Prevention

Evidence to Decision Documents (EtDs)

Features of the Evidence to Decision Document Format

- We have *italicised* the repeated sections across all EtDs: the first paragraph of the background section, as well as the Value and Equity sections.
- Where additional material is included within one of the *italicised* sections with repeated content, it is <u>underlined</u> to indicate this portion is new.
- Each EtD includes a Values section and an Equity section, which contain summaries of information from the respective core documents (see Appendices E, F and section 1.2).
- For 'Desirable' and 'Undesirable' effects, we first interpret where the point estimate lies in relation to the threshold. We then decide how certain we are in that effect, considering where the confidence interval lies in relation to the threshold. This is captured in our overall rating in the ‘Certainty of Evidence’ section. We are careful not to 'double count' the confidence interval by somehow integrating it in our description of the point estimate.
- For the ‘Balance of Effect’ section, we take into account both certainty and the point estimate.

Question 4.

Should delayed cord clamping vs. early cord clamping be used for preventing neonatal hypoglycaemia?	
POPULATION:	Babies at risk of neonatal hypoglycaemia
INTERVENTION:	delayed cord clamping
COMPARISON:	early cord clamping
MAIN OUTCOMES:	- Consideration will be given to the evidence (or lack thereof) for both Māori and non-Māori babies and their whānau. **Critical for making a decision:** 1. Hypoglycaemia (minimum effect size >=20 per 1000 babies) 2. Neurodevelopmental impairment (minimum effect size >=10 per 1000 babies) 3. Admission to special care nursery or neonatal intensive care nursery (minimum effect size >=20 per 1000 babies) 4. Adverse effects (for neonatal mortality minimum effect size >=1 per 1000 babies) 5. Fully breastfeeding at hospital discharge (minimum effect size >=20 per 1000 babies) **Important but not critical:** 1. Separation from the mother for treatment of hypoglycaemia before discharge home (minimum effect size >=20 per 1000 babies) 2. Hypoglycaemic injury on brain imaging (minimum effect size >=10 per 1000 babies) 3. Breastmilk feeding exclusively from birth to hospital discharge (minimum effect size >=20 per 1000 babies) 4. Duration of initial hospital stay (minimum effect size >=0.5 days per baby) 5. Cost (for whānau >=10 NZD per baby, for health system >=100 NZD per baby) **Less important for decision making:** 1. Time to blood glucose normalisation after intervention 2. Receipt of treatment for hypoglycaemia during initial hospital stay 3. Number of episodes of hypoglycaemia 4. Severity of hypoglycaemia 5. Duration of treatment
SETTING:	Any birth settings
PERSPECTIVE:	Clinical recommendation

BACKGROUND:	*Low blood glucose concentrations (hypoglycaemia) are common in newborn babies over the first few days after birth, particularly in those with recognised risk factors (infants of mothers with diabetes, or born preterm, low or high birthweight). Severe or prolonged hypoglycaemia can lead to brain injury, so early detection and treatment is recommended to reduce the risk of later developmental problems.* Waiting to clamp and cut the umbilical cord after birth allows time for the transfer of blood from the placenta to the baby. Delayed cord clamping has been shown to provide a variety of short- and long-term benefits for the baby. These include increased neonatal haemoglobin concentrations, and in preterm babies, decreased incidence of intraventricular haemorrhage, decreased hypotension, increased Apgar scores and decreased mortality. Once the cord is clamped and placental blood supply ceases, the newborn must adjust from dependence on their mother for fuel to initiating endogenous glucose production. Failure to adapt to this sudden interruption of glucose supply when the cord is clamped is the most common reason for neonatal hypoglycaemia. Placental transfusion through delayed cord clamping provides extra blood and may potentially help protect against hypoglycaemia, but there is a paucity of information on this.
CONFLICT OF INTERESTS:	CC, DH, JA JH, JR and LL are authors of cited paper.

ASSESSMENT

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	**Delayed cord clamping compared to early cord clamping results in** (1)**:** • Small reduction in neonatal hypoglycaemia (27 fewer per 1,000) [critical] • Moderate reduction in neurodevelopmental impairment at 12 to 24 months (35 fewer per 1,000) [critical] • Little to no effect on neurodevelopmental impairment at 24 to 48 months [critical] • Little to no effect on admission to special care nursery or neonatal intensive care nursery [critical] • Moderate reduction in neonatal mortality (19 fewer per 1,000) [adverse effects, critical] • Small increase in fully breastfeeding at hospital discharge [critical] • Little to no effect on duration of initial hospital stay [important] There is no data for the following outcomes: separation from the mother for treatment of hypoglycaemia before discharge home, hypoglycaemic injury on brain imaging, breastmilk feeding exclusively from birth to hospital discharge, cost.	**Delayed cord clamping compared to early cord clamping results in** (1) Little to no effect on blood glucose concentration during hospital stay, receipt of treatment for hypoglycaemia during initial hospital stay and severity of hypoglycaemia (1). Half of the studies were conducted in high-income countries, and the other half were conducted in low-income countries. Neonatal mortality reduction, with data predominantly from high-income countries, is observed only for preterm babies, as no events have been reported in term babies.

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with early cord clamping	Risk difference with delayed cord clamping
Hypoglycaemia [critical]	446 (6 RCTs)	⨁◯◯◯ Very low[a,b,c]	**RR 0.87** (0.53 to 1.30)	Study population	
				207 per 1,000	**27 fewer per 1,000** (97 fewer to 62 more)
Neurodevelopmental impairment at 12 to 24 months [critical]	1448 (2 RCTs)	⨁⨁◯◯ Low[a,c]	**RR 0.86** (0.71 to 1.04)	Study population	
				252 per 1,000	**35 fewer per 1,000** (73 fewer to 10 more)
Neurodevelopmental impairment at 24 to 48 months [critical]	673 (2 RCTs)	⨁⨁◯◯ Low[a,c]	**RR 0.97** (0.76 to 1.24)	Study population	
				249 per 1,000	**7 fewer per 1,000** (60 fewer to 60 more)
Admission to special care nursery or neonatal intensive care nursery [critical]	3122 (14 RCTs)	⨁⨁⨁◯ Moderate[a]	**RR 1.08** (0.81 to 1.45)	Study population	
				69 per 1,000	**5 more per 1,000** (13 fewer to 31 more)
Adverse effects-neonatal mortality [critical]	3041 (15 RCTs)	⨁⨁⨁◯ Moderate[a]	**RR 0.73** (0.55 to 0.98)	Study population	
				72 per 1,000	**19 fewer per 1,000** (32 fewer to 1 fewer)

In subgroup analyses, there was no interaction between gestational age (term vs preterm babies) and neonatal hypoglycaemia, neurodevelopmental impairment at 24 to 48 months, fully breastfeeding at hospital discharge, admission to special care nursery or neonatal intensive care nursery and duration of initial hospital stay.

Another systematic review and individual participant meta-analysis found that delayed cord clamping reduced the number of babies <32 weeks' gestation who needed later blood transfusion (13 trials; 2,128 babies; RR, 0.59; 95% CI, 0.47–0.73) (2).

Fully breastfeeding at hospital discharge [critical]	1564 (5 RCTs)	⊕⊕◯◯ Low[a,c]	**RR 1.04** (0.99 to 1.09)	Study population		
				711 per 1,000	**28 more per 1,000** (7 fewer to 64 more)	
Separation from the mother for treatment of hypoglycaemia before discharge home [important] - not measured	-	-	-	-	-	
Hypoglycaemic injury on brain imaging [important] - not measured	-	-	-	-	-	
Breastmilk feeding exclusively from birth to hospital discharge [important] - not measured	-	-	-	-	-	
Duration of initial hospital stay [important]	2082 (15 RCTs)	⊕⊕⊕◯ Moderate[c]	-	The mean duration of initial hospital stay [important	MD **0.19 days lower** (0.59 lower to 0.2 higher)	

					] was **24.5** days	
Cost [important] - not measured	-	-	-	-	-	

a.Downgraded one level of serious risk of bias due to overall moderate quality of this outcome.
b.Downgraded one level of serious indirectness due to variation in the definition of neonatal hypoglycaemia.
c.Downgraded one level for serious imprecision due to the confidence interval including the possibility of benefit and harm.
*Absolute effects were calculated based on the control group risk

Considerations for Māori
No additional data available

Considerations or Pacific
No additional data available

Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	**Considerations for Māori** No additional evidence available **Considerations for Pacific** No additional evidence available	Delayed cord clamping may increase the following risks for preterm babies: • hypothermia on admission (8 trials, 1,995 babies, RR 1.28 (1.06–1.56) (2) • polycythaemia (haematocrit >65%) (13 trials, 2,529 babies, RR 2.65 (1.61-4.37)) (3) • jaundice (mean difference in peak bilirubin +4.43 (1.15 to 7.71) µmol/L, 15 trials, 2,358 babies) (4)

		Most studies did not include babies who needed immediate resuscitation after birth. In cases where babies assigned to delayed cord clamping were deemed to require immediate resuscitation at birth, they frequently did not undergo the intervention, and occasionally, their outcomes were not included in the analysis.

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)
Hypoglycaemia [critical]	CRITICAL	⊕◯◯◯ Very low[a,b,c]
Neurodevelopmental impairment at 12 to 24 months [critical]	CRITICAL	⊕⊕◯◯ Low[a,c]
Neurodevelopmental impairment at 24 to 48 months [critical]	CRITICAL	⊕⊕◯◯ Low[a,c]
Admission to special care nursery or neonatal intensive care nursery [critical]	CRITICAL	⊕⊕⊕◯ Moderate[a]
Adverse effects- neonatal mortality [critical]	CRITICAL	⊕⊕⊕◯ Moderate[a]
Fully breastfeeding at hospital discharge [critical]	CRITICAL	⊕⊕◯◯ Low[a,c]
Separation from the mother for treatment of hypoglycaemia before discharge home [important] - not measured	IMPORTANT	-
Hypoglycaemic injury on brain imaging [important] - not measured	IMPORTANT	-
Breastmilk feeding exclusively from birth to hospital discharge [important] - not measured	IMPORTANT	-

Duration of initial hospital stay [important]	IMPORTANT	⊕⊕⊕◯ Moderate[c]	
Cost [important] - not measured	IMPORTANT	-	

a.Downgraded one level of serious risk of bias due to overall moderate quality of this outcome.
b.Downgraded one level of serious indirectness due to variation in the definition of neonatal hypoglycaemia.
c.Downgraded one level for serious imprecision due to the confidence interval including the possibility of benefit and harm.

Considerations for Māori

No additional evidence available

Considerations for Pacific

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	***Excerpts from Values summary document*** ***Uncertain value, possible variability*** • *Hypoglycaemia [critical]* • *Adverse effect [critical]* ***High value, no important variability*** • *Neurodevelopmental impairment [critical]* • *Fully breastfeeding at hospital discharge [critical]* • *Breastfeeding exclusively from birth to hospital discharge [important]* ***High value, probably no important variability*** • *Admission to special care nursery or neonatal intensive care nursery [critical]* • *Separation from the mother for treatment of hypoglycaemia before discharge home [important]* • *Duration of initial hospital stay [important]* ***Uncertain value and variability*** • *Hypoglycaemic injury on brain imaging [important]*	

	• *Cost [important]*	
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ● Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know	**Delayed cord clamping compared to early cord clamping:** Low certainty evidence showed • Small reduction in neonatal hypoglycaemia [critical] • Moderate reduction in neurodevelopmental impairment at 12 to 24 months [critical] • Little to no effect on neurodevelopmental impairment at 24 to 48 months [critical] • Little to no effect on admission to special care nursery or neonatal intensive care nursery [critical] • Moderate reduction on neonatal mortality [adverse effects, critical] • Small increase in fully breastfeeding at hospital discharge [critical] • Little to no effect on duration of initial hospital stay [important] **Considerations for Māori** No additional evidence available **Considerations for Pacific** No additional evidence available	**Delayed cord clamping compared to early cord clamping may increase the following for preterm babies:** • hypothermia on admission • polycythaemia (haematocrit >65%) • jaundice
Resources required How large are the resource requirements (costs)?"		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The cost of delayed cord clamping itself is generally minimal as it does not involve any expensive equipment or procedures. It simply involves waiting a short period of time before clamping and cutting the umbilical cord, which can be easily incorporated into standard birth practices. However, additional training is necessary for handling preterm babies, involving tasks such as maintaining appropriate warmth, recognising when delayed cord clamping should be reconsidered if the baby requires resuscitation, and securing intravenous access, especially in severely polycythemic preterm babies.	

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 did not do a systematic search for evidence about resource requirements.	

Cost effectiveness
Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ● Probably favors the intervention ○ Favors the intervention ○ Varies ○ No included studies	The need for any additional staffing time or training may be offset by long-term cost savings due to improved health outcomes. Delayed cord clamping may lead to potential cost savings due to its potential to reduce the risk of neonatal mortality in preterm babies.	
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	***Are there groups or settings that might be disadvantaged in relation to the problem or intervention of interest?*** *There is little published literature and therefore it is unclear if there are any groups or settings that might be disadvantaged in relation to the problem or intervention of interest.* ***Are there plausible reasons for anticipating differences in the relative effectiveness of the intervention for disadvantaged groups or settings?*** *There is little published literature. It is unlikely that the effectiveness of interventions would differ for disadvantaged groups or settings. However, within Aotearoa New Zealand, social determinants of health (e.g., colonisation, racism, income, education, employment and housing) are likely to have an impact on the implementation, and therefore the effectiveness, of interventions.* ***Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the intervention for the importance of the problem for disadvantaged groups or settings?*** *Māori babies (190/530, 35.8%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (7). *However, in the Sugar Babies study of 514 babies at risk of neonatal hypoglycaemia in Aotearoa New Zealand, the proportion of babies who*	

	developed hypoglycaemia was similar in Māori babies (79/150, 53%) to that in the whole cohort (260/514, 51%) (8). *Pacific babies (282/693, 40.7%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (7). *In the Sugar Babies study of 514 babies at risk of neonatal hypoglycaemia in Aotearoa New Zealand, the number of Pacific babies was very small, but the proportion who developed hypoglycaemia was similar to that in the whole cohort (6/16, 38% vs 260/514, 51%)* (8). *Asian babies (660/2068, 31.9%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (7). ***Are there important considerations that people implementing the intervention should consider in order to ensure that inequities are reduced, if possible, and that they are not increased?*** ***Consideration for Māori*** *In the Whānau Experience study* (5)*, participants expressed appreciation for the inclusion of prayer, karakia and tikanga before certain interventions.* *Māori are more likely to experience interpersonal, institutional, and structural racism, which requires intentional action on addressing racism within these three levels of racism* (9)(10)(11). *Additionally, a systematic literature review by Graham et al.* (12) *provides a summary of 20 years of data from Whānau Māori experiences in the public health and/or hospital system. A key barrier included perception of racism or discrimination amongst Whānau Māori. For instance, perceiving healthcare professionals to be uninterested in their health and wellbeing. Whānau Māori had good experiences when engaging with Māori healthcare providers when they provided whanaungatanga and were "just so welcoming"* (5). ***Consideration for Pacific*** *Some Pacific women interviewed in the Whānau Experience study reported difficulties with accessing the hospital due to cost, transportation and limited availability with work* (5). ***Other considerations*** *The Ministry of Health identify four priority groups for maternity care. These are Māori, Pacific, younger women (<25 years) and women with disabilities* (6). *Most pregnancy, hospital and well child care is free for Aotearoa New Zealand citizens and other eligible women, but accessing these services may incur costs that are challenging for families with limited resources. In addition, there may be a charge if families use some private or specialist services. In the 2014 Maternity Consumer Survey* (6) *71% of women reported that they had paid for at least one pregnancy-related service. Māori, Pacific and younger women were less likely to have paid for services.*	

Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	A recent study conducted in both private and public practice settings in Australia revealed that midwives strongly advocate for delayed cord clamping to be recognised as the standard procedure (13). Midwives were more likely to discuss cord clamping timing with parents and to clamp the cord later than obstetricians (14). In another recent study conducted in five tertiary hospitals in Saudi Arabia, a majority of midwives and obstetricians believed that delayed cord clamping is advantageous for both term and preterm babies, with potential benefits including enhanced long-term neurological development (15). **Considerations for Māori** No additional evidence available **Considerations for Pacific** 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	In a 2009 survey in Aotearoa New Zealand, 86% of midwives (n = 257; 3.5% Māori; 0.8% Pacific) reported leaving the umbilical cord unclamped for at least 3 minutes after vaginal birth (16) for healthy full-term babies. In an observational study conducted in Aotearoa New Zealand, which included term vaginal births (n=55, ethnicity not reported), the overall median cord clamping time was 3.5 minutes (IQR 2.18 to 5.68 minutes). There was a longer median cord clamping time associated with midwife-facilitated births (4.06 minutes; IQR 2.68–6.65 minutes) compared to obstetrician-facilitated births (2.13 minutes; IQR 1.48–3.28 minutes) (17). Delayed cord clamping is recommended in current international and national guidelines (18)(19)(20)(21). **Considerations for Māori** No additional evidence available	

	Considerations for Pacific 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	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors 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	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors 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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Question 5.

Should skin-to-skin contact vs. no skin-to-skin contact be used for the prevention of neonatal hypoglycaemia?	
POPULATION:	Babies at risk of neonatal hypoglycaemia
INTERVENTION:	skin-to-skin contact
COMPARISON:	no skin-to-skin contact
MAIN OUTCOMES:	- Consideration will be given to the evidence (or lack thereof) for both Māori and non-Māori babies and their whānau. **Critical for making a decision:** 1. Hypoglycaemia (minimum effect size >=20 per 1000 babies) 2. Neurodevelopmental impairment (minimum effect size >=10 per 1000 babies) 3. Admission to special care nursery or neonatal intensive care nursery (minimum effect size >=20 per 1000 babies) 4. Adverse effects (for neonatal mortality minimum effect size >=1 per 1000 babies) 5. Fully breastfeeding at hospital discharge (minimum effect size >=20 per 1000 babies) **Important but not critical:** 1. Separation from the mother for treatment of hypoglycaemia before discharge home (minimum effect size >=20 per 1000 babies) 2. Hypoglycaemic injury on brain imaging (minimum effect size >=10 per 1000 babies) 3. Breastmilk feeding exclusively from birth to hospital discharge (minimum effect size >=20 per 1000 babies) 4. Duration of initial hospital stay (minimum effect size >=0.5 days per baby) 5. Cost (for whānau >=10 NZD per baby, for health system >=100 NZD per baby) **Less important for decision making:** 1. Time to blood glucose normalisation after intervention 2. Receipt of treatment for hypoglycaemia during initial hospital stay 3. Number of episodes of hypoglycaemia 4. Severity of hypoglycaemia 5. Duration of treatment
SETTING:	Any birth settings

PERSPECTIVE:	Clinical recommendation
BACKGROUND:	*Low blood glucose concentrations (hypoglycaemia) are common in newborn babies over the first few days after birth, particularly in those with recognised risk factors (babies of mothers with diabetes, or born preterm, low or high birthweight). Severe or prolonged hypoglycaemia can lead to brain injury, so early detection and treatment are recommended to reduce the risk of later developmental problems.* Skin-to-skin contact between the mother and baby after birth has been demonstrated to promote breastfeeding and parent-infant bonding. Kangaroo Mother Care (KMC) specifically refers to extended skin-to-skin contact (at least 8 hours per day) for preterm and low birthweight babies, in combination with exclusive breastfeeding support. Skin-to-skin contact has been suggested to play a role in preventing neonatal hypoglycaemia, perhaps through encouraging early breastfeeding and/or helping the baby maintain a normal body temperature.
CONFLICT OF INTERESTS:	CC, DH, JA, JH, JR and LL are authors of cited papers.

ASSESSMENT

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	**Skin-to-skin contact compared to no skin-to-skin contact results in or is associated with** (1): • Large reduction in neonatal hypoglycaemia (111 fewer per 1,000) [critical] • Small reduction in admission to special care nursery or neonatal intensive care nursery (24 fewer per 1,000) [critical] • Large increase in fully breastfeeding at hospital discharge (157 more per 1,000) [critical] • Small reduction in the separation from the mother for treatment of hypoglycaemia before discharge home (40 fewer per 1,000) [important] • Large increase in exclusive breastmilk feeding from birth to hospital discharge (324 more per 1,000) [important] • Large reduction in duration of initial hospital stay (2.37 days fewer) [important] • No studies reported the following outcomes: neurodevelopmental impairment, hypoglycaemic injury on brain imaging, cost	**Skin-to-skin contact compared to no skin-to-skin contact results in** (1): • Large reduction in hypothermia (140 fewer per 1,000) • Moderate reduction in hyperthermia (81 fewer per 1,000) • Large increase exclusive breastmilk feeding from discharge to 3 months (205 more per 1,000) and 3 to 6 months (271 more per 1,000) Follow-up of an RCT conducted in Colombia (2) found no overall differences in mean intelligence scores

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 contact	Risk difference with skin-to-skin contact
Hypoglycaemia [critical]	922 (7 RCTs)	⨁⨁◯◯ Low[a,b,c]	**RR 0.32** (0.13 to 0.76)	Study population	
				163 per 1,000	**111 fewer per 1,000** (141 fewer to 39 fewer)
Neurodevelopmental impairment [critical] - not measured	-	-	-		
Admission to special care nursery or neonatal intensive care nursery [critical]	673 (4 RCTs)	⨁◯◯◯ Very low[d,e,f]	**RR 0.85** (0.45 to 1.60)	Study population	
				160 per 1,000	**24 fewer per 1,000** (88 fewer to 96 more)
Fully breastfeeding at hospital discharge [critical]	1341 (10 RCTs)	⨁◯◯◯ Very low[d,g,h]	**RR 1.24** (1.01 to 1.54)	Study population	
				656 per 1,000	**157 more per 1,000** (7 more to 354 more)
Separation from the mother for treatment of hypoglycaemia before discharge home [important]	816 (1 non-randomised study)	⨁⨁◯◯ Low	**OR 0.50** (0.25 to 1.00)	Study population	
				83 per 1,000	**40 fewer per 1,000** (61 fewer to 0 fewer)
Hypoglycaemic injury on brain imaging [important] - not measured	-	-	-	-	-
				Study population	

at 20 years between the adults who received skin-to-skin contact during the neonatal period and those who received standard care (139 participants, mean score 87.5 ± 13.8 vs 125 participants, 88.4 ± 13.9). However, a subgroup of 63 children who were identified as neurologically vulnerable (determined by neurologic examination, no details provided) at 6 months of age showed higher scores in intelligence and attention in adulthood if they had received skin-to-skin contact during the neonatal period. Moreover, young adults who had received skin-to-skin contact during the neonatal period had larger volumes of brain structures associated with intelligence, attention, memory, and coordination compared to those who received standard care (195 participants).

Harrison 2019 (3) found that neonatal skin-to-skin contact could improve learning and autonomic development in 3-month-old babies with complex congenital heart disease (20 participants). They reported increased engagement with a learning task, improved heart rate variability regulation during the task (reduced parasympathetic activation), and greater recovery afterwards (reduced heart rate).

Exclusive breastmilk feeding from birth to hospital discharge [important]	1250 (1 non-randomised study)	⨁⨁⨁◯ Moderate[d,i]	**OR 4.30** (3.19 to 5.81)	465 per 1,000	**324 more per 1,000** (270 more to 370 more)
Duration of initial hospital stay [important]	3437 (31 RCTs)	⨁◯◯◯ Very low[a,c,g,h]	-		MD **2.37 days fewer** (3.66 fewer to 1.08 fewer)
Cost [important] - not measured	-	-	-	-	-

a.Downgraded two levels of very serious risk of bias due to overall low study quality.
b.Downgraded one level for serious indirectness due to the definition of neonatal hypoglycaemia varied.
c.Upgraded one level for large effect.
d.Downgraded one level for serious risk of bias due to overall moderate to low study quality.
e.Downgraded one level for inconsistency due to significant heterogeneity.
f.Downgraded one level for serious imprecision due to the confidence interval including the possibility of benefit and harm.
g.Downgraded two levels for very serious inconsistency due to unexplained substantial heterogeneity.
h.Downgraded one level for publication bias due to asymmetry in the funnel plot.
i.Upgraded two levels for very large effect.
*Absolute effects were calculated based on the control group risk

Considerations for Māori
No additional data available
Considerations for Pacific
No additional data available

Study setting
Most of these studies (1) were conducted in low-, lower-middle- or upper-middle-income countries, limiting the relevance of findings to Aotearoa New Zealand. In high-income countries, two studies assessed neonatal hypoglycaemia and three assessed duration of initial hospital stay. In these studies, no difference in outcome was seen between the skin-to-skin and control groups. The one study assessing exclusive breastmilk feeding from birth to discharge was conducted in a high-income country.

Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Two studies found no difference in frequency (4)(5) or severity (5) of adverse events (apnoea (stopping breathing), desaturation (low blood oxygen) and regurgitation) in the skin-to-skin group compared to the control. Skin-to-skin contact has been identified as a potential risk factor for sudden unexpected postnatal collapse, which can lead to developmental problems in childhood or death (6)(7) However, only two cases were identified from 62,968 apparently healthy term babies (0.003%) (6). The authors concluded this rare potential complication does not outweigh the many benefits of skin-to-skin contact but highlights the need for monitoring babies during skin-to-skin contact.	

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 contact	Risk difference with skin-to-skin contact
Adverse effects [critical]	0 (2 RCTs)	⨁⨁◯◯ Low[a,b]	-	Two RCTs (n=151 babies) reported that the frequency of adverse events, including apnoea, desaturations and regurgitations were no different between the two groups.	

a.Downgraded one level for serious risk of bias due to overall moderate to low study quality.
b.Downgraded one level for imprecision due to no numbers being reported.

Considerations for Māori

No additional data available

Considerations for Pacific

No additional data 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)
Hypoglycaemia [critical]	CRITICAL	⨁⨁◯◯ Low[a,b,c]
Neurodevelopmental impairment [critical] - not measured	CRITICAL	-

Admission to special care nursery or neonatal intensive care nursery [critical]	CRITICAL	⨁◯◯◯ Very low[d,e,f]
Adverse effects [critical]	CRITICAL	⨁⨁◯◯ Low[d,g]
Fully breastfeeding at hospital discharge [critical]	CRITICAL	⨁◯◯◯ Very low[d,h,i]
Separation from the mother for treatment of hypoglycaemia before discharge home [important]	CRITICAL	⨁⨁◯◯ Low
Hypoglycaemic injury on brain imaging [important] - not measured	IMPORTANT	-
Exclusive breastmilk feeding from birth to hospital discharge [important]	IMPORTANT	⨁⨁⨁◯ Moderate[d,j]
Duration of initial hospital stay [important]	IMPORTANT	⨁◯◯◯ Very low[a,c,h,i]
Cost [important] - not measured	IMPORTANT	-

a.Downgraded two levels of very serious risk of bias due to overall low study quality.
b.Downgraded one level for serious indirectness due to the definition of neonatal hypoglycaemia varied.
c.Upgraded one level for large effect.
d.Downgraded one level for serious risk of bias due to overall moderate to low study quality.
e.Downgraded one level for inconsistency due to significant heterogeneity.
f.Downgraded one level for serious imprecision due to the confidence interval including the possibility of benefit and harm.
g.Downgraded one level for imprecision due to no numbers being reported.
h.Downgraded two levels for very serious inconsistency due to unexplained substantial heterogeneity.
i.Downgraded one level for publication bias due to asymmetry in the funnel plot.
j.Upgraded two levels for very large effect.

Considerations for Māori

No additional data available

Considerations for Pacific

No additional data 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	***Excerpts from Values summary document*** ***Uncertain value, possible variability*** • *Hypoglycaemia [critical]* • *Adverse effect [critical]* ***High value, no important variability*** • *Neurodevelopmental impairment [critical]* • *Fully breastfeeding at hospital discharge [critical]* • *Breastfeeding exclusively from birth to hospital discharge [important]* ***High value, probably no important variability*** • *Admission to special care nursery or neonatal intensive care nursery [critical]* • *Separation from the mother for treatment of hypoglycaemia before discharge home [important]* • *Duration of initial hospital stay [important]* ***Uncertain value and variability*** • *Hypoglycaemic injury on brain imaging [important]* • *Cost [important]*	
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ● Favors the intervention ○ Varies ○ Don't know	**Skin-to-skin contact compared to no skin-to-skin contact results in or is associated with** • Low certainty evidence showed • Large reduction in neonatal hypoglycaemia • Uncertain effect on admission to special care nursery or neonatal intensive care nursery • Large increase in fully breastfeeding at hospital discharge • Small reduction in the separation from the mother for treatment of hypoglycaemia before discharge home • Large increase in exclusive breastmilk feeding from birth to hospital discharge • Large reduction in the duration of initial hospital stay **Considerations for Māori** No additional data available **Considerations for Pacific** No additional data available	**Skin-to-skin contact compared to other treatment may result in** • Large reduction in hypothermia • Moderate reduction in hyperthermia • Large increase in exclusive breastmilk feeding from discharge to 3 months and 3 to 6 months
Resources required How large are the resource requirements (costs)?"		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	We did not do a systematic search for evidence about resource requirements. Skin-to-skin contact does not require any specific equipment, so the resources required are the training of health professionals and the time taken to educate parents and implement skin-to-skin. In the UK, the costs of establishing a program implementing skin-to-skin contact came from training staff and paying support staff to run the program, rather than any costs directly related to skin-to-skin contact (8).	
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 uncertain about the cost of staff time.	
Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ● Probably favors the intervention ○ Favors the intervention ○ Varies ○ No included studies	Lowson conducted an economic evaluation of a skin-to-skin program implemented in 18 UK neonatal units and found that skin-to-skin contact saved at least GBP £7.40 for every £1 invested due to reduced duration of hospital stay and reduced morbidity (8).	
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	***Are there groups or settings that might be disadvantaged in relation to the problem or intervention of interest?*** *There is little published literature and therefore it is unclear if there are any groups or settings that might be disadvantaged in relation to the problem or intervention of interest.* ***Are there plausible reasons for anticipating differences in the relative effectiveness of the intervention for disadvantaged groups or settings?*** *There is little published literature. It is unlikely that the effectiveness of interventions would differ for disadvantaged groups or settings. However, within Aotearoa New Zealand, social determinants of health (e.g., colonisation, racism, income, education, employment and*	

	housing) are likely to have an impact on the implementation, and therefore the effectiveness, of interventions. ***Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the intervention for the importance of the problem for disadvantaged groups or settings?*** *Māori babies (190/530, 35.8%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (11)*. However, in the Sugar Babies study of 514 babies at risk of neonatal hypoglycaemia in Aotearoa New Zealand, the proportion of babies who developed hypoglycaemia was similar in Māori babies (79/150, 53%) to that in the whole cohort (260/514, 51%)* (12)*.* *Pacific babies (282/693, 40.7%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (11)*.* *In the Sugar Babies study of 514 babies at risk of neonatal hypoglycaemia in Aotearoa New Zealand, the number of Pacific babies was very small, but the proportion who developed hypoglycaemia was similar to that in the whole cohort (6/16, 38% vs 260/514, 51%)* (12). *Asian babies (660/2068, 31.9%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (11). ***Are there important considerations that people implementing the intervention should consider in order to ensure that inequities are reduced, if possible, and that they are not increased?*** ***Consideration for Māori*** *In the Whānau Experience study* (9)*, participants expressed appreciation for the inclusion of karakia and tikanga before certain interventions.* *Māori are more likely to experience interpersonal, institutional, and structural racism, which requires intentional action on addressing racism within these three levels of racism* (13)(14)(15)*.* *Additionally, a systematic literature review by Graham et al.* (16) *provides a summary of 20 years of data from whānau Māori experiences in the public health and/or hospital system. A key barrier included perception of racism or discrimination amongst whānau Māori. For instance, perceiving healthcare professionals to be uninterested in their health and wellbeing. Whānau Māori had good experiences when engaging with Māori healthcare providers when they provided whanaungatanga and were "just so welcoming"* (16) ***Consideration for Pacific*** *Some Pacific women interviewed in the Whānau Experience study reported difficulties with accessing the hospital due to cost, transportation and limited availability with work* (9)*.* ***Other considerations***	

	The Ministry of Health identify four priority groups for maternity care. These are Māori, Pacific, younger women (<25 years) and women with disabilities (10)*. Most pregnancy, hospital and well child care is free for Aotearoa New Zealand citizens and other eligible women, but accessing these services may incur costs that are challenging for families with limited resources. In addition, there may be a charge if families use some private or specialist services. In the 2014 Maternity Consumer Survey* (10)*, 71% of women reported that they had paid for at least one pregnancy-related service. Māori, Pacific and younger women were less likely to have paid for services.*	
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 Whāunua Experience study (9), all mothers believed "skin-to-skin" and holding baby to the breast was the best way to comfort the child during the testing for neonatal hypoglycaemia. Some parents who were not offered the opportunity to support their child would have valued having the choice. **Considerations for Māori** Whānau Māori valued being offered skin-to-skin contact and then supported to breastfeed their pēpi during testing. All of these women believed that skin-to-skin by holding baby to their breast was the most effective way to soothe the baby. **Considerations for Pacific** Some Pacific mothers express a desire to hold their babies at the breast for early and continuous feeding to address concerns about potential hypoglycaemia	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies	Skin-to-skin contact is a routine practice in Aotearoa New Zealand. Kangaroo care is encouraged and practised in many hospitals and birthing centres as part of postnatal care. **Considerations for Māori** No additional data available **Considerations for Pacific**	

○ Don't know	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			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors 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	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors 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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Question 6.

Should thermal care vs. routine care be used for prevention of neonatal hypoglycaemia?

POPULATION:	Babies at risk of neonatal hypoglycaemia
INTERVENTION:	thermal care
COMPARISON:	routine care
MAIN OUTCOMES:	- Consideration will be given to the evidence (or lack thereof) for both Māori and non-Māori babies and their whānau. **Critical for making a decision:** 1. Hypoglycaemia (minimum effect size >=20 per 1000 babies) 2. Neurodevelopmental impairment (minimum effect size >=10 per 1000 babies) 3. Admission to special care nursery or neonatal intensive care nursery (minimum effect size >=20 per 1000 babies) 4. Adverse effects (for neonatal mortality minimum effect size >=1 per 1000 babies) 5. Fully breastfeeding at hospital discharge (minimum effect size >=20 per 1000 babies) **Important but not critical:** 1. Separation from the mother for treatment of hypoglycaemia before discharge home (minimum effect size >=20 per 1000 babies) 2. Hypoglycaemic injury on brain imaging (minimum effect size >=10 per 1000 babies) 3. Breastmilk feeding exclusively from birth to hospital discharge (minimum effect size >=20 per 1000 babies) 4. Duration of initial hospital stay (minimum effect size >=0.5 days per baby) 5. Cost (for whānau >=10 NZD per baby, for health system >=100 NZD per baby) **Less important for decision making:** 1. Time to blood glucose normalisation after intervention 2. Receipt of treatment for hypoglycaemia during initial hospital stay 3. Number of episodes of hypoglycaemia 4. Severity of hypoglycaemia 5. Duration of treatment
SETTING:	Any birth settings
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	*Low blood glucose concentrations (hypoglycaemia) are common in newborn babies over the first few days after birth, particularly in those with recognised risk factors (baby of mothers with diabetes, or born preterm, low or high birthweight). Severe or prolonged hypoglycaemia can lead to brain injury, so early detection and treatment is recommended to reduce the risk of later developmental problems.*

	Thermal care is an essential component of newborn care. It is a high-impact intervention that helps ensure the functional integrity of various neonatal biological systems. Since thermoregulation requires energy, low or decreasing body temperature may result in lower blood glucose concentrations. This means that thermal care may play a role in preventing neonatal hypoglycaemia. The intervention aimed at maintaining warmth typically involves a) applying barriers to heat loss on various body parts after birth, such as plastic bags, caps, or wraps; b) use external heat sources like skin-to-skin contact or heated/gel/chemical mattresses (1). For skin-to-skin contact, please refer to the skin-to-skin EtD.
CONFLICT OF INTERESTS:	DH, JA, JH, JR and LL are authors of cited papers.

ASSESSMENT

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	**Preterm/ low birthweight babies** Plastic bag/ wrap vs routine care (1) • Moderate reduction in hypoglycaemia (72 fewer per 1,000) [critical] • Large reduction in the duration of initial hospital stay (6.35 days lower) [important] Thermal mattress, thermal nest or thermal blanket: vs routine care (1)(2)(3)(4) • Little to no effect on hypoglycaemia [critical] • Moderate reduction in mortality (14 fewer per 1,000) [adverse effects, critical] • Large reduction in the duration of initial hospital stay (5 days lower) [important] **Term babies** Delaying bathing by at least 6 hours compared to early bathing (5) • Small reduction in hypoglycaemia (30 fewer per 1,000) [critical] • Small increase in fully breastfeeding at hospital discharge (44 more per 1,000) [critical] No studies reported any other critical or important outcomes.	**Preterm/ low birthweight babies** Plastic bag/ wrap vs routine care (1) • Little to no effect on initial blood glucose concentration • Large reduction in hypothermia on admission to NICU (244 fewer per 1,000) Thermal mattress vs routine care (1) • May increase core body temperature on admission to NICU (0.65 °C higher) • Large reduction in moderate hypothermia (<36°C) on admission to NICU (413 fewer per 1,000) A network meta-analysis (6) showed plastic bag and wrap were equally effective at maintaining

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with routine care	Risk difference with thermal care
Plastic wrap or bag: hypoglycaemia (Preterm/LBW) [critical]	389 (3 RCTs)	⊕⊕⊕◯ Moderate[a]	**RR 0.70** (0.47 to 1.03)	Study population	
				240 per 1,000	**72 fewer per 1,000** (127 fewer to 7 more)
Plastic wrap or bag: duration of initial hospital stay (Preterm/LBW) [important]	126 (2 RCTs)	⊕⊕◯◯ Low[b]	-	The mean plastic wrap or bag: duration of initial hospital stay (Preterm/LBW) [important] ranged from **46.6** days	MD **6.35 days lower** (17.37 lower to 4.56 higher)
Thermal mattress: hypoglycaemia (Preterm/LBW) [critical]	102 (1 RCT)	⊕◯◯◯ Very low[b,c]	**RR 1.02** (0.47 to 2.18)	Study population	
				204 per 1,000	**4 more per 1,000** (108 fewer to 241 more)
Thermal mattress: mortality (Preterm/LBW) [critical]	102 (1 RCT)	⊕◯◯◯ Very low[b,c]	**RR 0.31** (0.01 to 7.40)	Study population	
				20 per 1,000	**14 fewer per 1,000** (20 fewer to 131 more)
Thermal mattress: duration of initial hospital stay (Preterm/LBW) [important]	102 (1 RCT)	⊕◯◯◯ Very low[b]	-	The mean thermal mattress: duration of initial hospital stay (Preterm/LBW) [important] was **54** days	MD **5 days lower** (17.27 lower to 7.27 higher)
Thermal mattress, thermal nest or thermal blanket:	301 (2 RCTs)	⊕⊕◯◯ Low[c,d]	**RR 1.01** (0.60 to 1.71)	Study population	
				329 per 1,000	**3 more per 1,000**

body temperature. The plastic bag or wrap with thermal mattress was the most beneficial intervention for body temperature compared to routine care.

Term babies

Delaying bathing by at least 24 hours compared to early bathing (5)

- Moderate reduction in hypothermia (61 fewer per 1,000)

A study found no difference between cotton swaddling, aluminium coated fabric and a combination of the two in preventing hypothermia and hypoglycaemia when transferring the baby from the delivery room to the nursery (7).

A systematic review found that maternal warming during caesarean section with warmed air or fluid compared to no warmed air or fluid is likely to result in little to no effect on neonatal body temperature (8).

hypoglycaemia (Preterm/LBW) [critical]					(132 fewer to 233 more)
Early vs delayed bathing (6 hours): hypoglycaemia (Term) [critical]	2775 (3 non-randomised studies)	⊕◯◯◯ Very low[e]	**OR 0.39** (0.23 to 0.66)	Study population	
				49 per 1,000	**30 fewer per 1,000** (38 fewer to 16 fewer)
Early vs delayed bathing (6 hours): fully breastfeeding at hospital discharge (Term) [critical]	6768 (6 non-randomised studies)	⊕◯◯◯ Very low[e]	**OR 1.20** (1.08 to 1.34)	Study population	
				584 per 1,000	**44 more per 1,000** (19 more to 69 more)

a.Downgraded one level for serious indirectness due to large variations in the types of intervention.
b.Downgraded two levels for very serious imprecision due to wide confidence interval and small sample size.
c.Downgraded one level for serious risk of bias due to overall moderate to low quality of the included study (studies).
d.Downgraded one level for serious imprecision due to the confidence interval including the possibility of benefit and harm.
e.Downgraded two levels for very serious risk of bias due to overall low quality of the included study (studies).
*Absolute effects were calculated based on the control group risk

Considerations for Māori

No additional data available

Considerations for Pacific

No additional data available

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	**Preterm/ low birthweight babies** Plastic bag/ wrap compared to routine care (1) • Small increase in hyperthermia on admission to NICU (34 more per 1,000) [adverse effects, critical] Thermal mattress, thermal nest or thermal blanket vs routine care (1)(2)(3)(4) • Uncertain effect on hyperthermia (no events occurred in most groups) [adverse effects, critical] • No skin reactions with thermal mattress or thermal blanket [adverse effects, critical] **Term babies** No studies reported any other critical or important outcomes.	

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with routine care	Risk difference with thermal care
Plastic wrap or bag: hyperthermia on admission to NICU (Preterm/LBW) [critical]	1523 (12 RCTs)	⨁⨁⨁◯ Moderate[a]	**RR 3.91** (2.05 to 7.44)	Study population	
				12 per 1,000	**34 more per 1,000** (12 more to 75 more)
Thermal mattress: hyperthermia (Preterm/LBW) [critical]	126 (2 RCTs)	⨁◯◯◯ Very low[b,c]	**RR 4.63** (0.23 to 94.10)	Study population	
				0 per 1,000	**0 fewer per 1,000** (0 fewer to 0 fewer)

a.Downgraded one level for imprecision due to small event rate.
b.Downgraded one level for serious risk of bias due to overall moderate to low quality of the included study (studies).
c.Downgraded two levels for very serious imprecision due to wide confidence interval and small sample size.
*Absolute effects were calculated based on the control group risk

Considerations for Māori
No additional data available

Considerations for Pacific
No additional data 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)**	
	Plastic wrap or bag: hypoglycaemia (Preterm/LBW) [critical]	CRITICAL	⨁⨁⨁◯ Moderate[a]	
	Plastic wrap or bag: duration of initial hospital stay (Preterm/LBW) [important]	IMPORTANT	⨁⨁◯◯ Low[b]	
	Plastic wrap or bag: hyperthermia on admission to NICU (Preterm/LBW) [critical]	CRITICAL	⨁⨁⨁◯ Moderate[c]	
	Thermal mattress: hypoglycaemia (Preterm/LBW) [critical]	CRITICAL	⨁◯◯◯ Very low[b,d]	
	Thermal mattress: hyperthermia (Preterm/LBW) [critical]	NOT IMPORTANT	⨁◯◯◯ Very low[b,d]	
	Thermal mattress: mortality (Preterm/LBW) [critical]	CRITICAL	⨁◯◯◯ Very low[b,d]	
	Thermal mattress: duration of initial hospital stay (Preterm/LBW) [important]	IMPORTANT	⨁◯◯◯ Very low[b]	
	Thermal mattress, thermal nest or thermal blanket: hypoglycaemia (Preterm/LBW) [critical]	CRITICAL	⨁⨁◯◯ Low[d,e]	
	Early vs delayed bathing (6 hours): hypoglycaemia (Term) [critical]	CRITICAL	⨁◯◯◯ Very low[f]	
	Early vs delayed bathing (6 hours): fully breastfeeding at hospital discharge (Term) [critical]	CRITICAL	⨁◯◯◯ Very low[f]	

	a.Downgraded one level for serious indirectness due to large variations in the types of intervention. b.Downgraded two levels for very serious imprecision due to wide confidence interval and small sample size. c.Downgraded one level for imprecision due to small event rate. d.Downgraded one level for serious risk of bias due to overall moderate to low quality of the included study (studies). e.Downgraded one level for serious imprecision due to the confidence interval including the possibility of benefit and harm. f.Downgraded two levels for very serious risk of bias due to overall low quality of the included study (studies). **Considerations for Māori** No additional data available **Considerations for Pacific** No additional data 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	***Excerpts from Values summary document*** ***Uncertain value, possible variability*** • *Hypoglycaemia [critical]* • *Adverse effect [critical]* ***High value, no important variability*** • *Neurodevelopmental impairment [critical]* • *Fully breastfeeding at hospital discharge [critical]* • *Breastfeeding exclusively from birth to hospital discharge [important]* ***High value, probably no important variability*** • *Admission to special care nursery or neonatal intensive care nursery [critical]* • *Separation from the mother for treatment of hypoglycaemia before discharge home [important]* • *Duration of initial hospital stay [important]* ***Uncertain value and variability***	

	• *Hypoglycaemic injury on brain imaging [important]* • *Cost [important]*	
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ● Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know	Very low certainty evidence showed **Preterm/ low birthweight babies** <u>Plastic bag/ wrap compared to routine care</u> • Moderate reduction in hypoglycaemia [critical] • Large reduction in the duration of initial hospital stay [important] • Small increase in hyperthermia on admission to NICU [adverse effects, critical] • Little to no effect on initial blood glucose concentration • Large reduction in hypothermia on admission to NICU <u>Thermal mattress thermal nest or thermal blanket compared to routine care</u> • Little to no effect on hypoglycaemia [critical] • Uncertain effect on duration of initial hospital stay [important] • Uncertain effect on hyperthermia [adverse effects, critical] • Uncertain effect on mortality [adverse effects, critical] • No skin reactions with thermal mattress or thermal blanket [adverse effects, critical] • May increase core body temperature on admission to NICU • Large reduction in moderate hypothermia on admission to NICU **Term babies** <u>Delaying bathing by at least 6 hours compared to early bathing is associated with</u> • Uncertain effect on hypoglycaemia [critical] • Uncertain effect on fully breastfeeding at hospital discharge [critical] <u>Delaying bathing by at least 24 hours compared to early bathing is associated with</u> • Moderate reduction in hypothermia **Considerations for Māori** No additional data available **Considerations for Pacific** No additional data available	

Resources required How large are the resource requirements (costs)?"		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The plastic “Neo-wraps” used in Aotearoa New Zealand cost NZ$36 for a box of ten. The “TransWarmer” gel thermal mattresses used in Aotearoa New Zealand cost NZ$100 each.	
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 reasonably certain about the cost of the Neo-wraps and TransWarmer mattress as they are being used in Aotearoa New Zealand.	
Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ● Probably favors the intervention ○ Favors the intervention ○ Varies ○ No included studies	No information was found on the cost-effectiveness of the interventions.	
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	***Are there groups or settings that might be disadvantaged in relation to the problem or intervention of interest?*** *There is little published literature and therefore it is unclear if there are any groups or settings that might be disadvantaged in relation to the problem or intervention of interest.* ***Are there plausible reasons for anticipating differences in the relative effectiveness of the intervention for disadvantaged groups or settings?*** *There is little published literature. It is unlikely that the effectiveness of interventions would differ for disadvantaged groups or settings. However, within Aotearoa New Zealand, social determinants of health (e.g., colonisation, racism, income, education, employment and housing) are likely to have an impact on the implementation, and therefore the effectiveness, of interventions.* ***Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the intervention for the importance of the problem for disadvantaged groups or settings?*** *Māori babies (190/530, 35.8%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (11). *However, in the Sugar Babies study of 514 babies at risk of neonatal hypoglycaemia in Aotearoa New Zealand, the proportion of babies who developed hypoglycaemia was similar in Māori babies (79/150, 53%) to that in the whole cohort (260/514, 51%)* (12). *Pacific babies (282/693, 40.7%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (11).	

	In the Sugar Babies study of 514 babies at risk of neonatal hypoglycaemia in Aotearoa New Zealand, the number of Pacific babies was very small, but the proportion who developed hypoglycaemia was similar to that in the whole cohort (6/16, 38% vs 260/514, 51%) (12). *Asian babies (660/2068, 31.9%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (11). ***Are there important considerations that people implementing the intervention should consider in order to ensure that inequities are reduced, if possible, and that they are not increased?*** ***Consideration for Māori*** *In the Whānau Experience study* (9)*, participants expressed appreciation for the inclusion of karakia and tikanga before certain interventions.* *Māori are more likely to experience interpersonal, institutional, and structural racism, which requires intentional action on addressing racism within these three levels of racism* (13)(14)(15). *Additionally, a systematic literature review by Graham et al.* (16) *provides a summary of 20 years of data from Whānau Māori experiences in the public health and/or hospital system. A key barrier included perception of racism or discrimination amongst whānau Māori. For instance, perceiving healthcare professionals to be uninterested in their health and wellbeing. Whānau Māori had good experiences when engaging with Māori healthcare providers when they provided whanaungatanga and were "just so welcoming"* (16). ***Consideration for Pacific*** *Some Pacific women interviewed in the Whānau Experience study reported difficulties with accessing the hospital due to cost, transportation and limited availability with work* (9). ***Other considerations*** *The Ministry of Health identify four priority groups for maternity care. These are Māori, Pacific, younger women (<25 years) and women with disabilities* (10). *Most pregnancy, hospital and well child care is free for Aotearoa New Zealand citizens and other eligible women, but accessing these services may incur costs that are challenging for families with limited resources. In addition, there may be a charge if families use some private or specialist services. In the 2014 Maternity Consumer Survey* (10)*, 71% of women reported that they had paid for at least one pregnancy-related service. Māori, Pacific and younger women were less likely to have paid for services.*	
Acceptability Is the intervention acceptable to key stakeholders?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Two studies, conducted in Mexico and Canada, found that the use of plastic wrap was acceptable to neonatal staff (17)(18). Three studies reported that plastic wrap did not interfere with resuscitation (19)(20)(17), whilst two found that resuscitation affected the placement of the wrap (21)(22). Measuring oxygen saturation and body temperature was more challenging for babies in the plastic wrap. Little evidence was available on other interventions, but delayed bathing was suggested to be unacceptable to women in rural Uganda, due to the baby's perceived 'dirtiness' or 'vulnerability' (23). **Considerations for Māori** No additional data available **Considerations for Pacific** No additional 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 Neo-Wrap and TransWarmer mattress are currently used in Aotearoa New Zealand. The use of plastic wraps is feasible in Aotearoa New Zealand as they are already recommended in the Starship Guidelines for use in babies <32 weeks gestation for preventing hypothermia (24). **Considerations for Māori** No additional data available **Considerations for Pacific** 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			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors 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	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors 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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Question 7.

Should early feeding vs. delayed feeding be used for the prevention of neonatal hypoglycaemia?	
POPULATION:	Newborn babies at risk of neonatal hypoglycaemia
INTERVENTION:	early feeding
COMPARISON:	delayed feeding

MAIN OUTCOMES:	- Consideration will be given to the evidence (or lack thereof) for both Māori and non-Māori babies and their whānau. **Critical for making a decision:** 1. Hypoglycaemia (minimum effect size >=20 per 1000 babies) 2. Neurodevelopmental impairment (minimum effect size >=10 per 1000 babies) 3. Admission to special care nursery or neonatal intensive care nursery (minimum effect size >=20 per 1000 babies) 4. Adverse effects (for neonatal mortality minimum effect size >=1 per 1000 babies) 5. Fully breastfeeding at hospital discharge (minimum effect size >=20 per 1000 babies) **Important but not critical:** 1. Separation from the mother for treatment of hypoglycaemia before discharge home (minimum effect size >=20 per 1000 babies) 2. Hypoglycaemic injury on brain imaging (minimum effect size >=10 per 1000 babies) 3. Breastmilk feeding exclusively from birth to hospital discharge (minimum effect size >=20 per 1000 babies) 4. Duration of initial hospital stay (minimum effect size >=0.5 days per baby) 5. Cost (for whānau >=10 NZD per baby, for health system >=100 NZD per baby) **Less important for decision making:** 1. Time to blood glucose normalisation after intervention 2. Receipt of treatment for hypoglycaemia during initial hospital stay 3. Number of episodes of hypoglycaemia 4. Severity of hypoglycaemia 5. Duration of treatment
SETTING:	Any birth settings
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	*Low blood glucose concentrations (hypoglycaemia) are common in newborn infants over the first few days after birth, particularly in those with recognised risk factors (infants of mothers with diabetes, or born preterm, low or high birthweight). Severe or prolonged hypoglycaemia can lead to brain injury, so early detection and treatment is recommended to reduce the risk of later developmental problems.* Poor feeding may be a risk factor for neonatal hypoglycaemia, and early feeding has been widely recommended to prevent hypoglycaemia. For example, clinical practice guidelines from Queensland Health (1), the British Association of Perinatal Medicine (2) and WHO (3) recommend that breastfeeding be initiated within an hour of birth for the prevention of hypoglycaemia. However, the evidence supporting an association between early feeding and blood glucose concentrations or hypoglycaemia is limited, and the results are mixed (4).
CONFLICT OF INTERESTS:	CC, DH, JA, JH, JR and LL are authors of cited papers.

ASSESSMENT

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	**Early feeding compared to delayed feeding may be associated with** (4): • Large reduction in the incidence of neonatal hypoglycaemia (cohort studies: 278 fewer per 1,000; cross-sectional 137 fewer per 1,000) [critical] • Neonatal mortality (RCT: little to no effect; cohort study: small reduction (5 fewer per 1,000); cross-sectional study: moderate reduction (11 fewer per 1,000)) [adverse effect, critical] • Little to no effect on postpartum haemorrhage [adverse effect, critical] • Large increase in fully breastfeeding at hospital discharge (Cohort study, 442 more per 1,000) [critical] • Little to no effect on duration of initial hospital stay [important] No studies reported the following outcomes: neurodevelopmental impairment [critical], admission to special care nursery or neonatal intensive care nursery [critical], separation from the mother for treatment of hypoglycaemia before discharge home [important], hypoglycemic injury on brain imaging [important], cost [important].	Early feeding compared to delayed feeding may be associated with little to no difference in mean blood glucose concentration 1-3 hours after birth (4). In the systematic review (4) of studies reporting neonatal hypoglycaemia, 5/6 were conducted in India. Neonatal hypoglycaemia was defined as <2.5mmol/L or <2.2mmol/L. Early feeding was defined as within 1 hour of birth in two studies, within 2 hours in two studies, and undefined in two studies. Babies were breastfed in two studies and mode of feeding was undefined in four studies. Babies were preterm in one study, late preterm or term in two studies, term in one study and gestational age was not specified in two studies. All studies reporting adverse events were conducted in low- or lower-middle-income countries. Babies were breastfed in six of these studies, and the mode of feeding was undefined in one study. Babies were preterm in one study, and

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with delayed feeding	Risk difference with early feeding
Hypoglycaemia (cohort studies) [critical]	744 (4 non-randomised studies)	⨁⨁◯◯ Low[a,b,c]	**OR 0.19** (0.10 to 0.35)	Study population	
				385 per 1,000	**278 fewer per 1,000** (326 fewer to 205 fewer)
Hypoglycaemia (cross-sectional study) [critical]	196 (1 non-randomised study)	⨁◯◯◯ Very low[d]	**OR 0.48** (0.24 to 0.96)	Study population	
				323 per 1,000	**137 fewer per 1,000** (220 fewer to 9 fewer)

Neurodevelopmental impairment [critical] - not measured	-	-	-	-	-	
Admission to special care nursery or neonatal intensive care nursery [critical] - not measured	-	-	-	-	-	
Adverse effects - neonatal mortality (RCT) [critical]	4271 (1 RCT)	⊕◯◯◯ Very low[b]	**RR 1.01** (0.14 to 7.14)	Study population		
				1 per 1,000	**0 fewer per 1,000** (1 fewer to 6 more)	
Adverse effects - neonatal mortality (cohort studies) [critical]	132265 (3 non-randomised studies)	⊕⊕◯◯ Low	**OR 0.51** (0.37 to 0.72)	Study population		
				11 per 1,000	**5 fewer per 1,000** (7 fewer to 3 fewer)	
Adverse effects - neonatal mortality (cross-sectional study) [critical]	3182 (1 non-randomised study)	⊕⊕◯◯ Low	**OR 0.54** (0.32 to 0.92)	Study population		
				25 per 1,000	**11 fewer per 1,000** (17 fewer to 2 fewer)	
Adverse effects - postpartum haemorrhage (RCT) [critical]	4271 (1 RCT)	⊕⊕◯◯ Low[b]	**RR 0.94** (0.77 to 1.16)	Study population		
				83 per 1,000	**5 fewer per 1,000** (19 fewer to 13 more)	
Fully breastfeeding at hospital discharge (cohort) [critical]	99632 (1 non-randomised study)	⊕⊕⊕⊕ High[a]	**OR 7.76** (7.54 to 7.99)	Study population		
				390 per 1,000	**442 more per 1,000**	

gestational age was unspecified in six studies.

Of the studies reporting on mean blood glucose concentration 1-3 hours after birth, 3/4 were conducted in a high-income country. Babies were late preterm or term in three studies, and gestational age was not defined in one study.

					(438 more to 446 more)
Separation from the mother for treatment of hypoglycaemia before discharge home [important] - not measured	-	-	-	-	-
Hypoglycaemic injury on brain imaging [important] - not measured	-	-	-	-	-
Breastmilk feeding exclusively from birth to hospital discharge [important] - not measured	-	-	-	-	-
Duration of initial hospital stay (cohort) [important]	1673 (1 non-randomised study)	⊕◯◯◯ Very low	-	The mean duration of initial hospital stay (cohort) [important] was **2.3** days	MD **0.2 days fewer** (0.31 fewer to 0.09 fewer)
Cost [important] - not measured	-	-	-	-	-

a.Upgraded two levels due to very large effect.
b.Downgraded one level for serious risk of bias due to overall moderate to low quality of included studies (study).
c.Downgraded one level for serious indirectness due to variations in feeding timings across studies.
d.Downgraded two levels for very serious risk of bias due to the overall low quality of included studies (study).
*Absolute effects were calculated based on the control group risk

	Considerations for Māori No additional evidence available **Considerations for Pacific** 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	No studies reported adverse events associated with early feeding (4). **Considerations for Māori** No additional evidence available **Considerations for Pacific** 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)
Hypoglycaemia (cohort studies) [critical]	CRITICAL	⨁⨁◯◯ Low[a,b,c]
Hypoglycaemia (cross-sectional study) [critical]	CRITICAL	⨁◯◯◯ Very low[d]
Neurodevelopmental impairment [critical] - not measured	CRITICAL	-
Admission to special care nursery or neonatal intensive care nursery [critical] - not measured	CRITICAL	-

Adverse effects - neonatal mortality (RCT) [critical]	CRITICAL	⨁◯◯◯ Very low[b]
Adverse effects - neonatal mortality (cohort studies) [critical]	CRITICAL	⨁⨁◯◯ Low
Adverse effects - neonatal mortality (cross-sectional study) [critical]	CRITICAL	⨁⨁◯◯ Low
Adverse effects - postpartum haemorrhage (RCT) [critical]	CRITICAL	⨁⨁◯◯ Low[b]
Fully breastfeeding at hospital discharge (cohort) [critical]	CRITICAL	⨁⨁⨁⨁ High[a]
Separation from the mother for treatment of hypoglycaemia before discharge home [important] - not measured		-
Hypoglycaemic injury on brain imaging [important] - not measured		-
Breastmilk feeding exclusively from birth to hospital discharge [important] - not measured		-
Duration of initial hospital stay (cohort) [important]	IMPORTANT	⨁◯◯◯ Very low
Cost [important] - not measured		-

a.Upgraded two levels due to very large effect.
b.Downgraded one level for serious risk of bias due to overall moderate to low quality of included studies (study).
c.Downgraded one level for serious indirectness due to variations in feeding timings across studies.
d. Downgraded two levels for very serious riks of bias due to the overall low quality of included studies (study).

Considerations for Māori

No additional evidence available

Considerations for Pacific

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	***Excerpts from Values summary document*** ***Uncertain value, possible variability*** • *Hypoglycaemia [critical]* • *Adverse effect [critical]* ***High value, no important variability*** • *Neurodevelopmental impairment [critical]* • *Fully breastfeeding at hospital discharge [critical]* • *Breastfeeding exclusively from birth to hospital discharge [important]* ***High value, probably no important variability*** • *Admission to special care nursery or neonatal intensive care nursery [critical]* • *Separation from the mother for treatment of hypoglycaemia before discharge home [important]* • *Duration of initial hospital stay [important]* ***Uncertain value and variability*** • *Hypoglycaemic injury on brain imaging [important]* • *Cost [important]*	

Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ● Probably favors the intervention ○ Favors the intervention ○ Varies	Early feeding compared to delayed feeding: Low certainty evidence showed associations of • Large reduction in the hypoglycaemia [critical] • Small reduction in neonatal mortality [adverse effect, critical] • Little to no effect on postpartum haemorrhage [adverse effect, critical] • Large increase in fully breastfeeding at hospital discharge [critical] • Uncertain effect on duration of initial hospital stay [important] **Considerations for Māori** No additional evidence available **Considerations for Pacific**	Little to no effect on mean blood glucose concentration 1-3 hours after birth.

○ Don't know	No additional evidence available	

Resources required How large are the resource requirements (costs)?"		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Early feeding is unlikely to require additional resources. However, the location and timing of the resources required may change. The typical price range for 900g of formula in the community setting is approximately NZ$17 to $50. Pasteurised donor human milk costs NZ$33 cents per 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	We did not do a systematic search for evidence about resource requirements.	

● No included studies		
Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ● Probably favors the intervention ○ Favors the intervention ○ Varies ○ No included studies	We found no studies reporting the cost-effectiveness of early feeding (within an hour of birth) compared to delayed feeding (more than an hour after birth).	Early breastmilk feeding is associated with higher rates of exclusive breastmilk feeding later in infancy (5). In the United States, failure to comply with recommendations to exclusively breastfeed through to six months is estimated to cost US $13 billion annually (from medical care and indirect costs) and result in 911 preventable deaths per year (6).
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	***Are there groups or settings that might be disadvantaged in relation to the problem or intervention of interest?*** *There is little published literature and therefore it is unclear if there are any groups or settings that might be disadvantaged in relation to the problem or intervention of interest.* ***Are there plausible reasons for anticipating differences in the relative effectiveness of the intervention for disadvantaged groups or settings?*** *There is little published literature. It is unlikely that the effectiveness of interventions would differ for disadvantaged groups or settings. However, within Aotearoa New Zealand, social determinants of*	

	health (e.g., colonisation, racism, income, education, employment and housing) are likely to have an impact on the implementation, and therefore the effectiveness, of interventions. ***Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the intervention for the importance of the problem for disadvantaged groups or settings?*** *Māori babies (190/530, 35.8%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (9*). However, in the Sugar Babies study of 514 babies at risk of neonatal hypoglycaemia in Aotearoa New Zealand, the proportion of babies who developed hypoglycaemia was similar in Māori babies (79/150, 53%) to that in the whole cohort (260/514, 51%)* (10*).* *Pacific babies (282/693, 40.7%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (9*).* *In the Sugar Babies study of 514 babies at risk of neonatal hypoglycaemia in Aotearoa New Zealand, the number of Pacific babies was very small, but the proportion who developed hypoglycaemia was similar to that in the whole cohort (6/16, 38% vs 260/514, 51%)* (10*).* *Asian babies (660/2068, 31.9%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (9*).* ***Are there important considerations that people implementing the intervention should consider in order to ensure that inequities are reduced, if possible, and that they are not increased?*** ***Consideration for Māori*** In 6,685 singletons enrolled in the Growing Up in New Zealand cohort (11), breastfeeding initiation occurred for 97%. Compared to children of European mothers, children whose mothers were of Māori ethnicity were less likely to initiate breastfeeding. *In the Whānau Experience study* (7*), participants expressed appreciation for the inclusion of karakia and tikanga before certain interventions.* *Māori are more likely to experience interpersonal, institutional, and structural racism, which requires intentional action on addressing racism within these three levels of racism* (12, 13, 14*).* *Additionally, a systematic literature review by Graham et al.* (15*) provides a summary of 20 years of data from Whānau Māori experiences in the public health and/or hospital system. A key barrier included perception of racism or discrimination amongst whānau Māori. For instance, perceiving healthcare professionals to be uninterested in their health and wellbeing. Whānau Māori had good experiences when engaging with Māori healthcare providers when they provided whanaungatanga and were "just so welcoming"* (15*).* ***Consideration for Pacific***	

	In 6,685 singletons enrolled in the *Growing Up in New Zealand* cohort, breastfeeding initiation occurred for 97%. Compared to children of European mothers, children whose mothers were of Pacific ethnicity were less likely to initiate breastfeeding (11). *Some Pacific women interviewed in the Whānau Experience study reported difficulties with accessing the hospital due to cost, transportation and limited availability with work* (7*).* ***Other considerations*** *The Ministry of Health identify four priority groups for maternity care. These are Māori, Pacific, younger women (<25 years) and women with disabilities* (8*). Most pregnancy, hospital and well child care is free for Aotearoa New Zealand citizens and other eligible women, but accessing these services may incur costs that are challenging for families with limited resources. In addition, there may be a charge if families use some private or specialist services. In the 2014 Maternity Consumer Survey* (8), *71% of women reported that they had paid for at least one pregnancy-related service. Māori, Pacific and younger women were less likely to have paid for services.*	
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Cultural practices may delay feeding when understanding of early feeding benefits is lacking (16). One study highlights the need for a 'culturally aware and sensitive approach' to encouraging early milk feeding initiation due to cultural practices, such as those among Muslim women, that take precedence immediately after birth (17). In the Whānau Experiences study (7) of whānau/families with diverse cultural backgrounds including Māori, Pacific, and Asian ethnicities (studied because these groups have a higher likelihood of having a baby born at risk of neonatal hypoglycaemia), mothers reported a strong preference for breastfeeding. **Considerations for Māori** Whānau Māori value being offered and then supported to breastfeed their pēpi during testing. **Considerations for Pacific** One Pacific woman suggested that holding her baby at her breast for early and continuous feeding reduced hypoglycaemia risk.	
Feasibility Is the intervention feasible to implement?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	The Starship Child Health guideline for management of hypoglycaemia in the neonate advises breastfeeding is initiated within 1 hour of birth, prior to the first blood glucose concentration measurement (18). A 2014 study of compliance with clinical guidelines suggested only 9/22 neonatal units in Australia and Aotearoa New Zealand complied with the clinical guideline recommendation to feed babies within an hour of birth (19). Another study found feeding within an hour of birth was less likely among mothers giving birth for the first time, and those delivering by emergency or elective caesarean (20). **Considerations for Māori** No additional evidence available **Considerations for Pacific** 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	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors 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	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors 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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Question 8.

Should expressed breastmilk vs. other or no intervention be used for preventing or treating neonatal hypoglycaemia?	
POPULATION:	Babies at risk or with neonatal hypoglycaemia
INTERVENTION:	expressed breastmilk
COMPARISON:	other or no intervention
MAIN OUTCOMES:	- Consideration will be given to the evidence (or lack thereof) for both Māori and non-Māori babies and their whānau. **Critical for making a decision:** 1. Hypoglycaemia (minimum effect size >=20 per 1000 babies) 2. Neurodevelopmental impairment (minimum effect size >=10 per 1000 babies) 3. Admission to special care nursery or neonatal intensive care nursery (minimum effect size >=20 per 1000 babies) 4. Adverse effects (for neonatal mortality minimum effect size >=1 per 1000 babies) 5. Fully breastfeeding at hospital discharge (minimum effect size >=20 per 1000 babies) **Important but not critical:** 1. Separation from the mother for treatment of hypoglycaemia before discharge home (minimum effect size >=20 per 1000 babies) 2. Hypoglycaemic injury on brain imaging (minimum effect size >=10 per 1000 babies) 3. Breastmilk feeding exclusively from birth to hospital discharge (minimum effect size >=20 per 1000 babies) 4. Duration of initial hospital stay (minimum effect size >=0.5 days per baby) 5. Cost (for whānau >=10 NZD per baby, for health system >=100 NZD per baby) **Less important for decision making:** 1. Time to blood glucose normalisation after intervention 2. Receipt of treatment for hypoglycaemia during initial hospital stay 3. Number of episodes of hypoglycaemia

	4. Severity of hypoglycaemia 5. Duration of treatment
SETTING:	Any birth settings
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	*Low blood glucose concentrations (hypoglycaemia) are common in newborn babies over the first few days after birth, particularly in those with recognised risk factors (baby of mothers with diabetes, or born preterm, low or high birthweight). Severe or prolonged hypoglycaemia can lead to brain injury, so early detection and treatment is recommended to reduce the risk of later developmental problems.* While expressed breast milk provides optimal feeds for the baby, its effectiveness in preventing and treating neonatal hypoglycaemia is uncertain.
CONFLICT OF INTERESTS:	CC, DH, JA, JH, JR and LL are authors of cited papers.

ASSESSMENT

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ● Varies ○ Don't know	**Expressed breastmilk (mother's or donor's) compared to other or no intervention** (1) • Uncertain effect on preventing or treating neonatal hypoglycaemia [critical] • Large reduction in duration of initial hospital stay (RCT: 9.33 days lower; non-randomised study of intervention: 2 days lower) [important] • No studies reported any other critical or important outcomes	Rees et al (2) reported that among hypoglycaemic breastfed babies, there was a significant increase in blood glucose concentrations of 0.5 mmol/L when breastfeeding was supplemented with donor human milk and 0.4 mmol/L when supplemented with formula. In contrast, Harris et al (3) reported a significant additional increase in blood glucose concentration with formula feeds (+0.21 mmol/L, 95% CI 0.04 to 0.37) but no additional change in the blood glucose

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with other or no intervention	Risk difference with expressed breast milk
Neonatal hypoglycaemia	20 (1 RCT)	⨁◯◯◯ Very low[a,b]	-	One study reported no hypoglycaemic episodes in both groups (n=20).	

Neurodevelopmental impairment - not measured	-	-	-	-	-	
Admission to special care nursery or neonatal intensive care nursery - not measured	-	-	-	-	-	
Fully breastfeeding at hospital discharge - not measured	-	-	-	-	-	
Separation from the mother for treatment of hypoglycaemia before discharge home - not measured	-	-	-	-	-	
Hypoglycaemic injury on brain imaging - not measured	-	-	-	-	-	
Breastmilk feeding exclusively from birth to hospital discharge - not measured	-	-	-	-	-	
Duration of initial hospital stay - RCT	53 (1 RCT)	⊕◯◯◯ Very low[a,c]	-	The mean duration of initial hospital stay - RCT was **89.33** days	MD **9.33 days lower** (32.07 lower to 13.4 higher)	
Duration of initial hospital stay- non-randomised study of intervention	143 (1 non-randomised study)	⊕◯◯◯ Very low[a,c]	-	The mean duration of initial hospital stay- non-randomised study of intervention	MD **2 days lower** (12.39 lower to 8.39 higher)	

concentration of hypoglycaemic babies fed mother's expressed breastmilk (-0.1 mmol/L, 95% CI -0.21 to 0.05) in the first 48 hours after birth.

Offering expressed breastmilk to newborns in the NICU provides mothers with an emotional and psychological connection to their babies (4).

Early attainment of full enteral feeds with expressed breastmilk (mother's or donor's) is associated with a lower risk of septicaemia among preterm, extremely low birth weight babies (5).

					was **45.3** days	
Cost - not measured	-	-	-	-	-	

a.Downgraded one level of risk of bias due to overall unclear risk of bias.
b.Downgraded three levels of extreme serious imprecision due to the small sample size and no event occurring in each group.
c.Downgraded one level of serious imprecision due to wide confidence interval.
*Absolute effects were calculated based on the control group risk
Considerations for Māori
No additional data available
Considerations for Pacific
No additional data available

Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	No data on the outcome of interest. **Considerations for Māori** No additional data available **Considerations for Pacific** No additional data available	Mother's milk can become contaminated if not handled properly during expression, collection, transport, and storage, potentially leading to neonatal infections (6). Several outbreaks and case reports of neonatal infections have been previously linked to contaminated human milk containing Staphylococcus aureus, Escherichia coli, Serratia spp., Pseudomonas spp., Salmonella spp., Cytomegalovirus, and Acinetobacter baumannii pathogens, making safety and infection control an important issue

		in the NICU (7)(8). Screening breastmilk donors can mitigate the risk of infection. Infant formula can also become contaminated during handling (9)(10)(11) and has been associated with cases of foodborne illness in babies, including bacterial infections such as Salmonella, Cronobacter sakazakii (formerly Enterobacter sakazakii), and E. coli (12)(13)(14).

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)
Neonatal hypoglycaemia	CRITICAL	⊕◯◯◯ Very low[a,b]
Neurodevelopmental impairment - not measured	CRITICAL	-
Admission to special care nursery or neonatal intensive care nursery - not measured	CRITICAL	-
Adverse effects - not measured	CRITICAL	-
Fully breastfeeding at hospital discharge - not measured	CRITICAL	-
Separation from the mother for treatment of hypoglycaemia before discharge home - not measured	IMPORTANT	-

Hypoglycaemic injury on brain imaging - not measured	IMPORTANT	-
Breastmilk feeding exclusively from birth to hospital discharge - not measured	IMPORTANT	-
Duration of initial hospital stay - RCT	IMPORTANT	⊕◯◯◯ Very low[a,c]
Duration of initial hospital stay- non-randomised study of intervention	IMPORTANT	⊕◯◯◯ Very low[a,c]
Cost - not measured	IMPORTANT	-

a.Downgraded one level of risk of bias due to overall unclear risk of bias.
b.Downgraded three levels of extreme serious imprecision due to the small sample size and no event occurring in each group.
c.Downgraded one level of serious imprecision due to wide confidence interval.

Considerations for Māori

No additional data available

Considerations for Pacific

No additional data 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	***Excerpts from Values summary document*** ***Uncertain value, possible variability*** • *Hypoglycaemia [critical]* • *Adverse effect [critical]* ***High value, no important variability*** • *Neurodevelopmental impairment [critical]* • *Fully breastfeeding at hospital discharge [critical]* • *Breastfeeding exclusively from birth to hospital discharge [important]* ***High value, probably no important variability*** • *Admission to special care nursery or neonatal intensive care nursery [critical]*	

	• *Separation from the mother for treatment of hypoglycaemia before discharge home [important]* • *Duration of initial hospital stay [important]* ***Uncertain value and variability*** • *Hypoglycaemic injury on brain imaging [important]* • *Cost [important]*	
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ● Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know	**Expressed breastmilk (mother's or donor's) compared to other or no intervention** Very low certainty evidence showed • Uncertainty effect on neonatal hypoglycaemia • Uncertainty effect on the duration of hospital stay **Considerations for Māori** No additional data available **Considerations for Pacific** No additional data available	Conflicting evidence on the effect on blood glucose concentrations. Expressed breastmilk may improve the emotional and psychological connection mothers have with their babies.
Resources required How large are the resource requirements (costs)?"		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The resources required to collect and store expressed breastmilk are variable. The typical price range for 900g of formula in the community setting is approximately NZ $20 to $50. Pasteurised donor human milk costs NZ$33 per mL. However, the cost associated with collecting, storing, and feeding the baby with the mother's expressed breastmilk remains uncertain. The required resources can differ significantly based on various factors, including the method of expression (such as hand, manual, or electric pumps purchased by mothers or provided by the hospital), the presence or absence of proper expressed breastmilk storage facilities, equipment cleaning and re-use practices, as well as pasteurisation.	

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 of expressed breastmilk was not undertaken.	

Cost effectiveness
Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies	A systematic review comprising seven studies conducted in upper-middle-income countries, all of which focused on NICU settings and very low birth weight babies, suggests that all of these studies indicate that donor human milk interventions are cost-effective or cost-saving (15). However, none of the included studies assessed neonatal hypoglycaemia outcomes.	

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	We found no evidence to ascertain the impact of expressed breastmilk or donor human milk on health equity. ***Are there groups or settings that might be disadvantaged in relation to the problem or intervention of interest?*** *There is little published literature and therefore it is unclear if there are any groups or settings that might be disadvantaged in relation to the problem or intervention of interest.* ***Are there plausible reasons for anticipating differences in the relative effectiveness of the intervention for disadvantaged groups or settings?*** *There is little published literature. It is unlikely that the effectiveness of interventions would differ for disadvantaged groups or settings. However, within Aotearoa New Zealand, social determinants of health (e.g., colonisation, racism, income, education, employment and housing) are likely to have an impact on the implementation, and therefore the effectiveness, of interventions.* ***Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the intervention for the importance of the problem for disadvantaged groups or settings?*** *Māori babies (190/530, 35.8%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (17). *However, in the Sugar Babies study of 514 babies at risk of neonatal hypoglycaemia in Aotearoa New Zealand, the proportion of babies who developed hypoglycaemia was similar in Māori babies (79/150, 53%) to that in the whole cohort (260/514, 51%)* (18). *Pacific babies (282/693, 40.7%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (17). *In the Sugar Babies study of 514 babies at risk of neonatal hypoglycaemia in Aotearoa New Zealand, the number of Pacific babies was very small, but the proportion who developed hypoglycaemia was similar to that in the whole cohort (6/16, 38% vs 260/514, 51%)* (18). *Asian babies (660/2068, 31.9%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (17).	

	Are there important considerations that people implementing the intervention should consider in order to ensure that inequities are reduced, if possible, and that they are not increased? ***Consideration for Māori*** *In the Whānau Experience study* (19)*, participants expressed appreciation for the inclusion of karakia and tikanga before certain interventions.* *Māori are more likely to experience interpersonal, institutional, and structural racism, which requires intentional action on addressing racism within these three levels of racism* (20)(21)(22)*.* *Additionally, a systematic literature review by Graham et al.* (Graham et al., 2020*) provides a summary of 20 years of data from Whānau Māori experiences in the public health and/or hospital system. A key barrier included perception of racism or discrimination amongst whānau Māori. For instance, perceiving healthcare professionals to be uninterested in their health and wellbeing. Whānau Māori had good experiences when engaging with Māori healthcare providers when they provided whanaungatanga and were "just so welcoming"* (23)*.* ***Consideration for Pacific*** *Some Pacific women interviewed in the Whānau Experience study reported difficulties with accessing the hospital due to cost, transportation and limited availability with work* (19)*.* ***Other considerations*** *The Ministry of Health identify four priority groups for maternity care. These are Māori, Pacific, younger women (<25 years) and women with disabilities* (16)*). Most pregnancy, hospital and well child care is free for Aotearoa New Zealand citizens and other eligible women, but accessing these services may incur costs that are challenging for families with limited resources. In addition, there may be a charge if families use some private or specialist services. In the 2014 Maternity Consumer Survey* (16)*, 71% of women reported that they had paid for at least one pregnancy-related service. Māori, Pacific and younger women were less likely to have paid for services.*	
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no	A survey conducted in Aotearoa New Zealand explored mothers' and health professionals' views and experiences about donor human milk (24). Most mothers (n=496, ethnicity not	A qualitative study conducted in Australia, which involved

○ Probably yes ○ Yes ● Varies ○ Don't know	reported) donated (51.5%) or sought donor human milk (25.6%) for their babies and arranged donor human milk exchanges between individuals (51.9%). The health professional survey (n=283) reported that almost all respondents supported donor human milk use in hospitals (98.6%). The views of Māori participants were not reported separately. There is considerable variability in the maternal acceptability of giving expressed breastmilk to their babies. A study conducted in Eastern Africa (25) with 1,085 participants found that only 11% of respondents were willing to donate breastmilk, and 15% supported feeding their babies with expressed breastmilk. The primary reason for the low acceptance rate of breastmilk donation is the lack of information and misconceptions about the safety of breastmilk. In contrast, the majority (86%) of participants in a study conducted in the United States of America reported their willingness to donate breastmilk, and 77.4% of them agreed human milk banks are a viable alternative to feed babies when there is a shortage of formula feeds (26). **Considerations for Māori** No additional data available **Considerations for Pacific** No additional data available	participants selected from the admission register of the Neonatal Intensive Care Unit, found that mothers highly valued being taught how to express breastmilk. This skill enabled them to provide milk for their sick babies, influencing their feeding practices (4). In the Whāunua Experience Study (19), breastfeeding was highly valued by mothers, and the majority had a strong preference for breastfeeding as a treatment for neonatal hypoglycaemia compared to formula. **Considerations for Māori** Whānau Māori valued having supports in place to facilitate breastfeeding (19). **Considerations for Pacific** All Pacific mothers interviewed wanted to breastfeed their babies. Most (80%) had a strong preference to exclusively breastfeed and not use formula as a form of treatment. Only 2 participants (20%) accepted formula as a form of treatment (19).
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know	Establishing a human milk bank makes an adequate human milk supply more feasible. A study evaluating the milk bank established at Christchurch described the project as successful owing to the multidisciplinary team led by a neonatal nurse and the robust approach in its establishment, including detailed planning, audits, consultation processes, detailed mappings, literature reviews, and assessing its economic implications (27). However, it only prioritised pasteurised donated milk for preterm and unwell/sick babies admitted to the NICU (Waitaha Canterbury, Te Whatu Ora, Health New Zealand). Consequently, it is not currently an option for late preterm and term babies, who are most commonly considered for feeding as a treatment or preventative measure for hypoglycaemia. In the survey conducted in Aotearoa New Zealand, health professionals (n=232) felt human milk donation could be improved with better advocacy, access, affordability, and guideline development (24). Many guidelines on newborn care worldwide recommend giving newborn babies (both term and preterm babies) expressed breastmilk (mother's or donor's) to prevent or treat neonatal hypoglycaemia and for routine feeding of preterm babies admitted into neonatal intensive care or special care baby units (28)(29). **Considerations for Māori** No additional data available **Considerations for Pacific** No additional data available	There are currently six human milk banks in Aotearoa New Zealand. However, cost presents a significant barrier, and the supply is limited. As a result, these milk banks can only serve prioritised groups. Most babies at risk of hypoglycaemia do not fall within the currently prioritised groups. Many maternity hospitals in Aotearoa New Zealand have expressing equipment available for mothers to express their breastmilk.

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	Favors the comparison	Probably favors the comparison	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors 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	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors 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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Question 9.

Should oral dextrose gel vs. placebo be used for preventing neonatal hypoglycaemia?	
POPULATION:	Newborn babies judged to be at risk of hypoglycaemia
INTERVENTION:	oral dextrose gel

COMPARISON:	placebo
MAIN OUTCOMES:	- Consideration will be given to the evidence (or lack thereof) for both Māori and non-Māori babies and their whānau. **Critical for making a decision:** 1. Hypoglycaemia (minimum effect size >=20 per 1000 babies) 2. Neurodevelopmental impairment (minimum effect size >=10 per 1000 babies) 3. Admission to special care nursery or neonatal intensive care nursery (minimum effect size >=20 per 1000 babies) 4. Adverse effects (for neonatal mortality minimum effect size >=1 per 1000 babies) 5. Fully breastfeeding at hospital discharge (minimum effect size >=20 per 1000 babies) **Important but not critical:** 1. Separation from the mother for treatment of hypoglycaemia before discharge home (minimum effect size >=20 per 1000 babies) 2. Hypoglycaemic injury on brain imaging (minimum effect size >=10 per 1000 babies) 3. Breastmilk feeding exclusively from birth to hospital discharge (minimum effect size >=20 per 1000 babies) 4. Duration of initial hospital stay (minimum effect size >=0.5 days per baby) 5. Cost (for whānau >=10 NZD per baby, for health system >=100 NZD per baby) **Less important for decision making:** 1. Time to blood glucose normalisation after intervention 2. Receipt of treatment for hypoglycaemia during initial hospital stay 3. Number of episodes of hypoglycaemia 4. Severity of hypoglycaemia 5. Duration of treatment
SETTING:	Any birth settings
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	*Low blood glucose concentrations (hypoglycaemia) are common in newborn babies over the first few days after birth, particularly in those with recognised risk factors (babies of mothers with diabetes, or born preterm, low or high birthweight). Severe or prolonged hypoglycaemia can lead to brain injury, so early detection and treatment is recommended to reduce the risk of later developmental problems.* Current practice usually includes early identification of at-risk babies and prophylactic measures are advised. However, these measures usually involve use of formula milk or admission to the neonatal unit. Dextrose gel is non-invasive, inexpensive and effective for treatment of neonatal hypoglycaemia. If prophylactic dextrose gel reduced the incidence of neonatal hypoglycaemia, it potentially may reduce separation of mother and baby and support breastfeeding, as well as preventing brain injury.

CONFLICT OF INTERESTS:	DH, JA, JH, JR and LL are authors of cited papers.

ASSESSMENT

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	**Prophylactic oral dextrose compared to placebo gel or no gel results in** (1) : • Moderate reduction in hypoglycaemia (56 fewer per 1,000) [critical] • Little to no effect on neurodevelopmental impairment at ≥2 years [critical] • Moderate reduction in neurodevelopmental impairment at 6 to 7 years of age (84 fewer per 1,000) [critical] • Little to no effect on admission to special care nursery or neonatal intensive care nursery [critical] • Moderate reduction in fully breastfeeding at hospital discharge (84 fewer per 1,000) [critical] • Little to no effect on separation from mother for treatment of hypoglycaemia before discharge home [important] • Small increase in breastmilk feeding exclusively from birth to hospital discharge (30 more per 1,000) [important] • Little to no effect on duration of initial hospital stay [important] • No studies reported hypoglycaemic injury on brain injury, or cost	**Prophylactic oral dextrose compared to placebo gel or no gel results in** (1): Little to no effect on major neurological disability at ≥2 years (There is substantial heterogeneity for major neurological disability at two years of age or older (I-square = 85%, p = 0.009), with the direction of effect suggesting benefit in one study (3) and possible harm in the other, larger study (2). Uncertain effect on major neurological disability at six to seven years of age (85 fewer per 1,000). May reduce receipt of treatment for hypoglycaemia during initial hospital stay slightly (35 fewer per 1,000)). Little to no effect on the number of episodes of hypoglycaemia, and breastfeeding after hospital discharge (1).

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with placebo	Risk difference with oral dextrose gel
Hypoglycaemia [critical]	2548 (2 RCTs)	⨁⨁⨁⨁ High	**RR 0.87** (0.79 to 0.95)	Study population	
				433 per 1,000	**56 fewer per 1,000** (91 fewer to 22 fewer)
				Study population	

Neurodevelopmental impairment at ≥2 years [critical]	1553 (2 RCTs)	⨁⨁◯◯ Low[a,b]	**RR 1.03** (0.84 to 1.26)	193 per 1,000	**6 more per 1,000** (31 fewer to 50 more)	Dextrose gel used for prophylaxis or treatment of neonatal hypoglycaemia does not alter the neonatal gut microbiome (4).
Neurodevelopmental impairment at 6 to 7 years of age [critical]	308 (1 RCT)	⨁◯◯◯ Very low[c]	**RR 0.85** (0.68 to 1.07)	Study population		
				559 per 1,000	**84 fewer per 1,000** (179 fewer to 39 more)	
Admission to special care nursery or neonatal intensive care nursery [critical]	2548 (2 RCTs)	⨁⨁◯◯ Low[a,b]	**RR 1.03** (0.81 to 1.31)	Study population		
				95 per 1,000	**3 more per 1,000** (18 fewer to 29 more)	
Fully breastfeeding at hospital discharge [critical]	2523 (2 RCTs)	⨁◯◯◯ Very low[c]	**RR 1.09** (0.79 to 1.49)	Study population		
				928 per 1,000	**84 more per 1,000** (195 fewer to 455 more)	
Separation from mother for treatment of hypoglycaemia before discharge home [important]	2548 (2 RCTs)	⨁⨁◯◯ Low[b,d]	**RR 1.12** (0.81 to 1.55)	Study population		
				50 per 1,000	**6 more per 1,000** (9 fewer to 27 more)	
Hypoglycaemic injury on brain imaging [important] - not measured	-	-	-	-	-	
Breastmilk feeding exclusively from birth to hospital discharge [important]	2525 (2 RCTs)	⨁⨁⨁◯ Moderate[b]	**RR 1.06** (0.91 to 1.24)	Study population		
				500 per 1,000	**30 more per 1,000** (45 fewer to 120 more)	
Duration of initial hospital stay [important]	2537 (2 RCTs)	⨁⨁⨁◯ Moderate[b]	-	The mean duration of initial	MD **0.06 days higher**	

				hospital stay [important] was **3.20** days	(0.13 lower to 0.24 higher)
Cost [important] - not measured	-	-	-	-	-

a.Downgraded one level for serious inconsistency due to the substantial heterogeneity.
b.Downgraded one level for serious imprecision due to the confidence interval including the possibility of benefit and harm.
c.Downgraded three levels for extremely serious imprecision due to a very wide confidence interval suggesting markedly different inferences.
d.Downgraded two levels for very serious imprecision due to the wide confidence interval and low event rates.
*Absolute effects were calculated based on the control group risk

Considerations for Māori
In the hPOD trial of 2051 babies in Aotearoa New Zealand and Australia, the effects of prophylactic dextrose gel on the outcomes listed above were similar for the 116/238 Māori babies randomised (11.6%) compared to the findings for the whole cohort (unpublished data from (2)).
Considerations for Pacific
In the hPOD trial of 2051 babies in Aotearoa New Zealandand Australia, the number of Pacific babies was very small, the effects of prophylactic dextrose gel on the outcomes listed above were similar for the 56/116 Pacific babies randomised (5.7%) compared to the findings for the whole cohort (unpublished data from (2)).

Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

● Trivial
○ Small
○ Moderate
○ Large
○ Varies
○ Don't know

Prophylactic oral dextrose compared to placebo gel or no gel results in: (1)

- Little to no difference in short-term adverse effects [critical].

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with placebo	Risk difference with oral dextrose gel
Adverse effects [critical]	2510 (2 RCTs)	⨁⨁⨁◯ Moderate[a]	**RR 1.22** (0.64 to 2.33)	Study population	
				10 per 1,000	**2 more per 1,000** (4 fewer to 13 more)

a.Downgraded two levels for very serious imprecision due to the wide confidence interval and low event rates.
*Absolute effects were calculated based on the control group risk

Considerations for Māori
No additional data available

Considerations for Pacific
No additional data available

In a systematic review of buccal dextrose gel for the treatment of neonatal hypoglycaemia (5), no adverse events were reported in either the oral dextrose gel or the placebo gel group.

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)
Hypoglycaemia [critical]	CRITICAL	⨁⨁⨁⨁ High
Neurodevelopmental impairment at ≥2 years [critical]	CRITICAL	⨁⨁◯◯ Low[a,b]
Neurodevelopmental impairment at 6 to 7 years of age [critical]	CRITICAL	⨁◯◯◯ Very low[c]
Admission to special care nursery or neonatal intensive care nursery [critical]	CRITICAL	⨁⨁◯◯ Low[a,b]

Adverse effects [critical]	CRITICAL	⊕⊕⊕◯ Moderate[d]
Fully breastfeeding at hospital discharge [critical]	CRITICAL	⊕◯◯◯ Very low[c]
Separation from mother for treatment of hypoglycaemia before discharge home [important]	IMPORTANT	⊕⊕◯◯ Low[b,d]
Hypoglycaemic injury on brain imaging [important] - not measured	IMPORTANT	-
Breastmilk feeding exclusively from birth to hospital discharge [important]	IMPORTANT	⊕⊕⊕◯ Moderate[b]
Duration of initial hospital stay [important]	IMPORTANT	⊕⊕⊕◯ Moderate[b]
Cost [important] - not measured		-

a.Downgraded one level for serious inconsistency due to the substantial heterogeneity.
b.Downgraded one level for serious imprecision due to the confidence interval including the possibility of benefit and harm.
c.Downgraded three levels for extremely serious imprecision due to a very wide confidence interval suggesting markedly different inferences.
d.Downgraded two levels for very serious imprecision due to the wide confidence interval and low event rates.

Considerations for Māori

Because of the small numbers included in the available trials, the findings are less certain for Māori babies.

Considerations for Pacific

Because of the very small numbers included in the available trials, the findings are very uncertain for Pacific babies.

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	***Excerpts from Values summary document*** ***Uncertain value, possible variability*** • *Hypoglycaemia [critical]* • *Adverse effect [critical]* ***High value, no important variability*** • *Neurodevelopmental impairment [critical]* • *Fully breastfeeding at hospital discharge [critical]* • *Breastfeeding exclusively from birth to hospital discharge [important]* ***High value, probably no important variability*** • *Admission to special care nursery or neonatal intensive care nursery [critical]* • *Separation from the mother for treatment of hypoglycaemia before discharge home [important]* • *Duration of initial hospital stay [important]* ***Uncertain value and variability*** • *Hypoglycaemic injury on brain imaging [important]* • *Cost [important]*	
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ● Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know	Prophylactic oral dextrose compared to placebo gel or no gel: Moderate to low certainty evidence showed: • Moderate reduction in hypoglycaemia [critical] • Little to no effect on neurodevelopmental impairment at ≥ 2 years [critical] • Uncertain effect on neurodevelopmental impairment at 6 to 7 years of age [critical] • Little to no effect on admission to special care nursery or neonatal intensive care nursery [critical] • Uncertain effect on fully breastfeeding at hospital discharge [critical] • Little to no effect on separation from mother for treatment of hypoglycaemia before discharge home [important] • Small increase in breastmilk feeding exclusively from birth to hospital discharge [important] • Little to no effect on duration of initial hospital stay [important] **Considerations for Māori** Limited evidence suggests that the effects are similar for Māori babies. **Considerations for Pacific**	• Little to no effect on major neurological disability at ≥2 years • Uncertain effect on major neurological disability at 6 to 7 years of age • May reduce receipt of treatment for hypoglycaemia during initial hospital stay slightly • Little to no effect on the number of episodes of hypoglycaemia, and

	No specific evidence about effects for Pacific babies, but baseline risk is likely to be similar to other babies studied	breastfeeding after hospital discharge
Resources required How large are the resource requirements (costs)?"		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Cost of dextrose gel: use of single-dose syringes, priced at NZ $15.00 each (Biomed Ltd., Auckland, NZ). Cost of dextrose gel administration: US $7.38 (6) Minimal training is required to administer gel Time of applying the gel: 5 minutes. Additional time is required for prescriptions, sourcing gel and documenting administration.	Regarding dextrose gel treatment, most practitioners reported that the gel was easily available and that guidelines for its use were easy to access and understand (7).
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	High certainty about the cost of the gel There is no precise data on time; estimates are made based on experience.	

Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ● Probably favors the intervention ○ Favors the intervention ○ Varies ○ No included studies	Subjects who received prophylactic dextrose gel incurred costs to the health system of around United States US $14,000 over an 18 year time horizon, accruing 11.25 quality adjusted life years (QALYs), whereas those who did not receive prophylactic treatment incurred cost of around US $16,000 and experienced a utility of 11.10 QALYs (based on one study - early follow up showing benefits) (6).	

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	Dextrose gel does not require refrigeration, has a long shelf-life and is already being distributed around Aotearoa New Zealand. It can be used in any care setting and can be prescribed by a midwife. These factors are likely to favour equitable access in both rural and urban settings. ***Are there groups or settings that might be disadvantaged in relation to the problem or intervention of interest?*** *There is little published literature and therefore it is unclear if there are any groups or settings that might be disadvantaged in relation to the problem or intervention of interest.* ***Are there plausible reasons for anticipating differences in the relative effectiveness of the intervention for disadvantaged groups or settings?*** *There is little published literature. It is unlikely that the effectiveness of interventions would differ for disadvantaged groups or settings. However, within Aotearoa New Zealand, social determinants of health (e.g., colonisation, racism, income, education, employment and housing) are likely to have an impact on the implementation, and therefore the effectiveness, of interventions.* ***Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the intervention for the importance of the problem for disadvantaged groups or settings?*** *Māori babies (190/530, 35.8%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (9)*. However, in the Sugar Babies study of 514 babies at risk of neonatal hypoglycaemia in Aotearoa New Zealand, the proportion of babies who developed hypoglycaemia was similar in Māori babies (79/150, 53%) to that in the whole cohort (260/514, 51%)* (10)*.* *Pacific babies (282/693, 40.7%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (9)*.* *In the Sugar Babies study of 514 babies at risk of neonatal hypoglycaemia in Aotearoa New Zealand, the number of Pacific babies was very small, but the proportion who developed hypoglycaemia was similar to that in the whole cohort (6/16, 38% vs 260/514, 51%)* (10)*.* *Asian babies (660/2068, 31.9%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (9)*.* ***Are there important considerations that people implementing the intervention should consider in order to ensure that inequities are reduced, if possible, and that they are not increased?*** ***Consideration for Māori*** Effects of the intervention are likely to be similar in Māori babies to those reported above. *In the Whānau Experience study* (11)*, participants expressed appreciation for the inclusion of karakia and tikanga before certain interventions.*	

	Māori are more likely to experience interpersonal, institutional, and structural racism, which requires intentional action on addressing racism within these three levels of racism (12, 13, 14*).* *Additionally, a systematic literature review by Graham et al.* (15*) provides a summary of 20 years of data from Whānau Māori experiences in the public health and/or hospital system. A key barrier included perception of racism or discrimination amongst whānau Māori. For instance, perceiving healthcare professionals to be uninterested in their health and wellbeing. Whānau Māori had good experiences when engaging with Māori healthcare providers when they provided whanaungatanga and were "just so welcoming"* (15*).* ***Consideration for Pacific*** Effects of the intervention are likely to be similar in Pacific babies to those reported above. *Some Pacific women interviewed in the Whānau Experience study reported difficulties with accessing the hospital due to cost, transportation and limited availability with work* (11*).* ***Other considerations*** *The Ministry of Health identify four priority groups for maternity care. These are Māori, Pacific, younger women (<25 years) and women with disabilities* (8*). Most pregnancy, hospital and well child care is free for Aotearoa New Zealand citizens and other eligible women, but accessing these services may incur costs that are challenging for families with limited resources. In addition, there may be a charge if families use some private or specialist services. In the 2014 Maternity Consumer Survey* (8*), 71% of women reported that they had paid for at least one pregnancy-related service. Māori, Pacific and younger women were less likely to have paid for services.*	

Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Many Aotearoa New Zealand practitioners would consider implementing dextrose gel prophylaxis even if the clinical benefits are relatively small (7). When considering introducing dextrose gel prophylaxis, outcomes most often considered important by practitioners included reduced hypoglycaemia-associated cognitive impairment, improved breastfeeding, reduced use of formula to treat hypoglycaemia, reduced neonatal unit admission and reduced incidence of hypoglycaemia (7). In the Pre-hPOD trial, most parents found the gel acceptable (364/402, 91%) (3). **Considerations for Māori** Evidence from Whānau Experience Study (11) found Whānau Māori had positive experiences with buccal dextrose gel.	The DESiGN trial (16) showed that it was feasible to give the gel for treatment of hypoglycaemia in Aotearoa New Zealand, as most sites were giving it prior to the guidelines being published and implemented. Many studies in different countries have demonstrated the feasibility of implementing

	Considerations for Pacific Evidence from Whānau Experience Study found all Pacific mothers interviewed had either a positive or neutral perception of buccal dextrose gel.	dextrose gel for treatment, and its implementation has resulted in reduced NICU admissions and increased breastfeeding rates (17, 18, 19, 20, 21, 22, 23, 24, 25).

Feasibility **Is the intervention feasible to implement?**		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Before administering the gel, practitioners need to weigh the babies to determine the appropriate dosage. The timing of applying the gel may be problematic. Considerations for Māori No additional data available Considerations for Pacific No additional data available	Similar to above

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	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors 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	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors 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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Question 10.

Should formula vs. control be used for prevention of neonatal hypoglycaemia?	
POPULATION:	Babies at risk of neonatal hypoglycaemia
INTERVENTION:	formula
COMPARISON:	control
MAIN OUTCOMES:	- Consideration will be given to the evidence (or lack thereof) for both Māori and non-Māori babies and their whānau. **Critical for making a decision:** 1. Hypoglycaemia (minimum effect size >=20 per 1000 babies) 2. Neurodevelopmental impairment (minimum effect size >=10 per 1000 babies) 3. Admission to special care nursery or neonatal intensive care nursery (minimum effect size >=20 per 1000 babies)

	4. Adverse effects (for neonatal mortality minimum effect size >=1 per 1000 babies) 5. Fully breastfeeding at hospital discharge (minimum effect size >=20 per 1000 babies) **Important but not critical:** 1. Separation from the mother for treatment of hypoglycaemia before discharge home (minimum effect size >=20 per 1000 babies) 2. Hypoglycaemic injury on brain imaging (minimum effect size >=10 per 1000 babies) 3. Breastmilk feeding exclusively from birth to hospital discharge (minimum effect size >=20 per 1000 babies) 4. Duration of initial hospital stay (minimum effect size >=0.5 days per baby) 5. Cost (for whānau >=10 NZD per baby, for health system >=100 NZD per baby) **Less important for decision making:** 1. Time to blood glucose normalisation after intervention 2. Receipt of treatment for hypoglycaemia during initial hospital stay 3. Number of episodes of hypoglycaemia 4. Severity of hypoglycaemia 5. Duration of treatment
SETTING:	Any birth settings
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	*Low blood glucose concentrations (hypoglycaemia) are common in newborn babies over the first few days after birth, particularly in those with recognised risk factors (infants of mothers with diabetes, or born preterm, low or high birthweight). Severe or prolonged hypoglycaemia can lead to brain injury, so early detection and treatment is recommended to reduce the risk of later developmental problems.* Formula is sometimes used to prevent neonatal hypoglycaemia by providing an alternative source of glucose when breastfeeding is insufficient or not possible.
CONFLICT OF INTERESTS:	DH, JA, JH, JR and LL are authors of cited paper.

ASSESSMENT

Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	None of the studies reported any desirable effects for formula feeding (1) **Considerations for Māori** No additional data available **Considerations or Pacific** No additional data available	Tozier (2) conducted a chart review in the USA of 163 babies born to mothers with type 1 diabetes and reported that the first three blood glucose concentrations of babies fed colostrum (mothers' own milk) were no different from those of babies who received formula supplementation.

Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know	Formula compared to breastfeeding as first feed is associated with (1). • Large increase in neonatal hypoglycaemia (262 more er 1,000) [critical] • Large decrease in fully breastfeeding at hospital discharge (325 fewer per 1,000) [critical] • Moderate increase in the duration of hospital stay (1.2 days higher) [important]	Chertok 2009 (4) reported that among babies born to mothers with diabetes, breastfed babies had significantly higher mean blood glucose concentrations (3.20 mmol/L) compared to those who were formula fed for their first feed (2.68 mmol/L) (P = 0.002). Nicolas 2008 (5) reported that full-term babies without any risk factors who were breastfed presented much less hypoglycaemia than formula-fed neonates, with a statistically significant p-value of 0.0001 (numbers not provided).

Outcomes	№ 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 formula
Hypoglycaemia [critical]	621 (2 non-randomised studies)	⨁◯◯◯ Very low[a,b,c]	**OR 3.01** (0.53 to 17.13)	Study population	
				293 per 1,000	**262 more per 1,000** (113 fewer to 584 more)
Fully breastfeeding at hospital discharge [critical]	554 (1 non-randomised study)	⨁◯◯◯ Very low[a,d]	**OR 0.20** (0.13 to 0.30)	Study population	
				483 per 1,000	**325 fewer per 1,000** (374 fewer to 264 fewer)

Duration of initial hospital stay [important]	554 (1 non-randomised study)	⊕◯◯◯ Very low[a]	-	The mean duration of initial hospital stay [important] was **4.8** days	MD **1.2 days higher** (0.34 higher to 2.06 higher)

a.Downgraded two levels for very serious risk of bias due to included studies being of low quality.
b.Downgraded two levels for very serious inconsistency due to substantial heterogeneity.
c.Downgraded one level for serious imprecision due to wide confidence interval and small sample size.
d.Upgraded one level for large effect.
*Absolute effects were calculated based on the control group risk

Note: One of the included studies reported all three outcomes (3), but 61% of the babies in the formula group were admitted to the NICU before the initiation of feeding due to respiratory distress syndrome, transient tachypnoea of the newborn, and prematurity (apnoea, severe hypotonia, perinatal depression, and birth trauma), compared to only 22% in the breastfeeding group. Among those admitted to the Well Baby Nursery, there was no difference between the formula and breastfeeding groups in the incidence of hypoglycaemia (40% vs. 30%) or the duration of the initial hospital stay.Additionally, in one of the included studies that reported on the hypoglycaemia outcome, the average time to initial feeding was half an hour for the breastfeeding group and 2.6 hours for the formula group (4).

Considerations for Māori
No additional data available
Considerations or Pacific
No additional data 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	<table><tr><th>Outcomes</th><th>Importance</th><th>Certainty of the evidence (GRADE)</th></tr><tr><td>Hypoglycaemia [critical]</td><td>CRITICAL</td><td>⊕◯◯◯ Very low[a,b,c]</td></tr><tr><td>Neurodevelopmental impairment [critical] - not measured</td><td>CRITICAL</td><td>-</td></tr><tr><td>Admission to special care nursery or neonatal intensive care nursery [critical] - not measured</td><td>CRITICAL</td><td>-</td></tr><tr><td>Adverse effects [critical] - not measured</td><td>CRITICAL</td><td>-</td></tr><tr><td>Fully breastfeeding at hospital discharge [critical]</td><td>CRITICAL</td><td>⊕◯◯◯ Very low[a,d]</td></tr></table> a.Downgraded two levels for very serious risk of bias due to included studies being of low quality. b.Downgraded two levels for very serious inconsistency due to substantial heterogeneity. c.Downgraded one level for serious imprecision due to wide confidence interval and small sample size. d.Upgraded one level for large 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	*Excerpts from Values summary document* ***Uncertain value, possible variability*** • *Hypoglycaemia [critical]* • *Adverse effect [critical]* ***High value, no important variability*** • *Neurodevelopmental impairment [critical]* • *Fully breastfeeding at hospital discharge [critical]* • *Breastfeeding exclusively from birth to hospital discharge [important]* ***High value, probably no important variability***	

	• *Admission to special care nursery or neonatal intensive care nursery [critical]* • *Separation from the mother for treatment of hypoglycaemia before discharge home [important]* • *Duration of initial hospital stay [important]* ***Uncertain value and variability*** • *Hypoglycaemic injury on brain imaging [important]* • *Cost [important]*	
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
● Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know	Formula compared to breastfeeding Very low certainty evidence showed • Uncertain effect on neonatal hypoglycaemia [critical] • Uncertain effect on fully breastfeeding at hospital discharge [critical] • Uncertain effect on length of hospital stay [critical] **Considerations for Māori** No additional data available **Considerations for Pacific** No additional data available	Very low certainty evidence showed: No difference in early blood glucose concentrations between babies born to mothers with type 1 diabetes fed colostrum and those given formula. Uncertain effect on blood glucose concentrations in breastfed babies compared to formula-fed babies born to mothers with diabetes.
Resources required How large are the resource requirements (costs)?"		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The costs can vary depending on the type of formula used and the quantity required. The typical price range for a 900g container of formula in a community setting in New Zealand is approximately NZD $20 to $50. The estimated cost per litre of prepared Stage 1 baby formula in New Zealand would be approximately NZD $3.19 to $7.96. Additionally, resource requirements may include staff time for preparation and feeding, potential costs for additional feeding equipment, and considerations for storage and handling of the formula.	
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 of formula for the treatment of neonatal hypoglycaemia was not undertaken.	
Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ● Varies ○ No included studies	There are no studies that assess the specific cost-effectiveness of formula particularly in the context of preventing neonatal hypoglycaemia. However, a few studies suggest that formula is generally more cost-effective than donor human milk in the short term. In the long term, exclusive breastfeeding might offer cost savings compared to formula. A study conducted in Germany (6) comparing the costs of feeding preterm infants donor human milk, mother's own milk, and formula found that donor human milk was significantly more expensive than formula or mother's milk. The cost per litre of donor human milk was €306.95, with a total cost of €82.88 per litre for production and use. In contrast, formula costs €10.28 per litre. This suggests that formula has much lower direct costs than donor human milk.	

	Formula typically ranges from NZ$20 to $50 for a 900g container, depending on the type and quantity used. Additional costs of formula include factors such as staff time for preparation and feeding, as well as potential expenses for feeding equipment and storage. For comparison, oral dextrose gel is priced at approximately NZ$15 per single-dose syringe. The administration of dextrose gel costs an additional NZ$15(7) and requires minimal training. Thus, the cost of using formula as a prevention option is likely to be similar to that of dextrose gel.	
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	***Are there groups or settings that might be disadvantaged in relation to the problem or intervention of interest?*** *There is little published literature and therefore it is unclear if there are any groups or settings that might be disadvantaged in relation to the problem or intervention of interest.* ***Are there plausible reasons for anticipating differences in the relative effectiveness of the intervention for disadvantaged groups or settings?*** *There is little published literature. It is unlikely that the effectiveness of interventions would differ for disadvantaged groups or settings. However, within Aotearoa New Zealand, social determinants of health (e.g., colonisation, racism, income, education, employment and housing) are likely to have an impact on the implementation, and therefore the effectiveness, of interventions.* ***Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the intervention for the importance of the problem for disadvantaged groups or settings?*** *Māori babies (190/530, 35.8%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (10). *However, in the Sugar Babies study of 514 babies at risk of neonatal hypoglycaemia in Aotearoa New Zealand, the proportion of babies who developed hypoglycaemia was similar in Māori babies (79/150, 53%) to that in the whole cohort (260/514, 51%)* (11). *Pacific babies (282/693, 40.7%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (10).	

	In the Sugar Babies study of 514 babies at risk of neonatal hypoglycaemia in Aotearoa New Zealand, the number of Pacific babies was very small, but the proportion who developed hypoglycaemia was similar to that in the whole cohort (6/16, 38% vs 260/514, 51%) (11). *Asian babies (660/2068, 31.9%) are more likely to be at risk of hypoglycaemia than New Zealand Europeans (660/2529, 26.1%)* (10). ***Are there important considerations that people implementing the intervention should consider in order to ensure that inequities are reduced, if possible, and that they are not increased?*** ***Consideration for Māori*** *In the Whānau Experience study* (8), *participants expressed appreciation for the inclusion of karakia and tikanga before certain interventions.Māori are more likely to experience interpersonal, institutional, and structural racism, which requires intentional action on addressing racism within these three levels of racism* (12)(13)(14)*Additionally, a systematic literature review by Graham et al.* (15) *provides a summary of 20 years of data from Whānau Māori experiences in the public health and/or hospital system. A key barrier included perception of racism or discrimination amongst whānau Māori. For instance, perceiving healthcare professionals to be uninterested in their health and wellbeing. Whānau Māori had good experiences when engaging with Māori healthcare providers when they provided whanaungatanga and were "just so welcoming"* (15). ***Consideration for Pacific*** *Some Pacific women interviewed in the Whānau Experience study reported difficulties with accessing the hospital due to cost, transportation and limited availability with work* (8). ***Other considerations*** *The Ministry of Health identify four priority groups for maternity care. These are Māori, Pacific, younger women (<25 years) and women with disabilities* (9). *Most pregnancy, hospital and well child care is free for Aotearoa New Zealand citizens and other eligible women, but accessing these services may incur costs that are challenging for families with limited resources. In addition, there may be a charge if families use some private or specialist services. In the 2014 Maternity Consumer Survey* (9) *71% of women reported that they had paid for at least one pregnancy-related service. Māori, Pacific and younger women were less likely to have paid for services.*	
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 Whānau Experiences Study (8) , all Pacific mothers indicated a strong preference for breastfeeding their babies, with most favouring exclusive breastfeeding over formula feeding. Only 2 out of 10 participants in this group accepted formula. Similarly, among Asian mothers, some struggled with transitioning to formula feeding as they had initially planned to breastfeed exclusively. In the Growing Up in New Zealand cohort (16), exclusive breastfeeding was highly valued by many wāhine Māori due to its alignment with Tikanga Māori, indicating that formula use may be less acceptable, particularly when cultural traditions strongly emphasise breastfeeding. A survey in New Zealand (17) showed that health professionals viewed dextrose gel prophylaxis for neonatal hypoglycaemia positively because it can reduce the need for formula treatment. They preferred minimising formula use to support breastfeeding while ensuring effective treatment.	

Feasibility
Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Formula is widely available and used in most neonatal care settings.	

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	**Favors the comparison**	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors 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	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors 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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