EtD 4. Should lower parenteral fluid vs. Higher parenteral fluid be used for preterm infants receiving parenteral nutrition?

POPULATION:	Preterm infants receiving parenteral nutrition
INTERVENTION:	Lower parenteral fluid
COMPARISON:	Higher parenteral fluid
MAIN OUTCOMES:	**Critical outcomes** Mortality Necrotising enterocolitis Bronchopulmonary dysplasia Adverse effects – patent ductus arteriosus Faltering growth/body composition **Important but not critical** Neurodevelopmental impairment Fully breastfed or breastmilk feeding at hospital discharge Time to full enteral feeds Duration of initial hospital stay 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 guideline recommendation. Patient perspective
BACKGROUND:	The fluid and electrolyte requirements of preterm infants are unique due to significant fluid shifts in the first days and weeks after birth. At birth, preterm infants have an excess of extracellular fluid, which naturally decreases during the initial postnatal period. However, their immature organ systems often limit their ability to take in sufficient water and nutrients orally, leaving them unable to regulate water balance effectively. Inadequate water intake can lead to dehydration, while excessive water intake can cause complications such as heart and lung problems or intestinal damage. Intravenous or parenteral fluid therapy is, therefore, a critical aspect of neonatal care. It aims to maintain optimal hydration, electrolyte balance and nutritional support while minimising the risk of complications, such as patent ductus arteriosus (affecting the heart), bronchopulmonary dysplasia (affecting the lungs), or necrotising enterocolitis (causing intestinal damage). Fluid requirements vary with postnatal age and gradually increase during the first week after birth to meet growing metabolic demands. Parenteral fluid volumes are carefully adjusted based on factors such as birthweight, gestational age, clinical condition, blood biochemistry, and urine output. Excessive fluid intake has been linked to a higher risk of patent ductus arteriosus, bronchopulmonary dysplasia, and necrotising enterocolitis, underscoring the importance of precise fluid management. Conversely, insufficient fluid provision can result in dehydration, electrolyte imbalances and inadequate weight gain. Standardised fluid management which is then adjusted for individual requirements is essential to support the health and development of preterm infants. However, due to a lack of evidence, there is great variation in fluid management protocols in

	clinical practice.
CONFLICT OF INTERESTS:	None

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence is based on a Cochrane review [1] and observational studies [2] looking at whether early fluid restriction prevents bronchopulmonary dysplasia. 1 RCT [3] and 11 observational studies were identified [4-14]. The data from these additional studies has not been combined due to the heterogeneity of study design and populations and eras of clinical practice. **Restricted versus liberal fluids** **Mortality: RCT:** There was no difference for restricted versus liberal fluids for death (28 fewer per 1,000; 68 fewer to 34 more) [Critical]. **Bronchopulmonary dysplasia: RCT:** There was no difference for restricted versus liberal fluids for bronchopulmonary dysplasia (38 fewer per 1,000; 94 fewer to 36 more) [Critical]. **Bronchopulmonary dysplasia: Observational study:** A pre-post cohort study (Diderholm 2022) [6] found no significant difference in bronchopulmonary dysplasia (Restricted 24/63; 38% vs 41/112; 36%). A cohort study reported that significantly more infants in the high-fluid group developed bronchopulmonary dysplasia in week 1 (low fluid 10/51; 20% vs. intermediate fluid 27/102; 26% vs. high fluid 27/51;53%; P<0.001) [Critical]. **Necrotising enterocolitis (NEC): RCT:** Restricted fluids was associated with a decreased risk for NEC compared with liberal fluids (52 fewer per 1,000; 72 fewer to 12 fewer) [Critical]. **Adverse effects: RCT:** Restricted fluids were associated with a significant decrease in patent ductus arteriosus (144 fewer per 1,000; 189 fewer to 81 fewer) [Critical]. **Adverse effects: Observational study**: A pre-post cohort study (Diderholm 2022) found no significant difference in patent ductus arteriosus ligation (Restricted 20/63; 32% vs. 39/112; 34%). A cohort study (Stephens 2008) [14] reported that significantly more infants in the high-fluid group developed patent ductus arteriosus in week 1 (low fluid 3/51; 6% vs. intermediate fluid 7/102; 7% vs. high fluid 10/51; 20%; P=0.024) [Critical]. **No faltering growth/body composition**: **Observational study**: A pre-post cohort study (Diderholm 2022) found no significant difference in % weight change at day 8 of life (Restricted -9 +/-7% vs. Liberal -10 +/- 6%). A cohort study (Stephens 2008) reported that infants in the low-fluid group had significantly lower average daily weight loss during week 1 than infants in the intermediate or high-fluid group (-8.3 +/- 11.6 vs. -12.8 +/- 10 vs. -14.4 +/- 13 g/kg/day, respectively) [Critical].	The review by Bollaboina [2] included 5 studies of mixed design including a case control study, 3 cohort studies and a post-hoc analysis of a RCT. The methodological quality of the studies is good. The data were not pooled. The Bell systematic review only included 5 RCTs comparing liberal versus restricted water intake provided primarily via parenteral infusion [1]. Liberal water was considered the standard. There was variability between studies on the commencement and duration of water intake. The studies were conducted in the pre-surfactant era. There was inconsistency in the definition of the volume of fluids provided in the restricted and liberal groups Sweden [4]: Retrospective cohort study: Infants born 22-23 weeks' gestational age (n=36). Fluid balance data for infants in high humidification incubators (80 to 85%). USA [5]: Retrospective cohort study: Extremely low birthweight infants (n=226). Identified 151/226 (67%) of infants with moderate to severe bronchopulmonary dysplasia, 75/226 acted as controls.

	Fluid balance **Mortality: Observational studies:** A retrospective cohort study (Rallis 2024) found no significant difference in mortality between infants with fluid overload >/= 5% in first 24 hours (2/42; 5%) or those with no fluid overload (6/61; 10%). A retrospective chart review study (Levinson 2018) found no significant difference in mortality between infants receiving no additional/<15% additional fluids vs. >/=15% to 40% additional fluids vs. >/=40% additional fluids (1/112; 9% vs. 13/68; 19% vs. 4/20; 20%). A retrospective cohort study (Matsishita 2020) reported that 71/219 (32.4%) of infants died. Fluid overload in the first 72 hours after birth in an extremely preterm infant is associated with higher mortality rate (HR 3.07, 95%CI 1.71 to 5.53). Infants with severe fluid overload had a significantly higher mortality rate (72.2%) compared with groups with negative fluid balance (28.6%), mild (30.4%), and moderate (23.4%) fluid overload P = 0.002). Infants with severe fluid overload died significantly earlier during the neonatal intensive care unit stay than those without or less fluid overload (P < 0.0005) [Critical]. **Bronchopulmonary dysplasia: Observational studies:** A retrospective cohort study (Rallis 2024) found no significant difference in bronchopulmonary dysplasia between infants with fluid overload ≥5% in first 24 hours (20/42; 48%) or those with no fluid overload (23/61; 38%). A retrospective chart review study (Levinson 2018) found no significant difference in bronchopulmonary dysplasia between infants receiving no additional/<15% additional fluids vs. ≥15% to 40% additional fluids vs. ≥40% additional fluids (67/112; 60% vs. 49/68; 72% vs. 15/20; 75%) [Critical]. **Necrotising enterocolitis: Observational studies:** A retrospective chart review study (Levinson 2018) found no significant difference in bronchopulmonary dysplasia between infants receiving no additional/<15% additional fluids vs. ≥15% to 40% additional fluids vs. ≥40% additional fluids (9/112; 8% vs. 1/68; 1% vs. 2/20; 10%) [Critical]. **Adverse effects:** RCT: A RCT (Reller 1985) did not find a statistical difference in the incidence of haemodynamically stable patent ductus arteriosus between fluid intake and percent of birthweight loss during the first five days of life 17/26 (65.4%) in the restricted group 1 and 15/24 (62.5%) in the more restricted group 2 [Critical]. **Adverse effects:** Observational studies: A retrospective cohort study (Rallis 2024) found infants with fluid overload ≥5% in first 24 hours were more likely to be diagnosed with haemodynamically significant patent ductus arteriosus compared with infants without fluid overload (48% vs. 20% respectively; P=0.004). A retrospective chart review study (Levinson 2018) found no significant difference in patent ductus arteriosus between infants receiving no additional/<15% additional fluids vs. ≥15% to 40% additional fluids vs. ≥40% additional fluids (38/112; 34% vs. 30/68; 44% vs. 11/20; 55%). A retrospective cohort study (Mirza 2023) found that higher fluid intake in first 2 days of life is associated with prolonged duration of haemodynamically significant patent ductus arteriosus (hsPDA) in extremely preterm infants (Day 1: <1 week hsPDA median 110 (IQR 94 to 127) mL/kg/day vs. ≥1 week hsPDA median 130 (IQR 112 to 148) mL/kg/day; P<0.001 and Day 2: < 1 week hsPDA median 142 (IQR 125 to 154) mL/kg/day vs. ≥1 week hsPDA median 158 (IQR 135 to 180) mL/kg/day; P<0.009) [Critical]. **No faltering growth/body composition**: Observational study: A retrospective cohort study (Agren 2022) looked at fluid balance in infants 22-23 weeks' gestation. With a total fluid intake starting at a mean of 127 +/- 23 mL/kg/day on day 1, there was a maximum weight loss of -9+/-	[6] Sweden: Pre-Post cohort study: Infants born 22-26 weeks' gestation. N=63 restrictive regimen (initial total fluid volume of 65 mL/kg/day was recommended with a scheduled daily stepwise increase of 10 mL/kg/day up to 170 mL/kg/day). N=112 liberal regimen (total fluids were started at 95 mL/kg/day (GA 22–24 weeks) and 85 mL/kg/day (GA 25–26 weeks), respectively, daily stepwise increase of 10 mL/kg/day at clinical discretion. Taiwan: Retrospective chart review [7]: Infants (n=75) <32 weeks' gestation and birthweight <1500 g. USA: Retrospective chart review [9]: Very low birthweight infants (N=200). Fluid management day 1 of life. Three groups no additional/<15% additional fluids (n=112) received mean 100 +/- 13 mL/kg/day vs. >/=15% to 40% additional fluids received mean 132 +/- 16 mL/kg/day vs. >/=40% additional fluids received mean 157 +/- 20 mL/kg/day. USA: Prospective cohort [10]: Infants with birthweight 500 to 1500 g. Fluid management and bronchopulmonary dysplasia (n=865 of whom 224 (26%) had chronic lung disease). Brazil: Retrospective cohort study [11]: Infants with birthweight <1000 g (n=219) USA: Retrospective cohort [12]: Extremely preterm infants <29 weeks' gestation with haemodynamically significant patent ductus arteriosus

	5% at a mean postnatal age of 3 days. At 1-week postnatal age, mean weight loss was -2+/-7%, with 16/36 (44%) of infants having regain birthweight. The total fluid intake on day 7 was a mean of 178 +/-22 mL/kg/day. **Sepsis: Observational studies:** A retrospective cohort study (Rallis 2024) found no significant difference in sepsis between infants with fluid overload ≥5% in first 24 hours (14/42; 33%) or those with no fluid overload (26/61; 43%) [Important]. **Duration of hospital stay: Observational studies:** A retrospective cohort study (Rallis 2024) found no significant difference in length of stay between infants with fluid overload ≥5% in first 24 hours (median 83 days; IQR 64, 99) or those with no fluid overload (median 77; IQR 56,94) [Important]. **Fluids and risk/prevention of bronchopulmonary dysplasia** **Bronchopulmonary dysplasia:** Observational studies in systematic review: In a case-control study of 157 infants, a seven-day cumulative fluid overload threshold of 36.2% was the most accurate predictor for developing BPD in preterm neonates. A cohort study reported 159/389 infants with BPD; infants with a lower intake of energy and lipids and a higher intake of fluids in the first week after birth were more susceptible to BPD. In a retrospective cohort study of 191 preterm infants (23-28 weeks' gestational age), higher cumulative fluid balance was linked to increased odds of death (BPD). The absolute odds ratio (AOR) was 1.56 (95%CI 1.11-2.25). In a post-hoc analysis of an RCT including 1,382 ELBW infants, higher fluid intake and a lack of weight loss were significantly associated with a greater risk of death or BPD (p <0.001 and 0.006, respectively). Note that the RCT was conducted during the surfactant era. A prospective cohort study of 69 ventilated infants showed that a fluid volume of more than 131 mL/kg/day on day seven was associated with an increased risk of BPD (RR 2.09, 95% CI 1.14-3.85). **Bronchopulmonary dysplasia:** Observational study: A prospective cohort study (Marshall 1999) found that each 10 mL increase in fluids on day 2 of life was associated with an increase in BPD (OR 1.06; 95%CI 1.01 to 1.11). On each of the first five days of life, infants receiving greater amounts of fluid and experiencing less weight loss were at greater risk of developing BPD (Day 1 infants with BPD 120 +/-68 mL/kg/day vs. no BPD 100 +/- 26 mL/kg/day; P=0.0001; Day 5 infants with BPD 153 +/-39 mL/kg/day vs. no BPD 142 +/- 28 mL/kg/day; P=0.0002). A retrospective chart review (Guo 2015) found severe BPD was associated with higher volume of fluids received on Day 2 to 4 of life compared with infants with non-severe BPD (346.44 +/-42.38 mL/kg vs. 323.91 +/-27.62 mL/kg, p=0.007). Infants who received more than 345 mL/kg of total fluids from the 2nd to 4th days after birth were around 6.25 times more likely to develop severe BPD. A retrospective cohort study (Al-Jebawi 2020) found that during the first week after birth, the mean fluid intake was significantly higher in the moderate-severe BPD group than the control group. Higher fluid intake was associated with the risk of moderate to severe BPD (BPD fluid intake 172 +/- 41 mL/kg/day vs. control 147 +/- 14 mL/kg/day; P, 0.001; OR 1.03; 95%CI 1.01 to 1.04 [Critical]. **Desirable effects for Māori**	for < 1 week (n=50) and for >/=1 week (n=75). From Day 1- 4 of life the actual fluid intake was significantly higher than prescribed fluids in both groups. Greece: Retrospective cohort study [13]: 103 infants </= 30 weeks' gestation and </= 1500g. Infants started on 80-100 mL/kg/day. Looked at effects of fluid overload >5% in first 24 hours of life. USA: RCT [3]: very low birthweight infants 750 to 1500 g, 27 to 33 weeks' gestation. Infants in group 1 received a mean of 80 mL/kg/day of fluid on the first day of life; input was then gradually increased to 140 mL/kg/day by the fourth and fifth days of life. Infants in group 2 received an average of 65-70 mL/kg/day of fluid for the first three days of life, then input was increased to an average of 80 mL/kg/day by Day 5. USA: Retrospective cohort study [14]: 204 extremely low birthweight infants. Grouped into low-intermediate- and high-fluid intake. Day one Low (n=51) <96 mL/kg/day; intermediate (n=102) 96-125 mL/kg/day; high (n=51) >125 mL/kg/day. Day 5 Low <135 mL/kg/day; intermediate 135-170 mL/kg/day and high >170 mL/kg/day.

	None reported	

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with higher parenteral fluid	Risk difference with lower parenteral fluid
Mortality: RCT	582 (5 RCTs)	⨁⨁◯◯ Low[a,b]	**RR 0.81** (0.54 to 1.23)	Study population	
				148 per 1,000	**28 fewer per 1,000** (68 fewer to 34 more)
Necrotising enterocolitis: RCT	526 (4 RCTs)	⨁◯◯◯ Very low[a,b,c]	**RR 0.43** (0.21 to 0.87)	Study population	
				91 per 1,000	**52 fewer per 1,000** (72 fewer to 12 fewer)
Bronchopulmonary dysplasia: RCT	526 (4 RCTs)	⨁◯◯◯ Very low[a,b,d]	**RR 0.85** (0.63 to 1.14)	Study population	
				255 per 1,000	**38 fewer per 1,000** (94 fewer to 36 more)
Adverse effects: RCT assessed with: Patent ductus arteriosus	526 (4 RCTs)	⨁◯◯◯ Very low[a,b,c]	**RR 0.52** (0.37 to 0.73)	Study population	
				300 per 1,000	**144 fewer per 1,000** (189 fewer to 81 fewer)
Faltering growth/body composition: RCT assessed with weight loss (% of birthweight)	326 (3 RCTs)	⨁⨁◯◯ Low[a,b]	-	The mean faltering growth/body composition: RCT was **0**	MD **1.94 higher** (0.82 higher to 3.07 higher)
Neurodevelopmental impairment - not measured	-	-	-	-	-
Fully breastfed or breastmilk feeding at hospital discharge - not measured	-	-	-	-	-
Time to full enteral feeds - not measured	-	-	-	-	-
Duration of initial hospital stay - not measured	-	-	-	-	-
Sepsis: proven or suspected - not measured	-	-	-	-	-
Retinopathy of prematurity - not measured	-	-	-	-	-
Anaemia of prematurity - not measured	-	-	-	-	-
Cost: cost of intervention, cost of neonatal care and life-long cost - not measured	-	-	-	-	-
Time to full sucking feeds (<0.5 days) - not measured	-	-	-	-	-

a. Downgraded one level due to concerns of risk of bias
b. Downgraded one level due to indirectness due to lack of consistency in the regimens applied for commencing and the duration of restricted or liberal water intake
c. Downgraded one level for inconsistency with I2 >60%
d. Downgraded one level for imprecision with confidence intervals that cross the line of no effect

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	**Faltering growth or body composition: RCT:** Postnatal weight loss was higher with restricted versus liberal fluids (MD 1.94% of birthweight higher, 8.2 higher to 37 higher). **Undesirable effects for Māori** No additional data	The review by Bollaboina (2023) included 5 studies of mixed design including a case control study, 3 cohort studies and a post-hoc analysis of a RCT. The methodological quality of the studies is good. The data were not pooled. The Bell (2014) systematic review only included 5 RCTs comparing liberal versus restricted water intake provided primarily via intravascular infusion. Liberal water was considered the standard. There was variability between studies on the commencement and duration of water intake. The studies were conducted in the pre-surfactant era.

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	All of the observational studies and post-hoc analysis of a RCT in the Bollaboina (2023) review concurred that fluid restriction in the early days will decrease the risk of **bronchopulmonary dysplasia**. The quality of the evidence is good for observational studies. The Bell (2014) review found that restricted water intake significantly increased postnatal weight loss and significantly reduced the risks of patent ductus arteriosus and NEC. But there were associated non-significant trends for increased risk of dehydration and reduced risks of bronchopulmonary dysplasia, intracranial haemorrhage, and death. **Certainty of evidence for Māori** No additional data	The reviews do not consider sodium/potassium intake.

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 data	

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

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Lower parenteral fluid reduced postnatal weight but reduced the risk of **bronchopulmonary dysplasia**, patent ductus arteriosus and NEC. The risk of dehydration needs to be monitored. **Balance of effects for Māori** No additional data	

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Minimal resources needed. **Resources required for Māori** No additional data	

Certainty of evidence of required resources
What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Very low ○ Low ○ Moderate ● High ○ No included studies	No cost data identified **Certainty of evidence of required resources for Māori** No data identified	

Cost effectiveness

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

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No cost data identified **Cost effectiveness for Māori** No data identified	

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 all ethnicities and underrepresented groups. **Equity for underrepresented groups** Families living rurally or outside tertiary centres may experience variable IV fluid practices due to resource gaps or local protocols. Inconsistent care can impact infant outcomes and prolong hospitalisation. Nationally standardised, equity-informed guidance is essential to ensure all preterm infants receive safe and appropriate IV fluid therapy regardless of setting.	

Acceptability
Is the intervention acceptable to key interest-holders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Probably acceptable **Acceptability for Māori** No additional data	

Feasibility
Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Probably feasible **Feasibility for Māori** No evidence available	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	**Does not favour either the intervention or the comparison**	Probably favours the intervention	Favours the intervention	Varies	Don't know

	JUDGEMENT						
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
o	o	●	o	o

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