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

CONFLICT OF INTERESTS:	transitioning from parenteral nutrition.

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
○	●	○	○	○

Back to question list