

Executive summary

Introduction

Preterm infants have a gestational age below 37 weeks at birth and low-birth-weight (LBW) infants have a birth weight below 2.5 kg. Approximately 45% of all children under the age of five who die are newborns, and 60–80% of those newborns who die are premature and/or small for gestational age. Preterm and LBW infants have a 2- to 10-fold higher risk of mortality than infants born at term and with normal birth weight. Despite substantial progress over the last 10 years, the survival, health, growth and neurodevelopment of preterm and LBW infants remains concerning in many countries. Reasons include the complexities of caring for these vulnerable infants and preventing complications.

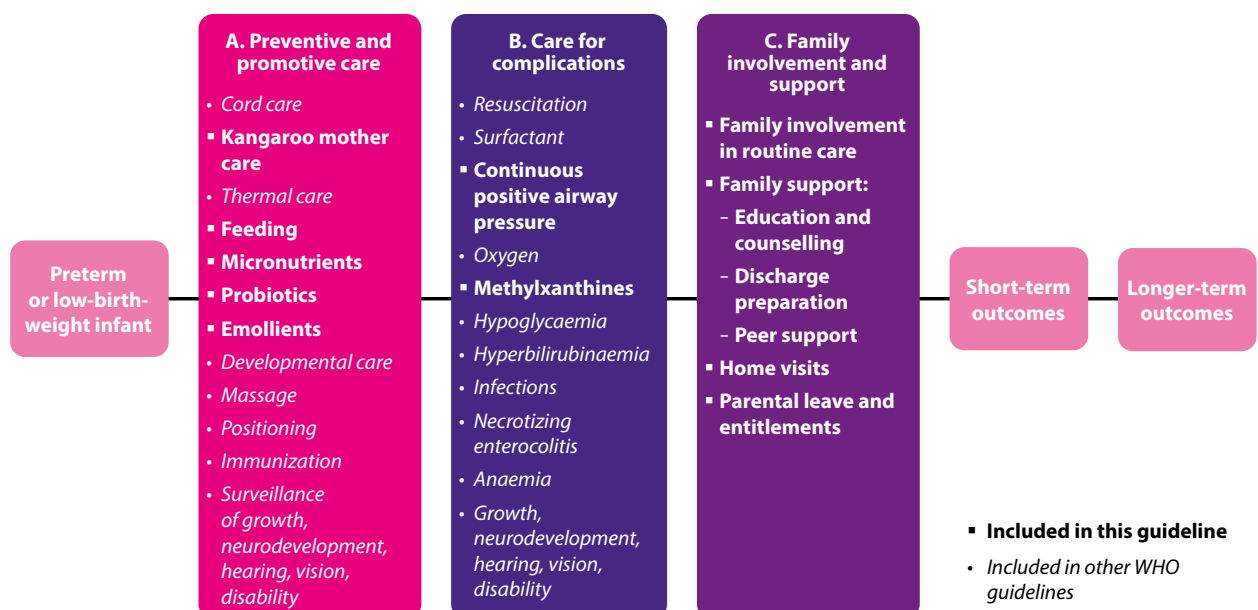
The care of preterm and LBW infants is a global priority. The WHO Departments of Maternal, Newborn, Child and Adolescent Health and Ageing (MCA) and Sexual and Reproductive Health and Research (SRH) have developed three guidelines for the care of preterm or LBW infants:

- *Guidelines on optimal feeding of low-birth-weight infants in low- and middle-income countries, 2011;*
- *WHO recommendations on interventions to improve preterm birth outcomes, 2015; and*
- *Recommendations for management of common childhood conditions, 2012.*

However, new evidence has emerged in many areas since the development of those guidelines. A review of 203 studies from low-, middle- and high-income countries about “what matters” to families about the care of their preterm or LBW infant reported that families want a positive outcome for their baby, to be involved in delivering care and to take an active role in deciding what interventions are given to their baby (these family values are listed in Table 1.1 in Chapter 1).

In December 2020, an international group of experts defined the scope and priority questions for the development of updated guidance about the care of preterm or LBW infants (see Figure 1 below, Table 1.2 in Chapter 1, and Web Annex A).

Figure 1. Scope of WHO recommendations for care of the preterm or low-birth-weight infant



Target audience

The recommendations in this guideline are intended to inform the development of national and subnational health policies, clinical protocols and programmatic guides. Therefore, the target audience includes national and subnational public health policy-makers, implementers and managers of maternal, newborn and child health programmes, health-care facility managers, supervisors/instructors for in-service training, health workers (including midwives, auxiliary nurse-midwives, nurses, paediatricians, neonatologists, general medical practitioners and community health workers), nongovernmental organizations, professional societies involved in the planning and management of maternal, newborn and child health services, academic staff involved in research and in the pre-service education and training of health workers, and those involved in the education of parents.

Guideline development methods

The guideline was developed using standard operating procedures in accordance with the process described in the *WHO handbook for guideline development*. This involved the convening of an Evidence Synthesis Team (EST) and an international Guideline Development Group (GDG) of experts. The process included: (i) identifying priority questions and outcomes, (ii) retrieval of the evidence, (iii) assessment and synthesis of the evidence, (iv) formulation of recommendations and write-up of the guideline, and (v) planning for dissemination, implementation, impact evaluation and updating of the recommendations.

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to appraise the quality and certainty of the quantitative evidence for each priority question, and for the qualitative evidence, the reviews were appraised using the GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative Research) tool. The DECIDE approach (Developing and Evaluating Communication strategies to support Informed Decisions and practice based on Evidence), an evidence-to-decision tool, was used to guide the evidence search, evidence synthesis and judgements on the different criteria by the EST, and the formulation of recommendations by the GDG. This included assessment of the effects (benefits and harms) of the interventions on infant outcomes, and consideration of the values of families and health workers, acceptability and feasibility of the interventions, the resources required, and equity.

Recommendations were developed using WHO Guidelines Review Committee criteria: “strong” recommendations are generally applicable to all preterm or LBW infants; “conditional” recommendations mean that the intervention is recommended under certain conditions; and a “good practice statement” was made for an intervention that was obviously beneficial and should be done in most circumstances, even though there was no, little or only very-low-certainty evidence. The GDG members examined and interpreted the evidence, formulated the wording of the final recommendations and provided related remarks and considerations at virtual meetings held between November 2021 and January 2022.

Recommendations

This guideline includes 25 recommendations and 1 good practice statement (see Table 1) for care of the preterm and LBW infant. Of the recommendations, 11 are new and 14 are updated, and the good practice statement is new. There are 11 strong recommendations for all preterm or LBW infants and 14 recommendations that are conditional on particular contexts or conditions.

Sixteen recommendations are for preventive and promotive care, six are for care for complications and three are for family involvement and support. A good practice statement was made for parental leave and entitlements because the GDG determined that these have obvious benefits, although there was little evidence available.

The GDG provided remarks related to all the recommendations and the good practice statement, where needed. Users of the guideline should refer to these remarks, which are presented prominently, along with the recommendations in Chapter 3 of the guideline.

Table 1. WHO recommendations for the care of the preterm (< 37 weeks' gestation) or low-birth-weight (< 2.5 kg) infant

Domain	Recommendation	Status	Strength/type
A. PREVENTIVE AND PROMOTIVE CARE			
A.1a Any KMC	Kangaroo mother care (KMC) is recommended as routine care for all preterm or low-birth-weight infants. KMC can be initiated in the health-care facility or at home and should be given for 8–24 hours per day (as many hours as possible). (<i>Strong recommendation, high-certainty evidence</i>)	Updated	Strong
A.1b Immediate KMC	Kangaroo mother care (KMC) for preterm or low-birth-weight infants should be started as soon as possible after birth. (<i>Strong recommendation, high-certainty evidence</i>)	New	Strong
A.2 Mother's own milk	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. (<i>Strong recommendation, low-certainty evidence</i>)	Updated	Strong
A.3 Donor human milk	When mother's own milk is not available, donor human milk may be considered for feeding of preterm or low-birth-weight (LBW) infants, including very preterm (< 32 weeks' gestation) or very LBW (< 1.5 kg) infants. (<i>Conditional recommendation, moderate-certainty evidence</i>)	Updated	Conditional
A.4 Multicomponent fortification of human milk	Multicomponent fortification of human milk is not routinely recommended for all preterm or low-birth-weight (LBW) infants but may be considered for very preterm (< 32 weeks' gestation) or very LBW (< 1.5 kg) infants who are fed mother's own milk or donor human milk. (<i>Conditional recommendation, low-to-moderate-certainty evidence</i>)	Updated	Conditional
A.5 Preterm formula	When mother's own milk and donor human milk are not available, nutrient-enriched preterm formula may be considered for very preterm (< 32 weeks' gestation) or very low-birth-weight (< 1.5 kg) infants. (<i>Conditional recommendation, low-certainty evidence</i>)	Updated	Conditional
A.6 Early initiation of enteral feeding	Preterm and low-birth-weight (LBW) infants, including very preterm (< 32 weeks' gestation) and very LBW (< 1.5 kg) infants, should be fed as early as possible from the first day after birth. Infants who are able to breastfeed should be put to the breast as soon as possible after birth. Infants who are unable to breastfeed should be given expressed mother's own milk as soon as it becomes available. If mother's own milk is not available, donor human milk should be given wherever possible. (<i>Strong recommendation, moderate-certainty evidence</i>)	Updated	Strong
A.7 Responsive and scheduled feeding	In health-care facilities, scheduled feeding may be considered rather than responsive feeding for preterm infants born before 34 weeks' gestation, until the infant is discharged. (<i>Conditional recommendation, low-certainty evidence</i>)	Updated	Conditional
A.8 Fast and slow advancement of feeding	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. (<i>Conditional recommendation, moderate-certainty evidence</i>)	Updated	Conditional

Domain	Recommendation	Status	Strength/type
A.9 Duration of exclusive breastfeeding	Preterm or low-birth-weight infants should be exclusively breastfed until 6 months of age. (<i>Strong recommendation, very-low-certainty evidence</i>)	Updated	Strong
A.10a Iron supplementation	Enteral iron supplementation is recommended for human milk-fed preterm or low-birth-weight infants who are not receiving iron from another source. (<i>Strong recommendation, moderate-certainty evidence</i>)	Updated	Strong
A.10b Zinc supplementation	Enteral zinc supplementation may be considered for human milk-fed preterm or low-birth-weight infants who are not receiving zinc from another source. (<i>Conditional recommendation, low-certainty evidence</i>)	Updated	Conditional
A.10c Vitamin D supplementation	Enteral vitamin D supplementation may be considered for human milk-fed preterm or low-birth-weight infants who are not receiving vitamin D from another source. (<i>Conditional recommendation, low-certainty evidence</i>)	Updated	Conditional
A.10d Vitamin A supplementation	Enteral vitamin A supplementation may be considered for human milk-fed very preterm (< 32 weeks' gestation) or very low-birth-weight (< 1.5 kg) infants who are not receiving vitamin A from another source. (<i>Conditional recommendation, low-certainty evidence</i>)	Updated	Conditional
A.11 Probiotics	Probiotics may be considered for human-milk-fed very preterm infants (< 32 weeks' gestation). (<i>Conditional recommendation, moderate-certainty evidence</i>)	New	Conditional
A.12 Emollients	Application of topical oil to the body of preterm or low-birth-weight infants may be considered. (<i>Conditional recommendation, low-certainty evidence</i>)	New	Conditional

B. CARE FOR COMPLICATIONS

B.1 CPAP for respiratory distress syndrome	Continuous positive airway pressure (CPAP) therapy is recommended in preterm infants with clinical signs of respiratory distress syndrome. (<i>Strong recommendation, moderate-certainty evidence</i>)	Updated	Strong
B.2 CPAP immediately after birth	Continuous positive airway pressure (CPAP) therapy may be considered immediately after birth for very preterm infants (< 32 weeks' gestation), with or without respiratory distress. (<i>Conditional recommendation, low-certainty evidence</i>)	New	Conditional
B.3 CPAP pressure source (bubble CPAP)	For preterm infants who need continuous positive airway pressure (CPAP) therapy, bubble CPAP may be considered rather than other pressure sources (e.g. ventilator CPAP). (<i>Conditional recommendation, low-certainty evidence</i>)	New	Conditional
B.4 Methylxanthines for treatment of apnoea	Caffeine is recommended for the treatment of apnoea in preterm infants. (<i>Strong recommendation, moderate-certainty evidence</i>)	New	Strong
B.5 Methylxanthines for extubation	Caffeine is recommended for the extubation of preterm infants born before 34 weeks' gestation. (<i>Strong recommendation, moderate-certainty evidence</i>)	New	Strong
B.6 Methylxanthines for prevention of apnoea	Caffeine may be considered for the prevention of apnoea in preterm infants born before 34 weeks' gestation. (<i>Conditional recommendation, low-certainty evidence</i>)	New	Conditional

Domain	Recommendation	Status	Strength/ type
C. FAMILY INVOLVEMENT AND SUPPORT			
C.1 Family involvement	Family involvement in the routine care of preterm or low-birth-weight infants in health-care facilities is recommended. (<i>Strong recommendation, low- to moderate-certainty evidence</i>)	New	Strong
C.2 Family support	Families of preterm or low-birth-weight infants should be given extra support to care for their infants, starting in health-care facilities from birth and continued during follow-up post-discharge. The support may include education, counselling and discharge preparation from health workers, and peer support. (<i>Conditional recommendation, very-low-certainty evidence</i>)	New	Conditional
C.3 Home visits	Home visits by trained health workers are recommended to support families to care for their preterm or low-birth-weight infant. (<i>Strong recommendation, moderate-certainty evidence</i>)	New	Strong
C.4 Parental leave and entitlements	Parental leave and entitlements should address the special needs of mothers, fathers and other primary caregivers of preterm or low-birth-weight infants. (<i>Good practice statement</i>)	New	Good practice statement