EtD 11. What is the recommended hang time for aqueous IV nutrition and lipid solutions for preterm infants?

POPULATION:	Preterm infants
INTERVENTION:	Parenteral nutrition aqueous phase or the lipid emulsion administration (hang) time of greater than 24 hours
COMPARISON:	Parenteral nutrition aqueous phase or the lipid emulsion administration (hang) time of 24 hours
MAIN OUTCOMES:	**Critical outcomes** Mortality Neurodevelopmental impairment Adverse effects Fully breastmilk feeding at hospital discharge **Important but not critical** Fully breastfeeding at hospital discharge Time to full enteral feeds Faltering growth/body composition Duration of initial hospital stay Bronchopulmonary dysplasia/chronic lung disease Necrotizing enterocolitis Sepsis: proven or suspected Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost **Less important for decision making** Time to full sucking feeds
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation: population perspective
BACKGROUND:	Parenteral nutrition (PN) is a vital intervention for preterm infants, providing essential nutrients to support growth and development until enteral feeding is sufficient. The duration of PN administration, or "hang time," has significant implications for safety, nutrient intake and cost. A hang time of 24 hours is common in many settings, aiming to minimise the risk of microbial contamination and associated infections while maintaining nutritional stability. However, extending hang time beyond 24 hours may reduce preparation and administration burdens on healthcare systems, potentially increasing efficiency and lowering costs. Accessing the intravenous lines to change the PN less often may reduce the risk of infection. Conversely, longer hang times could elevate the risk of bacterial contamination and nutrient degradation, raising safety concerns. Preterm infants are particularly vulnerable to infections and nutritional deficits due to their immature immune systems and high metabolic demands.

CONFLICT OF INTERESTS:	The following survey (Cormack et al, Reference 3) co-authors are on the Guideline Development Group: Barbara Cormack, Tanith Alexander.

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence is based on a Cochrane systematic review [1] which reported on optimal timing for changing giving sets and a before-after observational study that investigated shorter vs. longer hanging time [2]. The studies that included neonates for this evidence did not provide any supporting evidence for very preterm infants and the data that is available may not be generalisable to this population. Note that in these studies the intervention is external to the infant and are researching the changing of giving sets or bags of fluid. **Hang time PN solutions [2]** This study looked at changing hang times of the aqueous solution bags. Lipid bags were changed daily. Adverse events: Before-After study: Hang time: Longer hang times associated with reduced central line associated bloodstream infection (24 hours vs. 48 hours hang time for central line associated bloodstream infection per 1000-line days 0.8 vs. 0.4 respectively *P*<0.01) [Critical] Sepsis: Before-After study: Hang time: Large reduction in central venous catheter-related sepsis with longer hang times (4 fewer per 1,000; 4 fewer to 4 fewer)[Important]. Cost: cost of intervention, cost of neonatal care and life-long cost: Before-After study: Annual savings (AUD) - AUD$ 97 603.00/year with change to longer hang time (24 hours vs. 48 hours) [Important]. **Set replacement** [1] Adverse effects: RCT: Set replacement: Longer time between set changes had no significant reduction in infusate-related bloodstream infection at 48 hours + vs. 24 hours (25 fewer per 1,000; 45 fewer to 21 more). Longer time between set changes had no significant reduction in all-cause bloodstream infection for 48 hours + vs. 24 hours (48 fewer per 1,000; 143 fewer to 125 more) [Critical]. **Desirable effects for Māori** No additional evidence available	**Population information for included evidence** Cochrane systematic review [1]: For the two studies that included infants: One study included neonates admitted to the Neonatal Intensive Care Unit for whom intravenous lipid therapy was ordered (mean gestational age 34 weeks), the second study included neonates receiving parenteral nutrition (mean gestational age 32.8 weeks). Before-After study: Australia [2]. Median (inter-quartile range) gestational age (37 weeks (33,39) vs. 36 weeks (33,39)), mean (standard deviation) admission weight of 2442 g (101) versus 2476 g (104).

Outcomes	№ of participants	Certainty of the evidence	Relative effect	Anticipated absolute effects* (95% CI)

	(studies) Follow-up	(GRADE)	(95% CI)	Risk with parenteral nutrition aqueous phase or the lipid emulsion administration (hang) time of 24 hours	Risk difference with parenteral nutrition aqueous phase or the lipid emulsion administration (hang) time of greater than 24 hours
Mortality: RCT: set replacement: Lipid assessed with: 72 versus 24 hours (neonatal population only)	1189 (1 RCT)	⨁◯◯◯ Very low[a,b,c,]	**RR 1.79** (0.97 to 3.32)	Study population	
				44 per 1,000	**35 more per 1,000** (1 fewer to 102 more)
Neurodevelopmental impairment - not measured	-	-	-	-	-
Adverse effects: RCT: set replacement: 1 study lipids; 1 study lipid and aqueous solutions assessed with: Catheter-related bloodstream infection (48 hours + vs. 24 hours)	143 (2 RCTs)	⨁◯◯◯ Very low[f,g,h]	**RR 1.08** (0.07 to 16.95)	Study population	
				14 per 1,000	**1 more per 1,000** (13 fewer to 216 more)
Adverse effects: RCT: set replacement: lipid and aqueous solutions assessed with: Infusate-related bloodstream infection (48 hours + vs. 24 hours)	341 (1 RCT)	⨁◯◯◯ Very low[a,c,d]	**RR 0.58** (0.25 to 1.35)	Study population	
				60 per 1,000	**25 fewer per 1,000** (45 fewer to 21 more)
Adverse effects: RCT: set replacement: lipid and aqueous solutions assessed with: All-cause bloodstream infection (48 hours + vs. 24 hours)	148 (1 RCT)	⨁◯◯◯ Very low[a,c,d,]	**RR 0.81** (0.44 to 1.49)	Study population	
				255 per 1,000	**48 fewer per 1,000** (143 fewer to 125 more)
Adverse effects: Before-After study: Hang time aqueous solutions assessed with: central line–associated blood stream infection (CLABSI per 1000-line days)	260 (1 non-randomised study)	⨁◯◯◯ Very low[d,h]	-	24 hours vs. 48 hours hang time for CLABSI per 1000-line days 0.8 vs. 0.4 respectively *P*<0.01	
Fully breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Fully breastfeeding at hospital discharge - not measured	-	-	-	-	-
Time to full enteral feeds (days) - not measured	-	-	-	-	-
Faltering growth/body composition - not measured	-	-	-	-	-
Duration of initial hospital stay - not measured	-	-	-	-	-
Bronchopulmonary dysplasia - not measured	-	-	-	-	-
Necrotizing enterocolitis - not measured	-	-	-	-	-
Sepsis: proven or suspected: Before-After study: Hang time aqueous solutions assessed with: Central venous catheter-related	1011 (1 non-randomised study)	⨁◯◯◯ Very low[d,h]	not estimable	Study population	
				4 per 1,000	**4 fewer per 1,000**

sepsis					(4 fewer to 4 fewer)
Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost: Before-After study aqueous solutions assessed with: Annual savings (AUD)	260 (1 non-randomised study)	⨁◯◯◯ Very low[d,h]	-	Costs including purchasing and dispensing of standard or non-standard bags 48 hours = AUD190,153 vs. 24 hours = AUD287,756. Yearly savings of AUD 97,603.00 with change to longer hang time (24 hours vs. 48 hours).	
Time to full sucking feeds - not measured	-	-	-	-	-

a)Downgraded one level for risk of bias
b. Downgraded one level for indirectness as the evidence is unlikely to include any very or extremely preterm infants and the study reported on intravenous lipids
C) Downgraded two levels for imprecision with very wide confidence intervals that cross the line of no effect
d. Downgraded one level for indirectness as evidence is based on a single study
e. Upgraded one level for large effect
f. Downgraded two levels for inconsistency with I2= >80%
g. Downgraded two levels for indirectness. The study/studies did not report on whether the population included neonates or not

h. Downgraded two levels for risk of bias - before-after study in a single centre, no blinding, no confounding variables examined
i. Downgraded one level for imprecision as evidence is based on very few events

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	**Set replacement** [1] **Mortality: RCT:** Set replacement: No significant increase in risk of neonatal mortality for longer time between set change for lipid of 72 hours or more versus 24 hours (35 more per 1,000; 1 fewer to 102 more). [Critical] **Adverse effects: RCT**: Set replacement: Longer time between set changes had no significant effect in risk for catheter-related bloodstream infection at 48 hours + vs. 24 hours (1 more per 1,000; 13 fewer to 216 more) [Critical] **Undesirable effects for Māori** No additional evidence available	In the [1] review, mortality was reported in two studies Fox 1999 and Matlow 1999. Fox 1999 did not report mortality in the study, only that "Three patients in the 48-hour group died before samples were taken". The Cochrane review reflects that there were 3 deaths vs. 0 deaths. It does not mean there were no deaths in the 24-hour group. We have therefore not included this study for the outcome of mortality in this guideline question. The data is based on Matlow 1999 who noted that the excess deaths in the 72-hour group could not clearly be attributed to bacteraemia.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low	Very low certainty of evidence overall	

○ Low ○ Moderate ○ High ○ No included studies	**Certainty of evidence for Māori** No additional evidence available	

Outcomes	Importance	Certainty of the evidence (GRADE)
Mortality: RCT: set replacement: Lipid assessed with: 72 versus 24 hours (neonatal population only)	CRITICAL	⨁◯◯◯ Very low
Neurodevelopmental impairment - not measured	CRITICAL	-
Adverse effects: RCT: set replacement: 1 study lipids; 1 study lipid and aqueous solutions assessed with: Catheter-related bloodstream infection (48 hours + vs. 24 hours)	CRITICAL	⨁◯◯◯ Very low
Adverse effects: RCT: set replacement: lipid and aqueous solutions assessed with: Infusate-related bloodstream infection (48 hours + vs. 24 hours)	CRITICAL	⨁◯◯◯ Very low
Adverse effects: RCT: set replacement: lipid and aqueous solutions assessed with: All-cause bloodstream infection (48 hours + vs. 24 hours)	CRITICAL	⨁◯◯◯ Very low
Adverse effects: Before-After study: Hang time aqueous solutions assessed with: central line–associated blood stream infection (CLABSI per 1000-line days)	CRITICAL	⨁◯◯◯ Very low
Fully breastmilk feeding at hospital discharge - not measured	CRITICAL	-
Fully breastfeeding at hospital discharge - not measured	IMPORTANT	-
Time to full enteral feeds (days) - not measured	IMPORTANT	-
Faltering growth/body composition - not measured	IMPORTANT	-
Duration of initial hospital stay - not measured	IMPORTANT	-
Bronchopulmonary dysplasia - not measured	IMPORTANT	-
Necrotizing enterocolitis - not measured	IMPORTANT	-
Sepsis: proven or suspected: Before-After study: Hang time aqueous solutions assessed with: Central venous catheter-related sepsis	IMPORTANT	⨁◯◯◯ Very low
Retinopathy of prematurity - not measured	IMPORTANT	-
Anaemia of prematurity - not measured	IMPORTANT	-
Cost: cost of intervention, cost of neonatal care and life-long cost: Before-After study aqueous solutions assessed with: Annual savings (AUD)	IMPORTANT	⨁◯◯◯ Very low

Time to full sucking feeds - not measured	NOT IMPORTANT	-

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability **Values for Māori** No additional research available.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	**Longer versus shorter time between changing sets - Very low certainty evidence** Lipid: Uncertain effect on mortality (lipid 72 versus 24 hours), adverse effects (catheter-related bloodstream infection, infusate-related bloodstream infection, all-cause bloodstream infection) **Longer versus shorter hang time - Very low certainty evidence** Reduction in sepsis Probable reduction in adverse effect (central line-associated bloodstream infection per 1000-line days) Large reduction in costs of parenteral nutrition and neonatal nursing labour **Balance of effects for Māori** No additional evidence	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings	**Parenteral Nutrition Standard Solution Prices** **Aotearoa New Zealand Hospital A** Aqueous solution bags $140 per 750 mL bag SMOFLipid & Multi 12/Influvite syringe - $50.50	

○ Varies ○ Don't know	Giving sets: Aqueous solutions ($7.18 + $2.77 = $9.95) Lipid emulsion $7.82 *Current Hang Time:* Aqueous solution bags 48 hours SMOF Lipid is 50 mL syringe 48 hours (but some hospitals change lipid after 24 hours). **Aotearoa New Zealand Hospital B** Aqueous solution bags costs $117.50 SMOFLipid & Soluvit/Vitalipid syringe costs $71.04 Giving sets: Aqueous solutions ($7.18 + $2.77 = $9.95) Lipid emulsion $7.82 *Current Hang Times:* Aqueous solution (PN) bags and lines 96 hours SMOFLipid is 50 mL syringe and lines 48 hours ***Saving per infant to change*** aqueous solution bags and lines after 96 hours vs. 48 is $118 - $140 per 4 days ***Saving per infant to change*** lipid emulsion bags and lines after 48 hours vs. 24 is $117 - $158 per 4 days **Additional costs** Nursing time to administer IVN and change sets	

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	Although [2] is an Australian study, it is only based on a single centre. Event rates for central line associated bloodstream infection which was the primary outcome were extremely low. There is high certainty of the local resource requirements (costs). **Certainty of evidence of required resources for Māori** No additional evidence available	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison	Data from a before-after study [2]: Costs including purchasing and dispensing of standard or non-	

○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	standard bags 48 hours = AUD 190,153 vs. 24 hours = AUD 287,756. Yearly savings of AUD 97 603.00 with change to longer hang time (24 hours vs. 48 hours). Nurses survey (n=50; 82% response rate)– 68.3% had decreased workload, 80.5% indicated time changing PN was reduced. Assuming infants have parenteral nutrition for a mean of 10 to 12 days, the intervention is ~$700 to $900 per infant cheaper than the comparison. **Cost effectiveness for Māori** No additional evidence available	

Equity

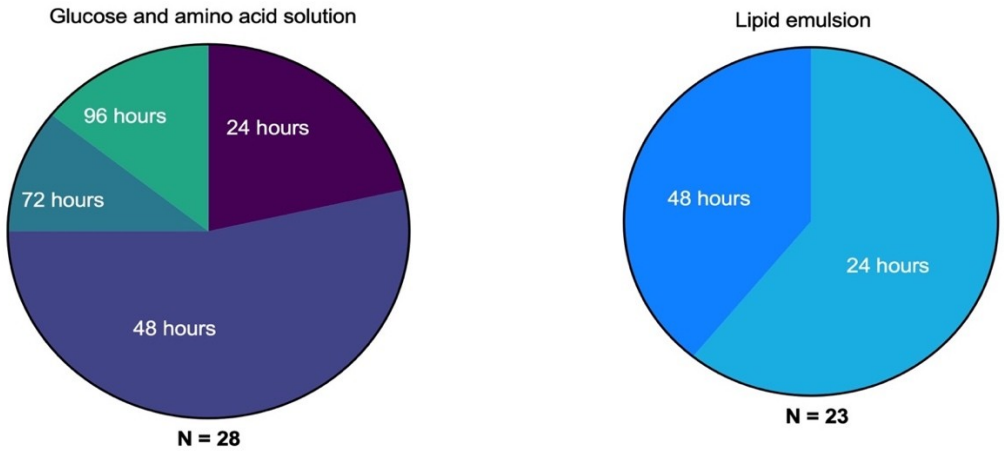
What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	**Equity for Māori** Influenced by the effects of colonisation, pēpi Māori are more likely to be born preterm, have more sepsis and neurodisability, both of which are associated with parenteral nutrition practices, and fewer survive. Thus, implementing standardised parenteral nutrition practices in Aotearoa New Zealand will contribute to achieving equitable health outcomes for preterm pēpi Māori and their whānau. **Equity for Pacific families** Implementing standardised parenteral nutrition practices in Aotearoa New Zealand will contribute directly to reducing health disparities for Pacific peoples **Equity for other underrepresented groups** Families from diverse backgrounds may not be informed about the safety and practical reasons behind hang time limits for parenteral nutrition. If errors occur, trust may be affected. Equity requires consistent safety protocols and proactive, inclusive communication that reassures and involves all families in understanding care procedures.	

Acceptability

Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	From a survey of Australasian neonatal dietitians conducted in 2024 [3]. **Parenteral nutrition hang times in NZ and Australian neonatal units**  	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Hang times (and administration set changes) of greater than 24 hours are in widespread use, so it is feasible in Aotearoa New Zealand. **Feasibility for Māori** No additional evidence available	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF	**Very low**	Low	Moderate	High			No included studies

	JUDGEMENT						
EVIDENCE							
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	**High**			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

References

1. Ullman, A.J.; Cooke, M.L.; Gillies, D.; Marsh, N.M.; Daud, A.; McGrail, M.R.; O'Riordan, E.; Rickard, C.M. Optimal timing for intravascular administration set replacement. *Cochrane Database Syst. Rev.* **2013**, *2013*, CD003588, doi:10.1002/14651858.CD003588.pub3.
2. Balegar, V.K.; Azeem, M.I.; Spence, K.; Badawi, N. Extending total parenteral nutrition hang time in the neonatal intensive care unit: is it safe and cost effective? *J. Paediatr. Child Health* **2013**, *49*, E57-61, doi:10.1111/jpc.12023.

3. Cormack, B.; Oliver, C.; Anscombe, Y.; Carson, G.; Allworth, S.; Gilroy, M.; Page D.; Little, H; Alexander,T.; Australasian Neonatal Dietitians Network (ANDiN). Progress and Variation in Nutrition Care for Preterm Infants in Australasia: Results From the 2024 Australasian Neonatal Dietitians Network Survey. *J Paediatr Child Health*. **2026** Jan 8. doi: 10.1111/jpc.70281. Epub ahead of print. PMID: 41503953.

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