WHO recommendations for care of the preterm or low-birth-weight infant

Web Annexes

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Web Annex A. Priority questions and outcomes

Recommendation No.	Domain	Population, intervention, comparator, outcome (PICO)
A.1a	**Any KMC**	Population: Preterm or low-birth-weight (LBW) infants (< 37 weeks or < 2.5 kg at birth) Intervention 1: KMC Comparator 1: Conventional newborn care Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Setting: Health-care facility or home in any country or setting Timing of intervention: From birth Subgroups: - Gestational age at birth (< 34 weeks, ≥ 34 weeks) - Birth weight (< 2.0 kg, ≥ 2.0 kg) - Daily duration of KMC achieved (< 8 hours, 8–16 hours, > 16 hours per day)
A.1b	**Immediate KMC**	Population: Preterm or LBW infants Intervention 2: KMC initiated early or immediately (within 24 hours after birth) Comparator 2: Initiating KMC later (more than 24 hours after birth) Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Setting: Health-care facility or home in any country or setting Timing of intervention: From birth Subgroups: - Gestational age at birth (< 34 weeks, ≥ 34 weeks) - Birth weight (< 2.0 kg, ≥ 2.0 kg) - Daily duration of KMC achieved (< 8 hours, 8–16 hours, > 16 hours per day)
A.2	**Mother's own milk**	Population: Preterm or LBW infants Intervention: Infant formula (term or preterm) Comparator: Mother's own milk Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: From birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg) - Type of milk in the control group (mother's own milk as the sole diet, mother's own milk not the sole diet)
A.3	**Donor human milk**	Population: Preterm or LBW infants Intervention: Infant formula Comparator: Donor human milk Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg) - Amount of donor milk in the control arm (donor milk provided as the sole diet, mixed with infant formula)

Recommendation No.	Domain	Population, intervention, comparator, outcome (PICO)
A.4	**Multicomponent fortification of human milk**	Population: Preterm or LBW infants Intervention: Human milk with multicomponent fortifier (human or non-human derived) Comparator: Human milk without multicomponent fortifier Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg) - Type of fortifier (human milk protein based, non-human milk protein based)
A.5	**Preterm formula**	Population: Preterm or LBW infants Intervention: Nutrient-enriched formula (or "preterm formula") Comparator: Standard formula (or "term formula") Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5kg, ≥ 1.5 kg)
A.6	**Early initiation of enteral feeding**	Population: Preterm or LBW infants Intervention: Early initiation of enteral feeding (< 72 hours) Comparator: Delayed initiation of enteral feeding (≥ 72 hours) Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 1 month of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg) - Timing of feed initiation (day 1, 2, 3) - Milk volume (< 15 ml/kg per day, ≥ 15 ml/kg per day) - Milk type (human milk, formula, and mixed human milk with formula)
A.7	**Responsive and scheduled feeding**	Population: Preterm or LBW infants who receive any enteral feeding Intervention: Responsive feeding based on infant cues Comparator: Scheduled feeding Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
A.8	**Fast and slow advancement of feeding**	Population: Preterm or LBW infants Intervention: Fast advancement of enteral feeds (≥ 30 ml/kg per day) Comparator: Slow advancement of enteral feeds (< 30 ml/kg per day)

Recommendation No.	Domain	Population, intervention, comparator, outcome (PICO)
		Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg) - Type of milk (human milk, formula milk)
A.9	**Duration of exclusive breastfeeding (EBF)**	Population: Preterm or LBW infants Intervention: EBF to < 6 months of age Comparator: EBF until 6 months of age Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
A.10a	**Iron supplementation**	Population: Preterm or LBW infants who are fed mother's own milk or donor human milk Intervention: Iron supplementation Comparator: No iron supplementation Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
A.10b	**Zinc supplementation**	Population: Preterm or LBW infants who are fed mother's own milk or donor human milk Intervention: Zinc supplementation Comparator: No zinc supplementation Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg) - Dose of elemental zinc (< 3 mg/day, 3–5 mg/day and > 5 mg/day)
A.10c	**Vitamin D supplementation**	Population: Preterm or LBW infants who are fed mother's own milk or donor human milk Intervention: Vitamin D supplementation Comparator: No vitamin D supplementation Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)

Recommendation No.	Domain	Population, intervention, comparator, outcome (PICO)
A.10d	**Vitamin A supplementation**	Population: Preterm or LBW infants who are fed mother's own milk or donor human milk Intervention: Vitamin A supplementation Comparator: No vitamin A supplementation Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
A.10e	**Calcium and phosphorous supplementation**	Population: Preterm or LBW infants who are fed mother's own milk or donor human milk Intervention: Calcium and phosphorous supplementation Comparator: No calcium and phosphorous supplementation Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or settings Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
A.10f	**Multiple micronutrient (MMN) supplementation**	Population: Preterm or LBW infants who are fed mother's own milk or donor human milk Intervention: Enteral MMN supplementation Comparator: No MMN supplementation Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
A.11	**Probiotics**	Population: Preterm or LBW infants Intervention: Any probiotics Comparator: No probiotics Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg) - Probiotic species (*Bifidobacterium* spp., *Lactobacillius* spp., other spp.) - Type of enteral feed (human milk, formula, mixed)
A.12a	**Emollients – oils**	Population: Preterm and LBW infants Intervention 1: Topical oil Comparator 1: No topical oil Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups:

Recommendation No.	Domain	Population, intervention, comparator, outcome (PICO)
		- Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
A.12b	**Emollients - ointments**	Population: Preterm and LBW infants Intervention 2: Topical ointment or cream Comparator 2: No topical ointment or cream Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
B.1a	**Any continuous positive airway pressure (CPAP)**	Population: Preterm infants with respiratory distress syndrome (RDS) Intervention 1: Any CPAP Comparator 1: Usual supplemental oxygen therapy by head box, face mask or nasal cannula Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: From birth Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
B.1b	**Early CPAP**	Population: Preterm infants with RDS Intervention 2: Early CPAP Comparator 2: Delayed CPAP Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: From birth Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
B.2a	**Immediate CPAP vs supplemental oxygen**	Population: Preterm infants immediately after birth Intervention 1: CPAP commencing immediately after birth Comparator 1: Supplemental oxygen by head box, face mask or nasal cannula Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Immediately after birth Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
B.2b	**Immediate CPAP vs mechanical ventilation**	Population: Preterm infants immediately after birth Intervention 2: CPAP commencing immediately after birth Comparator 2: Mechanical ventilation Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Immediately after birth Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks)

Recommendation No.	Domain	Population, intervention, comparator, outcome (PICO)
		- Birth weight (< 1.5 kg, ≥ 1.5 kg)
B.3	**CPAP pressure source (Bubble CPAP)**	Population: Preterm infants with RDS or post-extubation Intervention: Bubble CPAP pressure source Comparator: Other pressure sources (ventilator CPAP or Infant Flow Driver CPAP) Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Immediately after birth Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
B.4	**Methylxanthines for treatment of apnoea**	Population: Preterm infants Intervention: Any methylxanthine (aminophylline, theophylline, caffeine) at any dose Comparator: Placebo or no methylxanthine treatment Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
B.5	**Methylxanthines for extubation**	Population: Preterm infants (< 34 weeks) Intervention: Any methylxanthine (aminophylline, theophylline, caffeine) at any dose Comparator: Placebo or no methylxanthine treatment Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
B.6	**Methylxanthines for prevention of apnoea**	Population: Preterm infants (< 34 weeks) Intervention: Any methylxanthine (aminophylline, theophylline, caffeine) at any dose Comparator: Placebo or no methylxanthine treatment Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
C.1	**Family involvement**	Population: Hospitalized preterm or LBW infants Intervention: Interventions to involve families in their infant's routine health care Comparator: Usual hospital care Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Hospital in any country or setting Subgroups:

Recommendation No.	Domain	Population, intervention, comparator, outcome (PICO)
		- Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg) - Intensity of interventions (high intensity ≥ 12 hours per day, low intensity < 12 hours per day)
C.2a	**Family support – education and counselling**	Population: Families of preterm or LBW infants Intervention 1: Education and counselling interventions Comparator 2: Usual care Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
C.2b	**Family support – peer support**	Population: Families of preterm or LBW infants Intervention 2: Peer support interventions Comparator 2: Usual care Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
C.2c	**Family support – discharge preparedness**	Population: Families of preterm or LBW infants Intervention 3: Discharge preparedness interventions Comparator 3: Usual care Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
C.2d	**Family support – digital information**	Population: Families of preterm or LBW infants Intervention 4: Digital information interventions Comparator 4: Usual care Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)
C.3	**Home visits**	Population: Families of preterm or LBW infants Intervention: Home visits to support families to care for their preterm or LBW infant in the home Comparator: Usual care Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks)

Recommendation No.	Domain	Population, intervention, comparator, outcome (PICO)
		- Birth weight (< 1.5 kg, ≥ 1.5 kg)
C.4	**Parental leave and entitlements**	Population: Preterm or LBW infants Intervention: Parental leave and entitlements Comparator: Usual care Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country or setting Subgroups: - Gestational age at birth (< 32 weeks, ≥ 32 weeks) - Birth weight (< 1.5 kg, ≥ 1.5 kg)

CPAP: continuous positive airway pressure; EBF: exclusive breastfeeding; KMC: kangaroo mother care; LBW: low birth weight; MMN: multiple micronutrient; RDS: respiratory distress syndrome

Web Annex B. Detailed list of research priorities

Domain	Research questions *(Items in bold were prioritized by the Guideline Development Group)*
A.1a Any KMC	**What is the effectiveness of KMC on longer-term (i.e. up to 2 years of age, school-age, adolescence) growth, neuro-cognitive development, behaviour, mental health and disability outcomes?** **What are the key components of an implementation model that achieves high population-level coverage of KMC for more than 8 hours per day in high-income countries?** What is the effectiveness of KMC provided by the mother plus other family members compared with KMC provided only by the mother? What is the effectiveness of KMC compared with other approaches (e.g. oral sucrose) without KMC in reducing pain during procedures that are likely to be painful? What is the effectiveness and safety of KMC during transport of a preterm infant from the community to hospital, between hospitals, and within the hospital compared with standard methods of transport (e.g. transport incubator, incubator in the ambulance)? What is the effect of KMC on the physical and mental health and childcare practices of mothers, fathers, partners and family members? What is the effectiveness of prolonged skin-to-skin contact beyond the first hour of birth in newborns with normal size and weight?
A.1b Immediate KMC	**What is the effectiveness of immediate KMC in critically ill preterm and low-birth-weight (LBW) infants, such as infants who are mechanically ventilated or on blood pressure support (e.g. vasopressors)?** **How can immediate KMC be scaled up in routine health systems?**
A.2 Mother's own milk	**How can exclusive breastfeeding be promoted, supported and scaled up for preterm or LBW infants, especially those who are very preterm or very LBW?** **What are the most effective early feeding strategies for very preterm or very LBW infants, infants with illnesses (e.g. post-surgery), and infants with other conditions (e.g. doppler abnormalities, severe growth restriction)?**
A.3 Donor human milk	**What is the effectiveness, safety and feasibility of human milk banks in low- and middle-income countries?** When mother's own milk is not available, what is the effectiveness and safety of pasteurized compared with unpasteurized donor human milk?
A.4 Multicomponent fortification of human milk	What is the effect of multicomponent fortification of human milk on exclusive breastfeeding rates at 6 months of age in human milk-fed preterm or LBW infants?
A.7 Responsive and scheduled feeding	What is the effect of responsive feeding compared with different schedules of feeding (e.g. 2- or 3-hourly) in preterm or LBW infants?
A.8 Fast and slow advancement of feeding	What is the effectiveness of higher compared with lower increments in feeding volume (e.g. 40 vs 30 ml/kg per day) in preterm infants who need to be fed by an alternative feeding method to breastfeeding (e.g. gastric tube feeding or cup feeding)?
A.9 Duration of exclusive breastfeeding	What is the effect of shorter compared with longer duration of exclusive breastfeeding (e.g. less than six months vs six months or more) on long-term health, growth, neurodevelopment and metabolic (e.g. blood sugar, lipid profile) outcomes?

Domain	Research questions *(Items in bold were prioritized by the Guideline Development Group)*
A.10a Iron supplementation	What is the effect of different doses, timing and duration of supplementation with iron? What is the effect on biomarkers such as soluble transferrin receptor concentration? What is the effect in very preterm or very LBW infants?
A.10b Zinc supplementation	What is the effect of different doses, timing and duration of supplementation with zinc?
A.10c Vitamin D supplementation	What is the effect of different doses, timing and duration of supplementation with vitamin D? What is the effect on bone health? What is the effect on biomarkers such as 25-hydroxyvitamin D [25-(OH)D] concentration, alkaline phosphatase? What is the effect in very preterm or very LBW infants?
A.10d Vitamin A supplementation	What is the effect of different doses, timing and duration of supplementation with vitamin A? What is the effect on biomarkers such as retinol? What is the effect in very preterm or very LBW infants?
A.11 Probiotics	**What is the effectiveness and safety of probiotics in human-milk-fed infants?** **What is the effect of probiotics on immune function and gut microbiome in preterm or LBW infants?** **What are the most optimal probiotic compositions for preterm or LBW infants, i.e. the optimal combination of genera, species and strains?** **What is the optimal dosage and duration of probiotics for preterm or LBW infants?** **What is the effectiveness of probiotics alone compared with a combination of probiotics and prebiotics for preterm or LBW infants?** **What is the role of probiotics in prevention and management of postnatal growth restriction in preterm infants?**
A.12 Emollients	**What is the effect of emollients on mortality, invasive infection, sepsis, growth, and longer-term neurodevelopment in preterm or LBW infants in high-, middle- and low-income countries, especially in Africa?** **What is the effect of emollients on thermoprotection and the microbiome in preterm or LBW infants?** **Which emollients (which oils, which composition) are most effective and safe for preterm or LBW infants?** **What is the optimal regime (dose, frequency, duration) and mode of application (e.g. non-touch applications) for very or extremely preterm infants?**
B.1 Continuous positive airway pressure (CPAP) for respiratory distress syndrome	**What is the effectiveness of CPAP compared with humidified high-flow nasal cannulae and other forms of non-invasive ventilation in preterm and LBW infants with respiratory distress syndrome?**
B.2 CPAP immediately after birth	What is the effectiveness of starting CPAP immediately after birth regardless of respiratory distress?

Domain	Research questions *(Items in bold were prioritized by the Guideline Development Group)*
	What is the effect in very preterm infants?
B.4 Methylxanthines	What is the optimal timing of initiation, dosage and duration of caffeine therapy?
C.1 Family involvement	**What strategies can be used to increase family participation in the care of their preterm or LBW infants in intensive and special care units, and in settings without dedicated newborn units?**
C.2 Family support	**What is the most effective type of family support (including education, counselling, discharge preparation, peer support) for families of preterm or LBW infants?** How can social care services support parents of preterm or LBW infants? What is the effectiveness of digital health interventions (e.g. online video, mobile application [app], mHealth) in supporting parents of preterm or LBW infants?
C.3 Home visits	**What is the effectiveness of standard "in-person" home visits compared with "digital" home visits (e.g. online video, mobile application [app], mHealth) for post-discharge follow-up of preterm or LBW infants?** **What is the feasibility of "digital" home visits in high-, low- and middle-income countries?** What is the effectiveness of home visits from health workers who are specially trained in preterm and LBW infant care compared with home visits from routinely trained health workers, including community health workers? What is the optimal content, duration and frequency of home visits for preterm or LBW infants?
C.4 Parental leave and entitlements	What is the effect of parental entitlements including financial incentives and additional leave from work? Which types of entitlements are most effective? Which types of entitlements are most desirable for families? What should be the duration of parental leave and entitlements?
Other	What is the incremental cost-effectiveness of the recommendations in the guideline?

CPAP: continuous positive airway pressure; KMC: kangaroo mother care; LBW: low birth weight

Web Annex C. Changes from approved scope of guideline

Intervention	Population, intervention, comparator, outcome (PICO)	Change from approved scope and reason
Kangaroo mother care (KMC) scale-up	Population: Preterm or LBW infants Intervention: Package of health system interventions Comparator: No package of interventions or different packages of interventions Outcome: KMC coverage Plus: What are the components of the packages of health system interventions that achieve high (> 50%) KMC coverage?	Not included in this guideline as it will be included in a separate forthcoming guideline.
Methylxanthines for treatment of apnoea	Population: Preterm infants (< 37 weeks) with apnoea Intervention: Any methylxanthine (aminophylline, theophylline, caffeine) at any dose Comparator: Placebo or no methylxanthine treatment Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country Subgroups: Gestational age and birth weight (< 32 weeks or < 1.5 kg, ≥ 32 weeks or ≥ 1.5 kg)	Added to this guideline due to the availability of new evidence.
Methylxanthines for extubation	Population: Preterm infants (< 34 weeks) extubated Intervention: Any methylxanthine (aminophylline, theophylline, caffeine) at any dose Comparator: Placebo or no methylxanthine treatment Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country Subgroups: Gestational age and birth weight (< 32 weeks or < 1.5 kg, ≥ 32 weeks or ≥ 1.5 kg)	Added to this guideline due to the availability of new evidence.
Methylxanthines for prevention of apnoea	Population: Preterm infants (< 34 weeks) Intervention: Any methylxanthine (aminophylline, theophylline, caffeine) at any dose Comparator: Placebo or no methylxanthine treatment	Added to this guideline due to the availability of new evidence.

Intervention	Population, intervention, comparator, outcome (PICO)	Change from approved scope and reason
	Outcomes: All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up Timing of the intervention: Birth to 6 months of age Setting: Health-care facility or home in any country Subgroups: Gestational age and birth weight (< 32 weeks or < 1.5 kg, ≥ 32 weeks or ≥ 1.5 kg)	

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