolment to 120 days corrected age; mm/day)	CRITICAL	⨁◯◯◯ Very low
Faltering growth/body composition: RCT assessed with: Rate of head circumference gain from enrolment to 120 days corrected age; mm/day)	CRITICAL	⨁◯◯◯ Very low
Time to full enteral feeds - not measured	CRITICAL	-
Duration of initial hospital stay: RCT assessed with: Duration of birth hospitalisation	CRITICAL	⨁◯◯◯ Very low
Bronchopulmonary dysplasia - not measured	CRITICAL	-
Retinopathy of prematurity - not measured	CRITICAL	-
Anaemia of prematurity - not measured	CRITICAL	-
Sepsis: proven or suspected - 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	-
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	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		

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
○	○	○	●	○

References

1. 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.
2. Best, K.P.; Yelland, L.N.; Collins, C.T.; McPhee, A.J.; Rogers, G.B.; Choo, J.; Gibson, R.A.; Murguia-Peniche, T.; Varghese, J.; Cooper, T.R., et al. Growth of late preterm infants fed nutrient-enriched formula to 120 days corrected age-A randomized controlled trial. *Front Pediatr* **2023**, *11*, 1146089, doi:10.3389/fped.2023.1146089.

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