SUPPLEMENTARY MATERIAL

New World Health Organization recommendations for care of preterm or low birth weight infants: health policy

Running title: Care for preterm or low birth weight infants

Care of Preterm or Low Birthweight Infants Group

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Table S1. Interventions and systematic review research questions for care of preterm or LBW infants

Interventions		**Research questions/PICO**
Kangaroo Mother Care	Kangaroo mother care (KMC)	In preterm or LBW infants (P), what is the effect of KMC (I) compared to conventional neonatal care (C) on critical outcomes (O)? If KMC is effective then what is the effect of early-onset KMC (I) compared to late-onset KMC (C) on critical outcomes (O)? What is the effect of short (I) compared to longer (C) durations of KMC on critical outcomes (O)?
Feeding	Mother's own milk	In preterm or LBW infants (P), what is the effect of feeding mother's own milk (I) compared with feeding infant formula (C) on critical outcomes (O)?
	Donor human milk	In preterm or LBW infants who cannot be fed mother's own milk (P), what is the effect of feeding donor human milk (I) compared with feeding infant formula (C) on critical outcomes (O)?
	Infant formula	In preterm or LBW infants who cannot be fed mother's own milk or donor human milk (P), what is the effect of feeding nutrient enriched ('preterm') infant formula (I) compared with feeding standard infant ('term') formula (C) on critical outcomes (O)?
	Fortification	In preterm or LBW infants who are fed mother's own milk or donor human milk (P), what is the effect of multi-component fortification of milk (I) compared with no fortification (C) on critical outcomes (O)?
	Initiation of enteral feeding	In preterm or LBW infants (P) what is the effect of early initiation of enteral feeding (I) compared to delayed feeding (C) on critical outcomes (O)? If early then when should feeding be initiated? Does this effect differ in infants given full enteral feeding compared to infants given restricted volumes including minimal enteral feeding?
	Responsive feeding	In preterm or LBW infants who receive any enteral feeding (P), what is the effect of responsive feeding based on infants' cues (I) compared with scheduled feeding (C) on critical outcomes (O)?
	Volume advancement	In preterm or LBW infants who receive any enteral feeding (P), what is the effect of fast advancement of enteral feeds (I) versus slower rates of feed advancement (C) on critical outcomes (O)?
	Duration of exclusive breastfeeding	In preterm or LBW infants (P), what is the effect of exclusive breastfeeding for less than 6 months (I) compared with exclusive breastfeeding for 6 months (C) on critical outcomes (O)? If less than 6 months, then what is the optimal duration?

Micronutrients	Iron	In preterm or LBW infants who are fed mother's own milk or donor human milk (P), what is the effect of enteral iron supplementation (I) compared with no iron supplementation (C) on critical outcomes (O)?
	Zinc	In preterm or LBW infants who are fed mother's own milk or donor human milk (P), what is the effect of enteral zinc supplementation (I) compared with no zinc supplementation (C) on critical outcomes (O)?
	Vitamin D	In preterm or LBW infants who are fed mother's own milk or donor human milk (P), what is the effect of enteral vitamin D supplementation (I) compared with no vitamin D supplementation (C) on critical outcomes (O)?
	Vitamin A	In preterm or LBW infants who are fed mother's own milk or donor human milk (P), what is the effect of enteral vitamin A supplementation (I) compared with no vitamin A supplementation (C) on critical outcomes (O)?
	Calcium and phosphorous	In preterm or LBW infants who are fed mother's own milk or donor human milk (P), what is the effect of enteral CaP04 supplementation (I) compared with no CaP04 supplementation (C) on critical outcomes (O)?
	Multiple micronutrient supplements	In preterm or LBW infants who are fed mother's own milk or donor human milk (P), what is the effect of enteral multiple micronutrient supplements (I) compared with no enteral multiple micronutrient supplements (C) on critical outcomes (O)?
Probiotics	Probiotics	In preterm or LBW infants who are fed mother's own milk or donor human milk (P),, what is the effect of probiotics (I) versus no probiotics (C) on critical outcomes (O)?
Skin care	Emollients	In preterm or LBW infants (P) what is the effect of topical ointment, cream or oil applied to the skin (I) compared to routine skin care (C) on critical outcomes (O)?
Respiratory Distress Syndrome	CPAP for respiratory distress	In preterm infants with respiratory distress syndrome (P), what is the effect of any CPAP therapy (I) versus supportive care with oxygen therapy by head box, facemask or nasal cannula (C) on critical outcomes (O)?
	Early CPAP	In preterm infants with respiratory distress syndrome (P), what is the effect of early CPAP (I) versus late CPAP(C) on critical outcomes (O)?
	CPAP prophylaxis	In preterm infants less than 32w regardless of respiratory status (P) What is the effect of CPAP started immediately after birth (I) compared to supportive care with oxygen therapy by head box, facemask or nasal cannula (C) on critical outcomes (O)? -what is the effect of CPAP started immediately after birth (I) compared to mechanical ventilation (C) on critical outcomes (O)?

	CPAP pressure source	In preterm infants with respiratory distress syndrome, what is the effect of bubble (I) compared to other forms of CPAP (C) on critical outcomes (O)?
Apnoea	Methyl xanthines	In preterm infants, what is the effect of any methyl xanthine compared with no methyl xanthine on critical outcomes? What is the effect by indication (any, prevention, treatment), by type of methyl xanthine (eg caffeine, theophylline) and by gestational age or birthweight.
Family involvement and support	Family involvement	In hospitalised preterm or LBW infants (P) do interventions to involve families in the infant's routine health care (family involvement strategies, FIS) (I) compared to standard hospital or NICU care (C) improve critical outcomes (O)
	Family support	In preterm or LBW infants (P), do interventions to support the family to care for the infant in the home (I) compared to no or different interventions (C) improve critical outcomes (O)

PICO = population, intervention, comparator, outcome questions

Table S2. Evidence base

Framework	
Overview of systematic reviews	Edmond K, Strobel N. Evidence for Global Health Care Interventions for Preterm or Low Birth Weight Infants: An Overview of Systematic Reviews. Pediatrics. 2022 Aug 1;150(Suppl 1):e2022057092C. doi: 10.1542/peds.2022-057092C.
Values and acceptability	Hurt L, Odd D, Mann M, Beetham H, Dorgeat E, Isaac TC, et al. What matters to families about the healthcare of preterm or low birth weight babies: a qualitative evidence synthesis. medRxiv. 2022:2022.06.22.22276770. doi:10.1101/2022.06.22.22276770.
Supplies	UNICEF supply catalogue [website]. New York (NY): United Nations Children's Fund; 2018 (https://supply.unicef.org/)
Medical products	International medical products price guide, 2015 edition. Medford (MA): Management Sciences for Health; 2016 (https://mshpriceguide.org/en/home)
Health technologies	WHO compendium of innovative health technologies for low-resource settings: 2022. Geneva: World Health Organization; 2022 (https://apps.who.int/iris/handle/10665/355162)
WHO guidelines	
WHO guidelines	WHO recommendations for care of the preterm or low birth weight infant. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO
WHO annexes	Web Annexes. In: WHO recommendations for care of the preterm or low-birth-weight infant. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO
WHO GRADE tables	Web Supplement. Evidence base. In: WHO recommendations for care of the preterm or low-birth-weight infant. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO
Individual reviews	
Kangaroo mother care	Sivanandan S, Sankar MJ. Kangaroo mother care for preterm or low birth weight infants: A systematic review and meta-analysis. medRxiv. 2022:2022.09.14.22279053. doi:10.1101/2022.09.14.22279053. In Presss BMJ Global health
Mother's own milk	Strobel NA, Adams C, McAullay DR, Edmond KM. Mother's Own Milk Compared With Formula Milk for Feeding Preterm or Low Birth Weight Infants: Systematic Review and Meta-analysis. Pediatrics 2022; 150(Suppl 1). doi:10.1542/peds.2022-057092D.
Donor human milk	Quigley M, Embleton ND, McGuire W. Formula versus donor breast milk for feeding preterm or low birth weight infants. Cochrane Database Syst Rev 2019; 7(7): CD002971. doi:10.1002/14651858.CD002971.pub5.

Multicomponent fortifier	Brown JV, Lin L, Embleton ND, Harding JE, McGuire W. Multi-nutrient fortification of human milk for preterm infants. Cochrane Database Syst Rev 2020; 6(7): CD000343. doi:10.1002/14651858.CD000343.pub4.
Preterm formula	Walsh V, Brown JVE, Askie LM, Embleton ND, McGuire W. Nutrient-enriched formula versus standard formula for preterm infants. Cochrane Database Syst Rev 2019; 7(7): CD004204. doi:10.1002/14651858.CD004204.pub3.
Early initiation of enteral feeding	Chitale R, Ferguson K, Talej M, Yang WC, He S, Edmond KM, et al. Early Enteral Feeding for Preterm or Low Birth Weight Infants: a Systematic Review and Meta-analysis. Pediatrics 2022; 150(Suppl 1). doi:10.1542/peds.2022-057092E.
Responsive and scheduled feeding	Talej M, Smith ER, Lauria ME, Chitale R, Ferguson K, He S. Responsive Feeding for Preterm or Low Birth Weight Infants: A Systematic Review and Meta-analysis. Pediatrics 2022; 150(Suppl 1). doi:10.1542/peds.2022-057092F.
Advancement of feeding	Yang WC, Fogel A, Lauria ME, Ferguson K, Smith ER. Fast Feed Advancement for Preterm and Low Birth Weight Infants: A Systematic Review and Meta-analysis. Pediatrics 2022; 150(Suppl 1). doi:10.1542/peds.2022-057092G.
Duration of exclusive breastfeeding	Yang WC, Lauria ME, Fogel A, Ferguson K, Smith ER. Duration of Exclusive Breastfeeding for Preterm or Low Birth Weight Infants: A Systematic Review and Meta-analysis. Pediatrics 2022; 150(Suppl 1). doi:10.1542/peds.2022-057092H.
Iron supplementation	Manapurath RM, Gadapani Pathak B, Sinha B, Upadhyay RP, Choudhary TS, Chandola TR, et al. Enteral Iron Supplementation in Preterm or Low Birth Weight Infants: A Systematic Review and Meta-analysis. Pediatrics 2022; 150(Suppl 1). doi:10.1542/peds.2022-057092I.
Zinc supplementation	Sinha B, Dudeja N, Chowdhury R, Choudhary TS, Upadhyay RP, Rongsen-Chandola T, et al. Enteral Zinc Supplementation in Preterm or Low Birth Weight Infants: A Systematic Review and Meta-analysis. Pediatrics 2022; 150(Suppl 1). doi:10.1542/peds.2022-057092J.
Vitamin D supplementation	Kumar M, Shaikh S, Sinha B, Upadhyay RP, Choudhary TS, Chandola TR, et al. Enteral Vitamin D Supplementation in Preterm or Low Birth Weight Infants: A Systematic Review and Meta-analysis. Pediatrics 2022; 150(Suppl 1). doi:10.1542/peds.2022-057092K.
Vitamin A supplementation	Manapurath RM, Kumar M, Pathak BG, Chowdhury R, Sinha B, Choudhary T, et al. Enteral Low-Dose Vitamin A Supplementation in Preterm or Low Birth Weight Infants to Prevent Morbidity and Mortality: a Systematic Review and Meta-analysis. Pediatrics 2022; 150(Suppl 1). doi:10.1542/peds.2022-057092L.
Calcium and phosphorous supplementation	Kumar M, Chowdhury R, Sinha B, Upadhyay RP, Chandola TR, Mazumder S, et al. Enteral Calcium or Phosphorus Supplementation in Preterm or Low Birth Weight Infants: a Systematic Review and Meta-analysis. Pediatrics 2022; 150(Suppl 1). doi:10.1542/peds.2022-057092M.

Multiple micronutrient supplementation	Kumar M, Chowdhury R, Sinha B, Upadhyay RP, Chandola TR, Mazumder S, et al. Enteral Multiple Micronutrient Supplementation in Preterm and Low Birth Weight Infants: A Systematic Review and Meta-analysis. Pediatrics 2022; 150(Suppl 1). doi:10.1542/peds.2022-057092N.
Probiotics	Sharif S, Meader N, Oddie SJ, Rojas-Reyes MX, McGuire W. Probiotics to prevent necrotising enterocolitis in very preterm or very low birth weight infants. Cochrane Database Syst Rev 2020; 10(10): CD005496. doi:10.1002/14651858.CD005496.pub5.
Emollients	Cleminson J, McGuire W. Topical emollient for preventing infection in preterm infants. Cochrane Database Syst Rev 2021; 5(5): CD001150. doi:10.1002/14651858.CD001150.pub4.
CPAP for respiratory distress	Ho JJ, Subramaniam P, Davis PG. Continuous positive airway pressure (CPAP) for respiratory distress in preterm infants. Cochrane Database Syst Rev 2020; 10(10): CD002271. doi:10.1002/14651858.CD002271.pub3.
Early CPAP	Ho JJ, Subramaniam P, Sivakaanthan A, Davis PG. Early versus delayed continuous positive airway pressure (CPAP) for respiratory distress in preterm infants. Cochrane Database Syst Rev 2020; 10(10): CD002975. doi:10.1002/14651858.CD002975.pub2.
Prophylactic CPAP	Subramaniam P, Ho JJ, Davis PG. Prophylactic or very early initiation of continuous positive airway pressure (CPAP) for preterm infants. Cochrane Database Syst Rev 2021; 10(10): CD001243. doi:10.1002/14651858.CD001243.pub4.
Bubble CPAP	Prakash R, De Paoli AG, Davis PG, Oddie SJ, McGuire W. Bubble devices versus other pressure sources for nasal continuous positive airway pressure in preterm infants. Cochrane Database Syst Rev. 2023 Mar 31;3(3):CD015130. doi: 10.1002/14651858.CD015130.
Methyl xanthines	Marques K, Roehr CC, Bruschettini M, Davis PG, Soll R. Methylxanthine for the prevention and treatment of apnea in preterm infants. Cochrane Database Syst Rev 2022; (In Press).
Family involvement	North K, Whelan R, Folger LV, Lawford H, Olson I, Driker S, et al. Family Involvement in the Routine Care of Hospitalized Preterm or Low Birth Weight Infants: A Systematic Review and Meta-analysis. Pediatrics 2022; 150(Suppl 1). doi:10.1542/peds.2022-057092O.
Family support	Bedwell C, Lavender T, Tate N, Danna VA. Interventions to support parents, families and carers in caring for premature or low birth weight (LBW) infants in the home: a systematic review and meta-analysis. medRxiv. 2022:2022. doi:10.1101/2022.10.25.22281452. https://medrxiv.org/cgi/content/short/2022.10.25.22281452v1. Submitted
Home visits	Bedwell C, Lavender T, Tate N, Danna VA. Interventions to support parents, families and carers in caring for premature or low birth weight (LBW) infants in the home: a systematic review and meta-analysis. medRxiv. 2022:2022. doi:10.1101/2022.10.25.22281452. https://medrxiv.org/cgi/content/short/2022.10.25.22281452v1. Submitted

Table S3. Evidence to decision framework and methods

Domain	Questions to be answered	Methods	Rating
Benefits	How effective is the intervention?	Quantitative systematic reviews of effectiveness studies	Large, moderate, small, trivial, none, varies, don't know
Harms	Are there important adverse events reported by the study from the intervention?	Quantitative systematic reviews of effectiveness studies	Large, moderate, small, trivial, none, varies, don't know
Balance of effects	Does the balance between benefits and harms favour the intervention?	DECIDE[a] framework[40]	Favours intervention, probably favours intervention, probably favours no intervention, favours no intervention, varies, don't know
Certainty	What is the certainty of the effectiveness evidence?	GRADE[b] or GRADE CerQual[c] assessment of the certainty of the body of evidence[38,39]	Bias, imprecision, inconsistency, indirectness High, moderate, low, very low certainty
Values about outcomes	Is there important variability in the values or preferences a family might have about the outcomes that would impact judgments about the balance of effects	Qualitative systematic reviews of experimental, quasi-experimental and observational studies	Yes, probably yes, probably no, no, varies, don't know
Acceptability	Is the intervention acceptable?	Qualitative systematic reviews of experimental, quasi-experimental and observational studies	Yes, probably yes, probably no, no, varies, don't know
Resources	What resources are required and what are their costs?	Structured searches in resource, cost, feasibility and equity databases[d]	Negligible costs, low to moderate costs, large costs, varies, don't know
Feasibility	What is the feasibility of the intervention? Can it be easily or conveniently implemented? Is the intervention	Structured searches in resource, cost, feasibility and equity databases[d]	Yes, probably yes, probably no, no, varies, don't know

	acceptable and are the resources required achievable?		
Equity	Can the intervention be provided in low resource settings? Will the populations that need the intervention most receive it quickly and at low cost?	Structured searches in resource, cost,, feasibility and equity databases[d]	Yes, probably yes, probably no, no, varies, don't know

[a]DECIDE = The DECIDE framework (Developing and Evaluating Communication Strategies to support Informed Decisions and Practice based on Evidence[40]

[b]GRADE = Grading of Recommendations Assessment, Development and Evaluation[38]

[c]CERQual = Confidence in the Evidence from Reviews of Qualitative research[39]

[d]Searches = Structured searches in UNICEF supply catalogue,[41] International Medical Products Price Guide,[42] and the WHO compendium of innovative health technologies for low resource settings and health equity databases[43]

Table S4. Evidence-to-decision framework domains

Domain	Favors strong	Favors conditional
Balance of benefits to harms	Benefits highly outweigh harms	Benefits and harms more closely balanced
Quality of evidence	Higher certainty	Lower certainty
Values/preferences regarding outcomes	Benefits to harms assessment not impacted by variability in values/preferences regarding outcomes	Variability in values/preferences regarding outcomes that would impact benefits to harms assessment
Acceptability	Highly acceptable	Low or variable acceptability
Costs/resources	Cost savings/cost-effective	Costly/cost-ineffective
Feasibility	Feasible in intended settings	Unfeasible or feasibility varies in intended settings
Equity	Increases equity	Decreases equity or effects on equity variable

Table S5. Authors table for indexing in Pubmed

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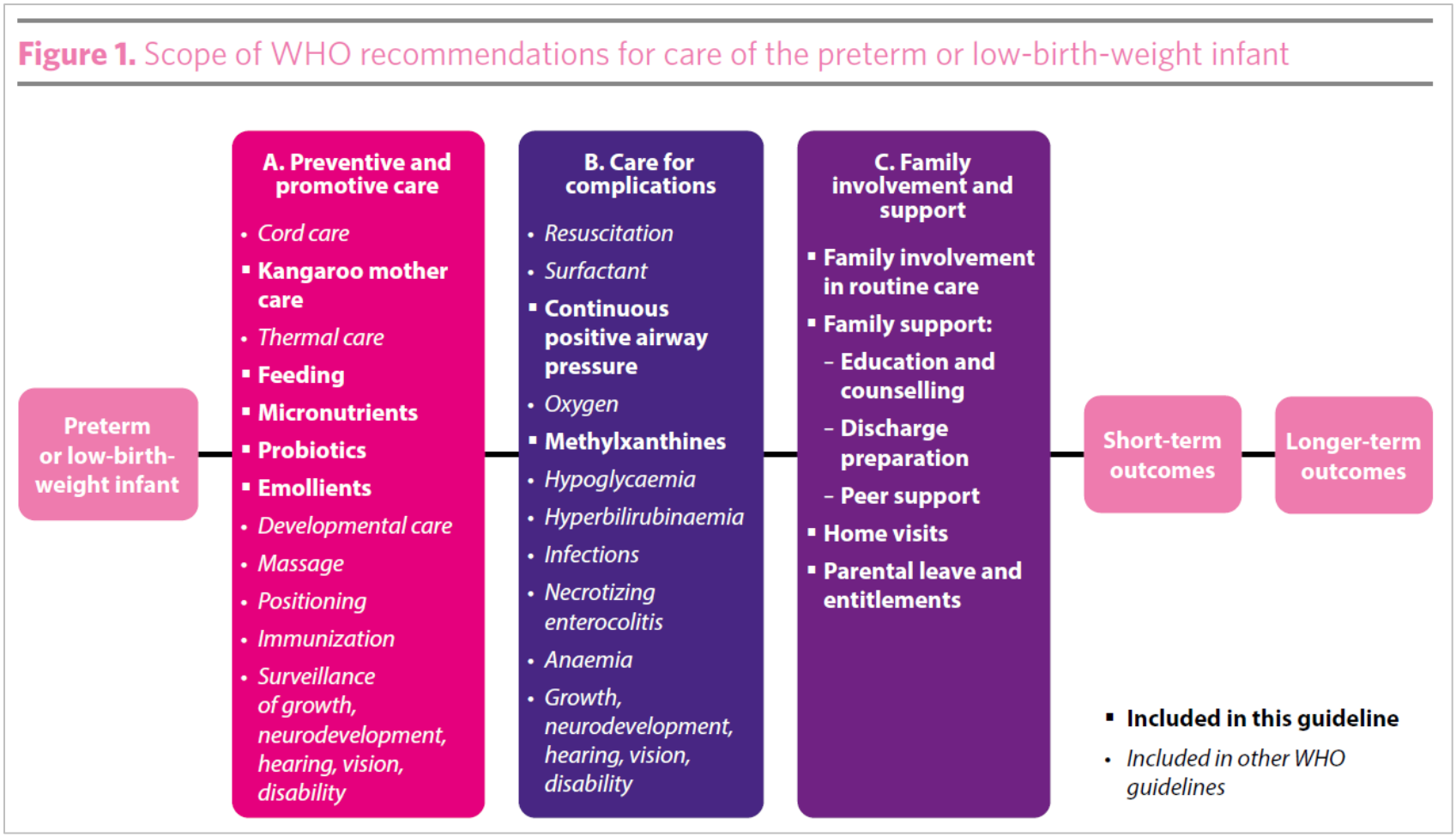
Figure S1. Scope of WHO recommendations for care of the preterm of low-birth-weight infant



Reference: WHO recommendations for care of the preterm or low birth weight infant. Geneva: World Health Organization; 2022.
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