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

	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.
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	**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 enternal 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 enternal 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	

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	

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 with-holding 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
○	●	○	○	○

References

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