

## A.8 FAST AND SLOW ADVANCEMENT OF FEEDING

### Recommendation and remarks

#### RECOMMENDATION A.8 (UPDATED)

**In preterm or low-birth-weight (LBW) infants, including very preterm (< 32 weeks' gestation) or very LBW (< 1.5 kg) infants, who need to be fed by an alternative feeding method to breastfeeding (e.g. gastric tube feeding or cup feeding), feed volumes can be increased by up to 30 ml/kg per day.** *(Conditional recommendation, moderate-certainty evidence)*

#### Remarks

- The recommendation is conditional on shared decision-making with parents; this includes informing parents about the benefits and risks and the need for further research.
- The GDG noted that the trials enrolled infants immediately after birth (i.e. day 1 – within 24 hours of birth) so results are generalizable to very early feeding of LBW infants from this time.
- All trials excluded babies with congenital anomalies and birth asphyxia, so careful consideration is needed in applying these recommendations to infants with these conditions. Feed advancement should be based on clinical judgement for these infants.
- All trials compared fast advancement (increments of 30–40 ml/kg per day) with slow advancement (increments of 15–25 ml/kg per day). So the GDG took the conservative value of 30 ml/kg per day as the threshold for fast feed advancement. This value is also consistent with many national guidelines.
- All studies were in hospitalized infants, so the GDG could not make a recommendation on feeding outside the hospital.
- The GDG did not make separate recommendations for babies fed formula milk versus human milk as there was insufficient evidence (only one trial gave formula as the sole diet while the remainder gave human milk only or a mix of human milk and formula).
- The GDG considered that advancement should continue until full maintenance feed volumes are reached. These volumes should be based on local guidelines.
- The GDG noted that further research is needed to understand the neurodevelopmental effects of fast feed advancement.

#### Background and definitions

There is substantial variation in the definitions of fast and slow advancement of enteral feeding volumes for preterm and LBW babies in the first weeks after birth. Advancement increments commonly vary between 10 and 40 ml/kg per day (93,94). Up to the 1990s, the standard of care was a conservative (“slow rate”) approach because of concerns about

feed intolerance (e.g. gagging, vomiting and apnoea post-feed) and necrotizing enterocolitis (56). In 2011, WHO recommended that feeds could be advanced by up to 30 ml/kg per day with careful monitoring for feed intolerance in infants weighing under 1.5 kg (19). However, there have been new studies published since that time (95).

## Summary of the evidence

OVERVIEW	A.8 Fast and slow advancement of feeding
<b>PICO</b>	<p><b>Population</b> – Preterm or LBW infants</p> <p><b>Intervention</b> – Fast advancement of enteral feeds (<math>\geq 30</math> ml/kg per day)</p> <p><b>Comparator</b> – Slow advancement of enteral feeds (<math>&lt; 30</math> ml/kg per day)</p> <p><b>Outcomes</b> – All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up</p>
<b>Timing, setting, subgroups</b>	<p><b>Timing of the intervention</b> – Birth to 6 months of age</p> <p><b>Setting</b> – Health-care facility or home in any country or setting</p> <p><b>Subgroups</b></p> <ul style="list-style-type: none"> <li>• Gestational age at birth (<math>&lt; 32</math> weeks, <math>\geq 32</math> weeks)</li> <li>• Birth weight (<math>&lt; 1.5</math> kg, <math>\geq 1.5</math> kg)</li> <li>• Type of milk (human milk, formula milk)</li> </ul>

### Effectiveness: Comparison – Fast versus slow advancement of enteral feeds

#### Sources and characteristics of the evidence

The effectiveness evidence was derived from a systematic review of 12 RCTs enrolling 4084 preterm or LBW infants (96). The trials were conducted in Bangladesh, Colombia, India, the Islamic Republic of Iran, Ireland, South Africa, Türkiye, the United Kingdom and the USA. The United Kingdom Speed of Increasing Milk Feeds trial (SIFT) was the largest trial ( $n=2973$ ) (97). Most studies included clinically stable infants and excluded those with perinatal asphyxia or haemodynamic instability. The infants were typically randomized on days 1–4 after birth. Intervention (fast advancement) increments ranged from 30 to 40 ml/kg per day. Comparator (slow advancement) increments ranged from 10 to 25 ml/kg per day. The target volume of full feeding ranged from 120 to 180 ml/kg per day. Seven studies enrolled very preterm infants born before 32 weeks' gestation. Three studies used human milk, one used infant formula, and seven used a combination of the two.

#### Critical outcomes

For fast compared with slow advancement of enteral feeding for preterm or LBW infants, 11 trials reported all-cause mortality, 12 reported morbidity (12 reported necrotizing enterocolitis, 9 sepsis, 2 apnoea), 6 reported growth outcomes (6 reported time to regain birth weight, 1 WAZ at discharge, 1 weight at discharge, 1 weight gain, 1 head circumference) and 1 reported neurodevelopmental outcomes (disability). (Full details are provided in GRADE Table A.8, in the Web Supplement.)

■ **Mortality:** Moderate-certainty evidence from 11 trials with a total of 4132 participants suggests little or no effect on all-cause mortality by hospital discharge (RR 0.93, 95% CI 0.73 to 1.18).

- **Morbidity:** Low-certainty evidence from two trials totalling 153 participants suggests a decrease in apnoea by hospital discharge (RR 0.72, 95% CI 0.47 to 1.12). Moderate-certainty evidence from 12 trials totalling 4291 participants suggests little or no effect on necrotizing enterocolitis by hospital discharge (RR 0.89, 95% CI 0.68 to 1.15). Moderate-certainty evidence from nine trials totalling 3648 participants suggests little or no effect on sepsis by hospital discharge (RR 0.92, 95% CI 0.83 to 1.03).
- **Growth:** High-certainty evidence from six trials totalling 993 participants suggests a decrease in time to regain birth weight by hospital discharge (MD -3.69, 95% CI -4.44 to -2.95). Low-certainty evidence from one trial with 2793 participants suggests little or no effect on WAZ by hospital discharge (MD 0.0, 95% CI -0.08 to 0.08). Low-certainty evidence from one trial with 131 participants suggests little or no effect on weight gain (in grams per kilogram per day) by hospital discharge (MD 0.5, 95% CI -1.19 to 2.19). Low-certainty evidence from one trial with 100 participants suggests little or no effect on weight in grams by hospital discharge (MD -29.0, 95% CI -74.89 to 16.89). Low-certainty evidence from one trial with 2793 participants suggests little or no effect on head circumference (head circumference z score) by hospital discharge (MD -0.1, 95% CI -0.22 to 0.02).
- **Neurodevelopment:** Low-certainty evidence from one trial of 2325 participants suggests little or no effect on neurodevelopment (neurodevelopmental disability measured using a validated test) at 24 months corrected age (RR 1.12, 95% CI 0.98 to 1.27).

### Other outcomes

There was a decrease in length of hospital stay (days to discharge) (MD -3.08, 95% CI -4.34 to -1.81; 7 trials, 3864 participants) and little or no effect on feed intolerance by hospital discharge (RR 0.92, 95% CI 0.77 to 1.10; 8 trials, 1114 participants).

### Subgroup analyses

No subgroup differences were seen for gestational age and birth weight for any critical outcome.

### Values and acceptability

The systematic review about what matters to families about the care of the preterm or LBW infant (see Table 1.1) reported that families want to be involved in delivering care to infants, including supporting nutrition, and want to take an active role in deciding what interventions are given to infants, including what and how they are fed (14). No specific evidence was located about whether families value fast versus slow feed advancement for their preterm or LBW baby or whether they find the different rates more or less acceptable.

## Summary of judgements

### Comparison: Fast vs slow advancement of enteral feeds (A.8)

#### Justification

- Evidence of moderate benefits: decrease in apnoea (*moderate-certainty evidence*), decrease in time to regain birth weight (*high-certainty evidence*), decreased length of hospital stay (*moderate-certainty evidence*)
- Evidence on harms uncertain: impaired neurodevelopment (*low-certainty evidence*)
- Evidence of little or no effect on: mortality, necrotizing enterocolitis, sepsis, weight gain, head circumference (*low-certainty evidence*), feed intolerance (*moderate-certainty evidence*)

### Evidence-to-Decision summary

<b>Desirable</b>	Small
<b>Undesirable</b>	Unknown
<b>Certainty</b>	Moderate
<b>Balance</b>	Probably favours fast feed advancement
<b>Values</b>	Uncertainty or variability about outcomes
<b>Acceptability</b>	Probably acceptable
<b>Resources</b>	Negligible
<b>Feasibility</b>	Probably feasible
<b>Equity</b>	Equitable

### Resources required and implementation considerations

#### Organization of care

Feed advancement should be based on clinical judgement for all infants at home and in health-care facilities. In facilities, there can be fast advancement of feed volumes by up to 30 ml/kg per day.

#### Infrastructure, equipment and supplies

National or local guidance on infrastructure, equipment and supplies for health-care facilities should be used.

#### Workforce, training, supervision and monitoring

Health workers at all levels can support mothers and families. Standardized packages are needed for training, supervision and monitoring.

#### Feasibility and equity

No specific evidence was located about the feasibility and equity of providing slow or fast feed advancement to preterm or LBW babies.