

## A.2 MOTHER'S OWN MILK

### Recommendation and remarks

#### RECOMMENDATION A.2 (UPDATED)

**Mother's own milk is recommended for feeding of preterm or low-birth-weight (LBW) infants, including very preterm (< 32 weeks' gestation) or very LBW (< 1.5 kg) infants.** (Strong recommendation, low-certainty evidence)

#### Remarks

- The GDG made a strong recommendation despite low-certainty evidence because of the consistent harm from infant formula on two critical outcomes (necrotizing enterocolitis and infection) and lack of evidence of benefit from infant formula.
- The GDG also considered that providing mother's own milk is the standard of care across all countries and the core of many national policies and programmes.
- Mothers should also be encouraged and supported before and after birth to provide their own breast-milk (including colostrum) for their infants.

### Background and definitions

Mother's own milk confers important immune and nutritional advantages for preterm and LBW infants (54-56). Artificial formulas can be manipulated to contain higher amounts of important nutrients (such as protein) than mother's own milk (55,57). However,

formula milks do not contain the antibodies and immune modulators and primers present in human milk that protect the immature gastro intestinal tract' of preterm and LBW infants (19,58,59). In 2011, WHO recommended that mother's own milk should be given to all preterm and LBW infants (19).

### Summary of the evidence

OVERVIEW	A.2 Mother's own milk
<b>PICO</b>	<p><b>Population</b> - Preterm or LBW infants</p> <p><b>Intervention</b> - Infant formula (term or preterm)</p> <p><b>Comparator</b> - Mother's own milk</p> <p><b>Outcomes</b> - All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up</p>
<b>Setting, timing, subgroups</b>	<p><b>Timing of the intervention</b> - From 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 (&lt; 32 weeks, ≥ 32 weeks)</li> <li>• Birth weight (&lt; 1.5 kg, ≥ 1.5 kg)</li> <li>• Type of milk in the control group (mother's own milk as the sole diet, mother's own milk not the sole diet)</li> </ul>

#### Effectiveness: Comparison - Any formula milk versus mother's own milk

##### Sources and characteristics of the evidence

The effectiveness evidence was derived from an updated systematic review of 42 studies reporting on 89 638 preterm or LBW infants from 20 countries (Australia, Belgium, Chile, China, Germany, Ghana, Greece, India, Israel, Italy, Japan, Nepal, the Netherlands, New Zealand, Poland, Romania, Spain, Sweden, the United Kingdom and the USA) (60).

Studies were included if they compared infants who received formula as the sole or predominant

(> 50%) diet (intervention group) with infants who received mother's own milk as the sole or predominant (> 50%) diet (comparison group) in the first 28 days after birth. Of the 89 638 participants, approximately 87% of infants were very preterm (< 32 weeks' gestation) or VLBW (< 1.5 kg). Studies typically excluded infants with congenital anomalies or gastrointestinal or neurological problems.

All the included studies were observational; there were no RCTs. Thirty-six studies were from hospitals and six were from the "whole population" (all infants born in the study area regardless of whether they

were admitted to hospital). The largest study (72 997 participants) was an observational study of all infants under 32 weeks' gestation admitted to 777 neonatal intensive care units (NICUs) in the USA. The studies used a combination of milks in the intervention and comparison groups.

In the intervention group, all 42 studies used formula milk as the sole or predominant (> 50%) diet. Among these studies, 24 studies gave formula milk as the sole diet, 13 mixed formula with mother's own milk, 5 mixed formula with donor milk and mother's own milk, and 6 did not state whether they mixed formula milk with other milks. Twenty-one studies used preterm formula, 5 used term formula, 2 used a combination of preterm and term formula, and 14 did not state which type of formula was used.

In the comparison group, all 42 studies used mother's own milk as the sole or predominant (> 50%) diet. Among these studies, 9 studies gave mother's own milk as the sole diet, 17 mixed mother's own milk with donor human milk, and the remainder did not state if they mixed mother's own milk with other milks. Twenty studies used fortifier, 6 did not use fortifier and 16 did not state whether fortifier was provided.

Babies all received their feeds from birth until discharge or 28 days of age. Twenty-five used parenteral nutrition, 10 did not use parenteral nutrition and the remainder did not state if parenteral nutrition was used.

### Critical outcomes

For the comparison of any formula milk with mother's own milk, 5 studies reported all-cause mortality, 15 studies reported morbidity (15 reported necrotizing enterocolitis, 15 severe infection), 7 studies reported growth (3 reported weight-for-age z score [WAZ], 3 WAZ change, 9 length, 3 length-for-age z score [LAZ], 9 head circumference) and 8 studies reported neurodevelopment (8 reported cognitive outcomes, 3 language outcomes). (Full details are provided in GRADE Table A.2, in the Web Supplement.)

- **Mortality:** Low-certainty evidence from five observational studies of 9673 participants suggests little or no effect on all-cause mortality at latest follow-up (mean 116 days) (OR 1.26, 95% CI 0.91 to 1.76).
- **Morbidity:** Low-certainty evidence from 15 observational studies totalling 3013 participants suggests an increase in necrotizing enterocolitis

at latest follow-up (mean 44 days) (OR 2.99, 95% CI 1.75 to 5.11). Very-low-certainty evidence from 15 observational studies totalling 2562 participants suggests an increase in severe infection at latest follow-up (mean 31 days) (OR 1.52, 95% CI 0.98 to 2.37).

- **Growth:** Very-low-certainty evidence from three observational studies totalling 271 participants suggests little or no effect on weight (weight-for-age z score [WAZ]) between 39 and 416 weeks (MD 0.02, 95% CI -0.28 to 0.31). Very-low-certainty evidence from four observational studies totalling 74 130 participants suggests little or no effect on weight (WAZ change) from birth to discharge (mean 52 days) (MD 0.14, 95% CI -0.76 to 1.05). Very-low-certainty evidence from nine observational studies totalling 1048 participants suggests little or no effect on length (in centimetres) at latest follow-up (mean 58 days) (MD 0.33, 95% CI -0.4 to 1.05). Very-low-certainty evidence from three observational studies totalling 271 participants suggests little or no effect on length (LAZ) at 39 to 416 weeks (MD 0.06, 95% CI -0.81 to 0.92). Very-low-certainty evidence from nine observational studies totalling 1550 participants suggests little or no effect on head circumference (in centimetres) at latest follow-up (mean 45 days) (MD 0.26, 95% CI -0.35 to 0.87).
- **Neurodevelopment:** Very-low-certainty evidence from eight observational studies totalling 1560 participants suggests little or no effect on cognitive development at follow-up (range: 91 to 416 weeks) (standardized mean difference [SMD] 1.3 standard deviation [SD] lower, 95% CI -3.53 to 0.93). Very-low-certainty evidence from three observational studies totalling 587 participants suggests little or no effect on language development at follow-up (range: 39-104 weeks) (SMD 0.02 SD lower, 95% CI -0.39 to 0.43).

### Subgroup analyses

There was no evidence of a subgroup difference by gestational age, birth weight, or type of milk in the control group 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). Two qualitative reviews reported that parents understood the importance of expressing breast-milk for the care of their baby but also found it challenging to express breast-milk unless supported by hospital staff and adequately informed about resources (61,62). Reviews also report that families value having formula available if their circumstances demand it – for example, work commitments, maternity leave, night-time feeding, father/partner support (14).

### Resources required and implementation considerations

#### Organization of care

Mother’s own milk should be provided through direct breastfeeding wherever possible. If direct breastfeeding is not possible, then breast-milk can be expressed and provided using cups and gastric tubes.

#### Infrastructure, equipment and supplies

Breastfeeding requires no specific infrastructure, equipment or supplies. If expressed breast-milk is needed, milk can be expressed by hand or using

a manual breast pump. Supplies are also needed for cup and gastric tube feeding. National or local guidance for health-care facilities should be used.

#### Workforce, training, supervision and monitoring

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

#### Feasibility and equity

Difficulties related to breastfeeding and expressing breast-milk in hospitals can include lack of privacy, inadequate training from busy health workers, and feelings of stress and inadequacy from mothers and families (63). There are also studies that report difficulties in providing mother’s own milk when the mother and baby return home from hospital, including difficulties balancing work commitments, maternity leave, night-time feeding and father and partner support (14). There are many studies that report problems in sourcing clean water to reconstitute infant formula and wash receptacles in resource-limited settings (64,65).

## Summary of judgements

### Comparison: Any formula milk vs mother’s own milk (A.2)

#### Justification

- No evidence of benefits of infant formula
- Evidence of moderate harms from using infant formula instead of mother’s own milk: increased necrotizing enterocolitis (*low-certainty evidence*) and increased infections (*very-low-certainty evidence*)
- Evidence of little or no effect of using infant formula on mortality (*low-certainty evidence*), weight gain (*very-low-certainty evidence*) and neurodevelopment (*very-low-certainty evidence*)
- No evidence on other critical outcomes

### Evidence-to-Decision summary

<b>Benefits</b>	Benefits of infant formula are trivial or none
<b>Harms</b>	Harms of infant formula are moderate
<b>Certainty</b>	Low
<b>Balance</b>	Does not favour infant formula, favours mother’s own milk
<b>Values</b>	Probably no important uncertainty or variability about outcomes
<b>Acceptability</b>	Acceptability of infant formula varies, acceptability of mother’s own milk does not vary
<b>Resources</b>	Low to moderate (costs of infant formula), negligible (costs of mother’s own milk)
<b>Feasibility</b>	Feasibility of infant formula varies, feasibility of mother’s own milk does not vary, where it is available
<b>Equity</b>	Equity of infant formula varies, equity of mother’s own milk does not vary