Enteral Multiple Micronutrient Supplementation in Preterm and Low Birth Weight Infants: A Systematic Review and Meta-analysis

Mohan Kumar, MD,[a] Ranadip Chowdhury, PhD,[a,b] Bireshwar Sinha, MD,[a,b] Ravi Prakash Upadhyay, MD,[a,b] Temsunaro Rongsen Chandola, PhD,[a] Sarmila Mazumder, PhD,[a] Sunita Taneja, PhD,[a] Karen Edmond, PhD,[c] Rajiv Bahl, PhD,[c] Nita Bhandari, PhD,[a] Usha Ramakrishnan, PhD,[d,e] Juan A. Rivera, PhD,[f] Sonia Tandon, MPH,[e] Christopher P. Duggan, MD, MPH,[g,i] Enju Liu, PhD,[g,h] Wafaie Fawzi,[i,j] Karim Manji,[k] Tarun Shankar Choudhary, MD[a,l]

abstract

OBJECTIVES: To assess effects of supplementation with 3 or more micronutrients (multiple micronutrients; MMN) compared to no MMN in human milk-fed preterm and low birth weight (LBW) infants.

RESULTS: Data on a subgroup of 414 preterm or LBW infants from 2 randomized controlled trials (4 reports) were included. The certainty of evidence ranged from low to very low. For growth outcomes in the MMN compared to the non-MMN group, there was a small increase in weight-for-age (2 trials, 383 participants) and height-for-age z-scores (2 trials, 372 participants); a small decrease in wasting (2 trials, 398 participants); small increases in stunting (2 trials, 399 participants); and an increase in underweight (2 trials, 396 participants). For neurodevelopment outcomes at 78 weeks, we found small increases in Bayley Scales of Infant Development, Version III (BISD-III), scores (cognition, receptive language, expressive language, fine motor, gross motor) in the MMN compared to the non-MMN group (1 trial, 27 participants). There were no studies examining dose or timing of supplementation.

CONCLUSIONS: Evidence is insufficient to determine whether enteral MMN supplementation to preterm or LBW infants who are fed mother's own milk is associated with benefit or harm. More trials are needed to generate evidence on mortality, morbidity, growth, and neurodevelopment.

[a]Centre for Health Research and Development, Society for Applied Studies, New Delhi, India; [b]DBT/Wellcome India Alliance Clinical and Public health Fellow, Hyderabad, India; [c]Department of Maternal, Newborn, Child, and Adolescent Health and Aging, World Health Organization, Geneva, Switzerland; [d]Hubert Department of Global Health, Emory University, Atlanta, Georgia; [e]Doctoral Program in Nutrition and Health Sciences, Laney Graduate School, Emory University, Atlanta, Georgia; [f]Instituto Nacional de Salud Pública, Cuernavaca, Morelos, Mexico; [g]Division of Gastroenterology, Hepatology, and Nutrition, Center for Nutrition, and [hi]Institutional Centers for Clinical and Translational Research, Boston Children's Hospital, Boston, Massachusetts; [i]Departments of Nutrition and [j]Global Health and Population, Harvard T H Chan School of Public Health, Boston, Massachusetts; [k]Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania; and [l]Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway

Drs Kumar, Edmond, and Choudhary conceptualized and designed the study, designed the data collection instruments, collected data, conducted the initial analyses, and prepared the initial draft, and reviewed and revised the manuscript; Drs Bahl and Chowdhury conceptualized and designed the study, and reviewed and revised the manuscript; Drs Sinha, Upadhyay, Chandola, Mazumder, Taneja, Bhandari, Ramakrishnan, Rivera, Duggan, Liu, Fawzi, Manji, and Ms Tandon reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

This study is registered at PROSPERO, #CRD42021238975, https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021238975.

DOI: https://doi.org/2022057092N

Accepted for publication May 16, 2022

Address correspondence to Tarun Shankar Choudhary, MD, Centre for Health Research and Development, Society for Applied Studies, 45 Kalu Sarai, New Delhi 110016, India. E-mail: tarun.choudhary@sas.org.in

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Preterm (<37 weeks' gestation) and low birth weight (<2.5 kg) (LBW) infants have high risks of mortality and morbidity, and many are born with low stores of micronutrients. Human milk may not be sufficient for adequate postnatal skeletal growth and development in preterm and LBW infants.[1–4] Multiple micronutrients (MMN) such as vitamin A, vitamin D, B vitamins (ie, thiamine, riboflavin, niacin, pyridoxine, and folate), vitamin C, vitamin E, zinc, iron, and magnesium are considered to be important for infant growth and development.[4,5] MMNs are commonly combined together into specially formulated "syrups" for preterm and LBW infants and provided to human milk-fed preterm and LBW infants across high income and low and middle income countries.[4]

There have been many systematic reviews of MMN supplementation during pregnancy and early childhood[6–9]; however, to our knowledge, there has been no systematic review of the effect of MMN on health, growth, and developmental outcomes in preterm or LBW infants fed mother's own milk in high-, low-, and middle-income settings.

Our primary objective was to assess the effect of MMN during infancy on mortality, morbidity, growth, and neurodevelopmental outcomes in preterm or LBW infants who are fed mother's own milk or donor human milk. Secondary objectives were to determine the optimal time of initiation, dose, and duration of MMN during infancy.

METHODS

Registration 4 C X

The protocol for this review was registered in PROSPERO (PROSPERO 2021 #CRD42021238975).[10]

Inclusion Criteria

We included studies that were either randomized controlled trials (RCTs) or nonrandomized trials (quasi-randomized), including cluster-randomized trials but not crossover trials, in which individual LBW (birth weight <2.5 kg) or preterm infants (<37 weeks' gestational age) who were fed mother's own milk or donor human milk were either: allocated to receive enteral MMN syrups, and compared with a control group (placebo or none), or allocated to different regimens of MMN syrups (to compare dosage, duration, and timing of initiation).

In this review, MMN were defined as supplements containing at least 3 or more of the following micronutrients: vitamin A, vitamin D, B vitamins (ie, thiamine, riboflavin, niacin, pyridoxine, or folate), vitamin C, vitamin E, iron, or zinc in 1 formulation.[5]

Exclusion Criteria

We excluded studies in which MMN were mixed with multicomponent breast milk "fortifier" and where infants were fed formula milk.

Search and Extraction

A comprehensive search was conducted in the Cochrane Central Register of Controlled Trials (2016, Issue 3) in the Cochrane Library via the Cochrane Register of Studies Online, Medline via PubMed, and Embase from inception to March 24, 2021, using the search terms in Appendices 1 and 2.

The trials used varying doses of MMN supplementation (Appendix 8). The MMN supplement in the Tanzania trial contained vitamin C, E, thiamine, riboflavin, niacin, pyridoxine, folate, and vitamin B12. The MMN in the Mexico trial had the same nutrients, plus vitamins A and D, iron, zinc, and magnesium. The Tanzania trial had 4 arms, MMN alone, MMN plus zinc, zinc alone, and placebo. Thus, we combined the MMN alone and MMN plus zinc arms into the intervention group and the 2 non-MMN groups into the comparator group (placebo and zinc alone). The Mexico trial had 2 arms. The intervention group was MMN, vitamin A, and iron. The comparator was vitamin A and iron. Mothers in the Mexico trial received MMN or iron during pregnancy and their babies were rerandomized and the MMN supplementation was started at 3 months and continued until 24 months of age. The Tanzania trial commenced supplementation at 66 weeks of age and continued until18 months of age.

The risk of bias assessment is summarized in Appendix 4 for the two trials. Overall, 2 reports had some concerns of risk of bias[18,19] because of bias arising from randomization process, and 2 reports had high risk of bias[17,20] because of bias arising from randomization process, missing outcome data, and measurement of the outcome.

For growth outcomes, from enrollment (mean [SD], 7 [1.41] weeks) to latest follow-up (mean [SD], 91 [18.38] weeks), the mean change between infants who received MMN and infants who did not receive MMN: weight for height z-score (WHZ) was −0.01 (95% CI −0.31 to 0.29, I^2 = 0.00%, low certainty evidence, 2 trials, 358 participants)[18,20]; height for age z-score (HAZ) was 0.07 (95% CI −0.19 to 0.33, I^2 = 0.00%, low certainty evidence, 2 trials, 372 participants)[18,20]; and weight for age z-score (WAZ) was 0.05 (95% CI −0.20 to 0.30, I^2 = 0.00%, low certainty evidence, 2 trials, 383 participants) (Table 1).[18,20]

TABLE 1 Summary of Findings for Critical Outcomes

MMN Supplementation Compared With No Supplementation for Preterm and/or LBW Infants

Outcomes	No. of Participants (Studies) Follow-up	Certainty of the Evidence (GRADE)	Relative Effect (95% CI)	Anticipated Absolute Effects	
				Risk With No Supplementation	Risk Difference With MMN Supplementation
Wasting follow-up: latest mean (SD) 91 (18.38) wk; median (IQR) 91 (78–104) wk	398 (2 RCTs)	⨁⨁◯◯ Lowa	RR 0.86 (0.50–1.48)	129 per 1000	18 fewer per 1000 (64 fewer–62 more)
Stunting follow-up: latest mean (SD) 91 (18.38) wk; median (IQR) 91 (78–104) wk	399 (2 RCTs)	⨁⨁◯◯ Low[a]	RR 1.17 (0.83–1.66)	227 per 1000	39 more per 1000 (39 fewer–150 more)
Underweight follow-up: latest mean (SD) 91 (18.38) wk; median (IQR) 91 (78–104) wk	396 (2 RCTs)	⨁⨁◯◯ Low[a]	RR 1.22 (0.85–1.76)	179 per 1000	39 more per 1000 (27 fewer–136 more)
Change in WHZ between baseline mean (SD) 7 (1.41) wk; median (IQR) 7 (6–8) wk and endline mean (SD) 91 (18.38) wk; median (IQR) 91 (78–104) wk	358 (2 RCTs)	⨁⨁◯◯ Low[a]	—	The mean change in WHZ was −0.57 SD	MD 0.01 SD lower (0.31 lower–0.29 higher)
Change in HAZ between baseline mean (SD) 7 (1.41) wk; median (IQR) 7 (6–8) wk and endline mean (SD) 91 (18.38) wk; median (IQR) 91 (78–104) wk	372 (2 RCTs)	⨁⨁◯◯ Low[a]	—	The mean change in HAZ was −0.34 SD	MD 0.07 SD higher (0.19 lower–0.33 higher)
Change in WAZ between baseline mean (SD) 7 (1.41) wk; median (IQR) 7 (6–8) wk and endline mean (SD) 91 (18.38) wk; median (IQR) 91 (78–104) wk	383 (2 RCTs)	⨁⨁◯◯ Low[a]	—	The mean change in WAZ was −0.23 SD	MD 0.05 SD higher (0.2 lower–0.3 higher)
WHZ follow-up: latest mean (SD) 91 (18.38) wk; median (IQR) 91 (78–104) wk	385 (2 RCTs)	⨁⨁◯◯ Low[a]	—	The mean WHZ was −0.47 SD	MD 0.04 SD lower (0.3 lower–0.22 higher)
HAZ follow-up: latest mean (SD) 91 (18.38) wk; median (IQR) 91 (78–104) wk	392 (2 RCTs)	⨁⨁◯◯ Low[a]	—	The mean HAZ was −1.21 SD	MD 0.06 SD lower (0.28 lower–0.17 higher)
WAZ follow-up: latest mean (SD) 91 (18.38) wk; median (IQR) 91 (78–104) wk	392 (2 RCTs)	⨁⨁◯◯ Low[a]	—	The mean WAZ was −1.03 SD	MD 0.01 SD lower (0.27 lower–0.25 higher)
BSID-III scores					
Cognition follow-up: latest wk (78 wk)	27 (1 RCT)	⨁◯◯◯ Very low[b]	—	The mean BSID-III scores cognition was 47.76	MD 2.64 higher (0.48 lower–5.76 higher)
Receptive language follow-up: latest wk (78 wk)	27 (1 RCT)	⨁◯◯◯ Very low[b]	—	The mean BSID-III scores receptive language was 17.71	MD 1.19 higher (0.33 lower–2.71 higher)
Expressive language follow-up: latest wk (78 wk)	27 (1 RCT)	⨁◯◯◯ Very low[b]	—	The mean BSID-III scores expressive language was 18.76	MD 0.94 higher (1.13 lower –3.01 higher)
Fine motor follow-up: latest wk (78 wk)	27 (1 RCT)	⨁◯◯◯ Very low[b]	—	The mean BSID-III scores fine motor was 33.47	MD 1.03 higher (1.13 lower–3.19 higher)
Gross motor follow-up: latest wk (78 wk)	27 (1 RCT)	⨁◯◯◯ Very low[b]	—	The mean BSID-III scores gross motor was 46.76	MD 1.14 higher (0.56 lower–2.84 higher)

The risk in the intervention group (and its 95% CI) is on the basis of the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). Explanations: high certainty, we are very confident that the true effect lies close to that of the estimate of the effect; moderate certainty, we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; low certainty, our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect; very low certainty, we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect. Patient or population**:** preterm and/or LBW infants. Setting: any high-, middle-, or low-income country; at home or in the health facility. Intervention: multiple micronutrient supplementation. Comparison: no supplementation. IQR, interquartile ratio; —, not applicable.

[a] Downgraded 2 levels for: serious risk of bias; serious imprecision (wide CI).

[b] Downgraded 3 levels for: very serious risk of bias; serious inconsistency (only 1 study, so inconsistency could not be assessed); very serious imprecision (wide CI, suboptimal sample size).

At latest follow-up (mean [SD] 91 [18.38] weeks), the MDs between the infants who received MMN and those who did not receive MMN in WHZ's was −0.04 (95% CI −0.30 to 0.22, I^2 = 0.00%, low certainty evidence, 2 trials, 385 participants)[18,20]; HAZ's was −0.06 (MD −0.06, 95% CI −0.28 to 0.17, I^2 = 17.22%, low certainty evidence, 2 trials, 392 participants)[18,20]; and WAZ's was −0.01 (95% CI −0.27 to 0.25, I^2 = 0.00%, low certainty evidence, 2 trials, 392 participants).[18,20]

At latest follow-up (mean [SD] 91 [18.38] weeks), when comparing infants who received MMN to those who did not receive MMN, the RR for wasting (WHZ < −2 SD score) was 0.86 (95% CI 0.50–1.48, I^2 = 0.00%, low certainty evidence, 2 trials, 398 participants)[18,20]; the RR for stunting (HAZ < −2 SD score) was 1.17 (95% CI 0.83–1.66, I^2 = 0.00%, low certainty evidence, 2 trials, 399 participants)[18,20]; and the RR for underweight (WAZ < −2 SD score) was 1.22 (95% CI 0.85–1.76, I^2 = 0.00%, low certainty evidence, 2 trials, 396 participants).[18,20]

At latest follow-up (78 weeks), the MDs between infants who received MMN and those who did not receive MMN in BISD-III, development scores for: cognitive development was 2.64 (95% CI −0.48 to 5.76, very low certainty evidence, 1 trial, 27 participants)[17]; language development was 1.19 (95% CI −0.33 to 2.71, very low certainty evidence, 1 trial, 27 participants)[17]; expressive language was 0.94 (95% CI −1.13 to 3.01, very low certainty evidence, 1 trial, 27 participants)[17]; fine motor development was 1.03 (95% CI −1.13 to 3.19, very low certainty evidence, 1 trial, 27 participants)[17]; and gross motor score development was 1.14 (1 trial, 27 participants, MD, 95% CI –0.56 to 2.84, very low certainty evidence).[17]

There were insufficient data to perform our prespecified subgroup analyses: gestational age, birth weight, and income level of the country.

DISCUSSION

Data on a subgroup of 414 preterm or LBW infants from 2 RCTs (4 reports) were included in our systematic review. Evidence was insufficient to understand the effects of MMN on mortality, morbidity, growth, and neurodevelopment. There were also no studies examining dose, timing of initiation, and duration of supplementation with MMN.

Using GRADE criteria,[15] we judged the quality of the evidence to be low to very low for all outcomes. The number of participants included in the systematic review was low (n = 414) and the participants were from small subgroups of 2 randomized trials. We downgraded 2 levels for serious imprecision. The trials were not designed to examine effects in preterm or LBW infants, though the Tanzania trial did test for subgroup differences between LBW and non-LBW infants.[17–19] The trials included also used varying types and doses of MMN supplementation, though heterogeneity in the meta-analyses was low. There were insufficient data to stratify our analyses by birth weight, gestational age, and income setting, and we could not perform prespecified subgroup analyses. Strengths of the review include the rigorous methods, the comprehensive literature search, and the community-based settings of the trials.

Overall, we found consistently small increases in all BSID-III scores (cognition, receptive language, expressive language, fine motor, and gross motor) in the MMN compared with non-MMN supplemented infants that may be of clinical significance, though CIs were wide and crossed the line of no effect for all domains. There were only 27 infants in the neurodevelopmental analysis and results were very low certainty. This also highlights an important research gap in understanding the effect of MMN on neurodevelopment in young preterm and LBW infants. For growth outcomes, we found small changes from enrollment to follow-up in wasting, stunting, underweight, and WAZ's, HAZ's, and WHZ's. These effects were all of uncertain clinical significance, and CIs were also wide and crossed the line of no effect for all growth outcomes.

There are many studies that show important beneficial effects of MMNs when given in childhood (6–59 months) on child growth and neurodevelopment.[8,9] There are also studies which show effect on these outcomes when given in pregnancy.[6,7] A number of reviews,[21–26] including those published in this supplement, report important effects of single micronutrients, especially of iron supplementation.[27,28] There are also studies that report possible interactions between iron supplementation on indices of zinc[29] and copper[30] status, zinc supplementation on iron and copper status,[31] and calcium on iron absorption and ascorbic acid on iron status.[32,33] We planned this review specifically to understand the synergistic effects of MMNs and potential harms in combining MMNs for preterm or LBW infants. However, because of the paucity of data we were unable to assess these "combined"

effects. To our knowledge, there have been no other systematic reviews that compared enteral MMN supplementation for preterm or LBW infants fed mother's own milk or donor human milk with no supplementation or placebo.

Overall, MMNs are used widely for preterm and LBW infants in most countries globally. It is of concern that there is such little evidence of their benefits and harms, especially because provision of MMNs is so common in newborns and their mothers. More trials are needed to understand the effects of MMN in preterm and LBW infants. Data on enteral supplementation of preterm or LBW infants fed mother's own milk or donor human milk with MMN are currently insufficient to allow recommendations for practice.

ACKNOWLEDGMENTS

The Society for Applied Studies thanks the core support provided by the Department of Maternal, Newborn, Child and Adolescent Health, World Health Organization, Geneva (World Health Organization Collaborating Centre IND–158).

ABBREVIATIONS

BISD-III: Bayley Scales of Infant Development, Version III
CI: confidence interval
GRADE: Grading of Recommendations Assessment, Development, and Evaluation
HAZ: height for age z-score
LBW: low birth weight
MD: mean difference
MMN: multiple micronutrient
RCT: randomized controlled trial
RR: relative risk
WAZ: weight for age z-score
WHZ: weight for height z-score

FUNDING: Funding was provided from the Department of Maternal, Newborn, Child, and Adolescent Health and Aging, World Health Organization (WHO), Geneva, Switzerland, for this systematic review. Dr. Duggan was supported in part by the National Institutes of Health (#K24DK104676 and #2P30 DK040561). Supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (#NICHD R01 HD048969–01). The sponsor (WHO) commissioned the review for a guideline development group meeting for development of WHO recommendations on care of the preterm or low birth weight infant. The sponsor assisted in formulating the research question and provided inputs on the synthesis of the results and manuscript.

CONFLICT OF INTEREST DISCLAIMER: The authors have indicated they have no conflicts relevant to this article to disclose.

REFERENCES

1. Ballard O, Morrow AL. Human milk composition: nutrients and bioactive factors. *Pediatr Clin North Am*. 2013;60(1):49–74
2. Beltrand J, Alison M, Nicolescu R, et al. Bone mineral content at birth is determined both by birth weight and fetal growth pattern. *Pediatr Res*. 2008;64(1):86–90
3. Bhatia J. Human milk and the premature infant. *Ann Nutr Metab*. 2013;62(Suppl 3):8–14
4. Tam E, Keats EC, Rind F, Das JK, Bhutta AZA. Micronutrient supplementation and fortification interventions on health and development outcomes among children under 5 in low- and middle-income countries: a systematic review and meta-analysis. *Nutrients*. 2020;12(2):E289
5. World Health Organization. *Guidelines On Optimal Feeding of Low Birth Weight Infants in Low- And Middle-Income Countries*. Geneva: World Health Organization; 2011
6. Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev*. 2017;4(4):CD004905
7. Keats EC, Haider BA, Tam E, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev*. 2019;3(3):CD004905
8. Ramakrishnan U, Goldenberg T, Allen LH. Do multiple micronutrient interventions improve child health, growth, and development? *J Nutr*. 2011;141(11):2066–2075
9. Smuts CM, Lombard CJ, Benadé AJ, et al. International Research on Infant Supplementation (IRIS) Study Group. Efficacy of a foodlet-based multiple micronutrient supplement for preventing growth faltering, anemia, and micronutrient deficiency of infants: the four country IRIS trial pooled data analysis. *J Nutr*. 2005;135(3):631S–638S
10. Choudhary TSB, Chowdhury R, Upadhyay R, et al. Enteral multiple micronutrient supplementation in preterm or low birth weight infants. Available at: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021238975. Accessed November 16, 2022
11. Higgins JPTTJ, Chandler J, Cumpston M, et al, eds. Cochrane Handbook for Systematic Reviews of Interventions version 6.2. Cochrane, 2021. Available at: www.training.cochrane.org/handbook. Accessed November 16, 2022
12. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898
13. Mavridis D, Salanti G. How to assess publication bias: funnel plot, trim-and-fill method and selection models. *Evid Based Ment Health*. 2014;17(1):30

14. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557–560

15. Schünemann HBJ, Guyatt G, Oxman A, eds. *GRADE Handbook For Grading Quality of Evidence and Strength of Recommendations*. Available at: guidelinedevelopment.org/handbook. Accessed June 30, 2022

16. McMaster University. GRADEpro GDT: GRADEpro guideline development tool. [software]. Evidence Prime lAfhgocgo

17. Locks LM, Manji KP, McDonald CM, et al. The effect of daily zinc and/or multivitamin supplements on early childhood development in Tanzania: results from a randomized controlled trial. *Matern Child Nutr*. 2017;13(2):e12306

18. Locks LM, Manji KP, McDonald CM, et al. Effect of zinc and multivitamin supplementation on the growth of Tanzanian children aged 6-84 wk: a randomized, placebo-controlled, double-blind trial. *Am J Clin Nutr*. 2016;103(3):910–918

19. McDonald CM, Manji KP, Kisenge R, et al. Daily zinc but not multivitamin supplementation reduces diarrhea and upper respiratory infections in Tanzanian infants: a randomized, double-blind, placebo-controlled clinical trial. *J Nutr*. 2015;145(9):2153–2160

20. Ramakrishnan U, Neufeld LM, Flores R, Rivera J, Martorell R. Multiple micronutrient supplementation during early childhood increases child size at 2 y of age only among high compliers. *Am J Clin Nutr*. 2009;89(4):1125–1131

21. Darlow BA, Graham PJ, Rojas-Reyes MX. Vitamin A supplementation to prevent mortality and short- and long-term morbidity in very low birth weight infants. *Cochrane Database Syst Rev*. 2016;2016(8):CD000501

22. Haider BA, Sharma R, Bhutta ZA. Neonatal vitamin A supplementation for the prevention of mortality and morbidity in term neonates in low- and middle-income countries. *Cochrane Database Syst Rev*. 2017;2(2):CD006980

23. Harding JE, Wilson J, Brown J. Calcium and phosphorus supplementation of human milk for preterm infants. *Cochrane Database Syst Rev*. 2017;2(2):CD003310

24. Huey SL, Acharya N, Silver A, et al. Effects of oral vitamin D supplementation on linear growth and other health outcomes among children under five years of age. *Cochrane Database Syst Rev*. 2020;12(12):CD012875

25. Tan ML, Abrams SA, Osborn DA. Vitamin D supplementation for term breastfed infants to prevent vitamin D deficiency and improve bone health. *Cochrane Database Syst Rev*. 2020;12(12):CD013046

26. Zittermann A, Pilz S, Berthold HK. Serum 25-hydroxyvitamin D response to vitamin D supplementation in infants: a systematic review and meta-analysis of clinical intervention trials. *Eur J Nutr*. 2020;59(1):359–369

27. McCarthy EK, Dempsey EM, Kiely ME. Iron supplementation in preterm and low birth weight infants: a systematic review of intervention studies. *Nutr Rev*. 2019;77(12):865–877

28. Mills RJ, Davies MW. Enteral iron supplementation in preterm and low birth weight infants. *Cochrane Database Syst Rev*. 2012;(3):CD005095

29. Sandström B, Davidsson L, Cederblad A, Lönnerdal B. Oral iron, dietary ligands and zinc absorption. *J Nutr*. 1985;115(3):411–414

30. Sandström B. Micronutrient interactions: effects on absorption and bioavailability. *Br J Nutr*. 2001;85(Suppl 2):S181–S185

31. Yadrick MK, Kenney MA, Winterfeldt EA. Iron, copper, and zinc status: response to supplementation with zinc or zinc and iron in adult females. *Am J Clin Nutr*. 1989;49(1):145–150

32. Hallberg L, Bengtsson C, Lapidus L, Lindstedt G, Lundberg PA, Hultén L. Screening for iron deficiency: an analysis based on bone-marrow examinations and serum ferritin determinations in a population sample of women. *Br J Haematol*. 1993;85(4):787–798

33. Hallberg L, Brune M, Erlandsson M, Sandberg AS, Rossander-Hultén L. Calcium: effect of different amounts on nonheme- and heme-iron absorption in humans. *Am J Clin Nutr*. 1991;53(1):112–119