TEHRAN UNIVERSITY OF MEDICAL SCIENCES

Prenatal and lactation Supplementation

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01

Perenatal supplementation

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Background

1. Micronutrient deficiencies are a key contributing factor to poor health and suboptimal development outcomes, and they especially affect women and children who reside in low- and middle-income countries (LMICs)

2. They often result from diets that chronically lack diversity or proper and sufficient nutrients, and in some cases, from infections and/or chronic disease that inhibit proper nutrient absorption

Darnton-Hill, I.; Mkparu, U.C. Micronutrients in pregnancy in low- and middle-income countries. *Nutrients* **2015**, *7*, 1744–1768

3. Micronutrient deficiencies are of particular concern as they will threaten the survival and well-being of women of reproductive age (WRA) and their infants, and may put subsequent generations of children at risk due to the intergenerational transfer of malnutrition

4. Micronutrient deficiencies are often exacerbated during pregnancy due to increased nutritional requirements and, in LMICs, often appear concurrently (deficiencies in two or more micronutrients)

- FAO; IFAD; WHO; WFP; UNICEF. *The State of Food Security and Nutrition in the World 2019. Safeguarding against Economic Slowdowns and Downturns*; FAO: Rome, Italy, 2019.
- UNICEF. *The State of the World's Children 2019. Children, Food and Nutrition: Growing Well in a Changing World*; UNICEF: New York, NY, USA, 2019.

02

Common Deficiencies

Vitamin A

01

vitamin A deficiency affects approximately 15.3% (95% CI 6.0–24.6%) of pregnant women.

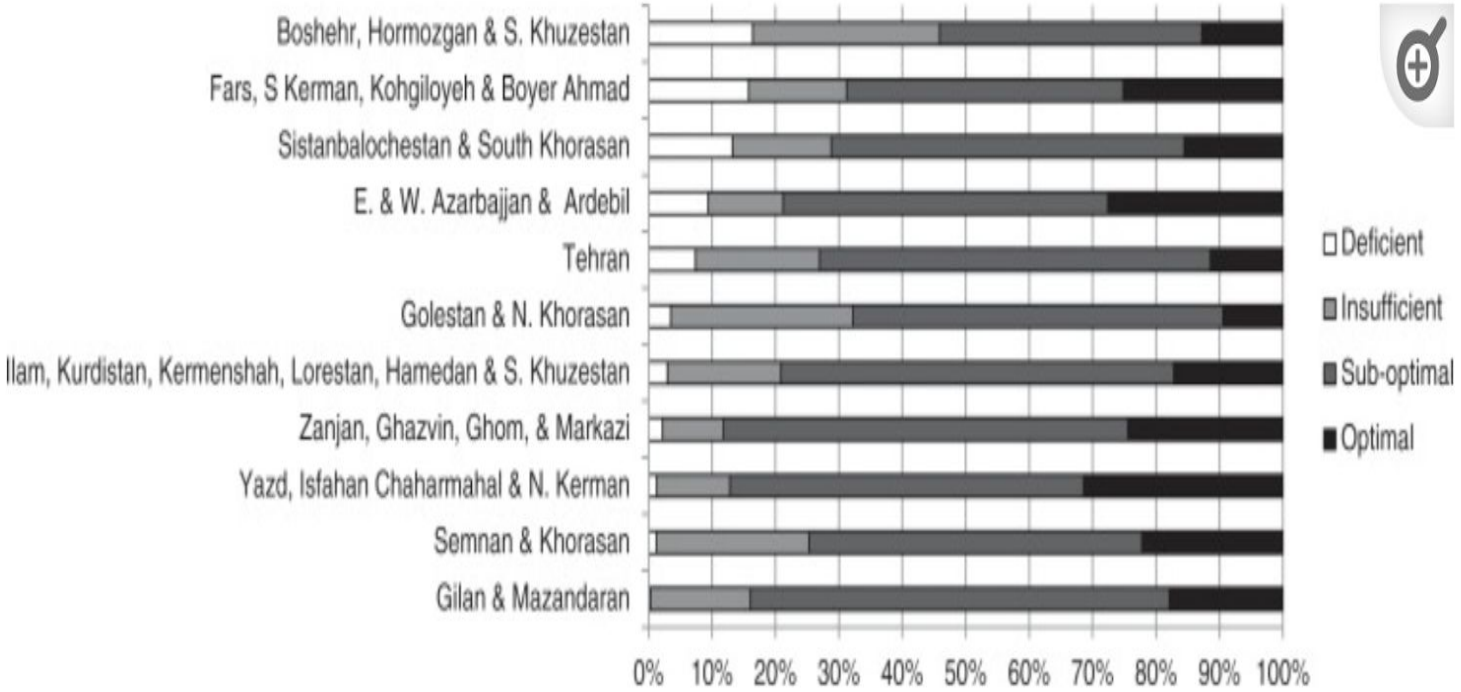
Vitamin A

02

vitamin A deficiency affects approximately 6.6% of Iranian pregnant women.

- Black, R.E.; Victora, C.G.; Walker, S.P.; Bhutta, Z.A.; Christian, P.; de Onis, M.; Ezzati, M.; Grantham-McGregor, S.; Katz, J.; Martorell, R.; et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet* **2013**, *382*, 427–451
- Olang, B., Abdollahi, Z., Neshati, R., Ali, M. A., Naghavi, M., & Yngve, A. (2014). Vitamin A status in pregnant women in Iran in 2001 and its relationship with province and gestational age. *Food & nutrition research*, *58*, 10.3402/fnr.v58.25707. https://doi.org/10.3402/fnr.v58.25707

Fig. 1 Vitamin A deficiencies among Iranian pregnant women.



Percentage distribution of vitamin A status in the 11 regions of Iran.

- Olang, B., Abdollahi, Z., Neshati, R., Ali, M. A., Naghavi, M., & Yngve, A. (2014). Vitamin A status in pregnant women in Iran in 2001 and its relationship with province and gestational age. *Food & nutrition research*, *58*, 10.3402/fnr.v58.25707. https://doi.org/10.3402/fnr.v58.25707

Vitamin A deficiency

Serum concentration of retinol <20 microg/dL appears to indicate a deficient status, and is associated with an increased risk of preterm delivery and maternal anaemia.

- Czuba, Lindsay C et al. “Plasma Retinoid Concentrations Are Altered in Pregnant Women.” Nutrients vol. 14,7 1365. 25 Mar. 2022, doi:10.3390/nu14071365

Iron deficiency

01

Prenatal iron deficiency is one common example with a high global prevalence of 19.2% (95% confidence interval (CI) 17.1–21.5%)

Iron deficiency

02

Concerning pregnancy anemia, Iran's details are unknown. The overall estimate of anemia prevalence in Iranian pregnant women was 13.6 (95% CI: 8.3 - 18.9)

- Black, R.E.; Victora, C.G.; Walker, S.P.; Bhutta, Z.A.; Christian, P.; de Onis, M.; Ezzati, M.; Grantham-McGregor, S.; Katz, J.; Martorell, R.; et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet* **2013**, *382*, 427–451
- Barooti, Esmat & Rezazadeh kermani, Mohammad & Sadeghirad, Behnam & Motaghi, Shahrzad & Tayeri, Soodabeh & Arabi, Minoo & Salahi, Saman & Haghdoost, AliAkbar. (2010). Prevalence of Iron Deficiency Anemia among Iranian Pregnant Women; a Systematic Review and Meta-analysis. Journal of Reproduction & Infertility. 11. 17-24.

Iron deficiency

iron deficiency can cause serious health complications, including:

intrauterine growth restriction, which means that the baby's growth is too slow, low birth weight, premature labor, anemia in the newborn, breathing issues in the baby at birth

- https://www.medicalnewstoday.com/articles/anemia-in-pregnancy-2#complications

Zinc deficiency

01

Globally, around 82% of pregnant women have experienced a lower zinc intake capacity as compared to the recommended dietary intake

Zinc deficiency

02

It has been suggested that maternal zinc supplementation can reduce preterm birth

- Endalifer ML, Azeze GG, Diress G, Bizuneh AD, Demelash H. A systematic review protocol on the epidemiology of zinc deficiency and associated factors during pregnancy in Africa. Journal of Global Health Reports. 2020;4:e2020021. doi:10.29392/001c.12501
- Ota, E.; Mori, R.; Middleton, P.; Tobe-Gai, R.; Mahomed, K.; Miyazaki, C.; Bhutta, Z.A. Zinc supplementation for improving pregnancy and infant outcome. *Cochrane Database Syst. Rev.* **2015**

Vitamin D deficiency

01

The prevalence of vitamin D deficiency in Iranian pregnant women based on cutoff point of 10, 20 ng/ml was estimated to be 42%, 56% respectively

Vitamin D deficiency

02

lead to pre-eclampsia, and subsequently increase the risks of preterm birth, small-for-gestational age (SGA) and perinatal mortality

- Dror, D.K. Vitamin D status during pregnancy: Maternal, fetal, and postnatal outcomes. *Curr. Opin. Obs. Gynecol.* **2011**, *23*, 422–426
- Badfar G, Shohani M, Mansouri A, Soleymani A, Azami M. Vitamin D status in Iranian pregnant women and newborns: a systematic review and meta-analysis study. Expert Rev Endocrinol Metab. 2017 Sep;12(5):379-389. doi: 10.1080/17446651.2017.1365596. PMID: 30058894.

Insufficient Ca

01

The prevalence of Ca deficiency is 33.5% in Iranian pregnant women.

Insufficient Ca

02

linked to the development of hypertension, which is a leading cause of maternal mortality, morbidity, fetal growth restriction and preterm birth

- Abbasian, Maryam & Chaman, Reza & Delvarianzadeh, Mehri & Amiri, Mohammad & Raei, Mehdi & Norouzi, Pirasteh & Zadeh, Azam. (2012). Investigating the Prevalence of Calcium Deficiency and Some of its Influencing Factors in Pregnant Women and their Neonates. Knowledge & Health. 7. 44-48.
- Ortega, R.M.; Martinez, R.M.; Lopez-Sobaler, A.M.; Andres, P.; Quintas, M.E. Influence of calcium intake on gestational hypertension. *Ann. Nutr. Metab.* **1999**, *43*, 37–46

Folate & Iodine

01

The prevalence of folate deficiency was >20% in many countries with lower income economies but was typically <5% in countries with higher income economies.

Folate & Iodine

02

The prevalence of Iodine deficiency was reported 22.7% in Iranian pregnant woman in 2018.

- Jamshidi M, Naghibzadeh-Tahami A, Maleki E, Borhaninejad V, Alizadeh H, Farokhnia M et al . An assessment of urinary Iodine in pregnant women: brief report. Tehran Univ Med J. 2018; 76 (3) :216-220
- Rogers, L. M., Cordero, A. M., Pfeiffer, C. M., Hausman, D. B., Tsang, B. L., De-Regil, L. M., Rosenthal, J., Razzaghi, H., Wong, E. C., Weakland, A. P., & Bailey, L. B. (2018). Global folate status in women of reproductive age: a systematic review with emphasis on methodological issues. Annals of the New York Academy of Sciences, 1431(1), 35–57. https://doi.org/10.1111/nyas.13963

Folate & Iodine

Severely impair fetal development, leading to neural tube defects (NTDS) and an increased risk of mental retardation and cretinism, respectively

- De-Regil, L.M.; Pena-Rosas, J.P.; Fernandez-Gaxiola, A.C.; Rayco-Solon, P. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. *Cochrane Database Syst. Rev.* **2015**
- Dunn, J.T. Iodine supplementation and the prevention of cretinism. *Ann. N. Y. Acad. Sci.* **1993**, *678*, 158–168

03

Current Strategies and Interventions

- ✔ Micronutrient supplementation is another common strategy, often used for short-term, preventive purposes targeting specific at-risk population groups.

- ✔ Supplementation is a recommended part of routine antenatal care to overcome complications associated with micronutrient deficiencies during pregnancy, and to support maternal health and fetal development

WHO Recommendation

The World Health Organization (WHO) recommends:

- Daily iron and folic acid (IFA) supplementation with 30–60 mg of elemental iron and 400 µg (0.4 mg) folic acid recommended for pregnant women to prevent maternal anemia, puerperal sepsis, low birth weight and preterm birth.

- In populations where anemia prevalence is **less than 20%**, or where side effects from daily supplementation are severe, the WHO recommends intermittent (once weekly) supplementation with 120 mg of elemental iron and 2800 µg folic acid instead.

- WHO. *WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience*; World Health Organization: Geneva, Switzerland, 2016.

WHO Recommendation

- Daily calcium supplementation (1.5–2.9 g oral elemental calcium) in populations with low dietary calcium intake.
- Daily or weekly vitamin A supplementation (up to 10,000 IU or 25,000 IU, respectively) where vitamin A deficiency is a severe public health problem
- Zinc supplementation is only recommended where rigorous research supports its provision, and vitamin D supplementation is not recommended for pregnant women to improve maternal and perinatal outcomes

- WHO. *WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience*; World Health Organization: Geneva, Switzerland, 2016

The new findings of research suggested the use of the form beta-carotene vitamin A instead of retinol form:

- Beta-carotene is converted to vitamin A in the body on an ‘as required’ basis which reduces the risk of vitamin A toxicity. This makes it safe during pregnancy when high levels of vitamin A itself (retinol) should be avoided

- Not generally available as a single supplement. Commonly available as part of a multivitamin and mineral formula.

RDA Recommendation

Table 1. Daily Recommended Dietary Allowance for Vitamins, Micronutrients and Macronutrients for Pregnancy.

Vitamins, Micronutrients and Macronutrients	Unit	Institute of Medicine Recommended Dietary Allowance (RDA) for Pregnancy		
		14–18 Years	19–30 Years	31–50 Years
Vitamin A (retinol)	µg	750	770	770
Vitamin B1 (thiamin)	mg	1.4	1.4	1.4
Vitamin B2 (riboflavin)	mg	1.4	1.4	1.4
Vitamin B3 (niacin)	mg	18	18	18
Vitamin B5 (pantothenic acid)	mg	*6*	*6*	*6*
Vitamin B6 (pyridoxine)	mg	1.9	1.9	1.9
Vitamin B7 (biotin)	µg	*30*	*30*	*30*
Vitamin B9 (folate)	µg	600	600	600
Vitamin B12 (cobalamine)	µg	2.6	2.6	2.6
Vitamin C (ascorbate)	mg	80	85	85
Vitamin D (cholecalciferol)	IU	15	15	15
Vitamin E (tocopherol acetate)	mg	15	15	15
Vitamin K (phytomenadione)	µg	*75*	*90*	*90*
Choline	mg	*450*	*450*	*450*
Calcium	mg	1300	1000	1000
Chromium	g	*29*	*30*	*30*

RDA Recommendation

Table 1. Daily Recommended Dietary Allowance for Vitamins, Micronutrients and Macronutrients for Pregnancy.

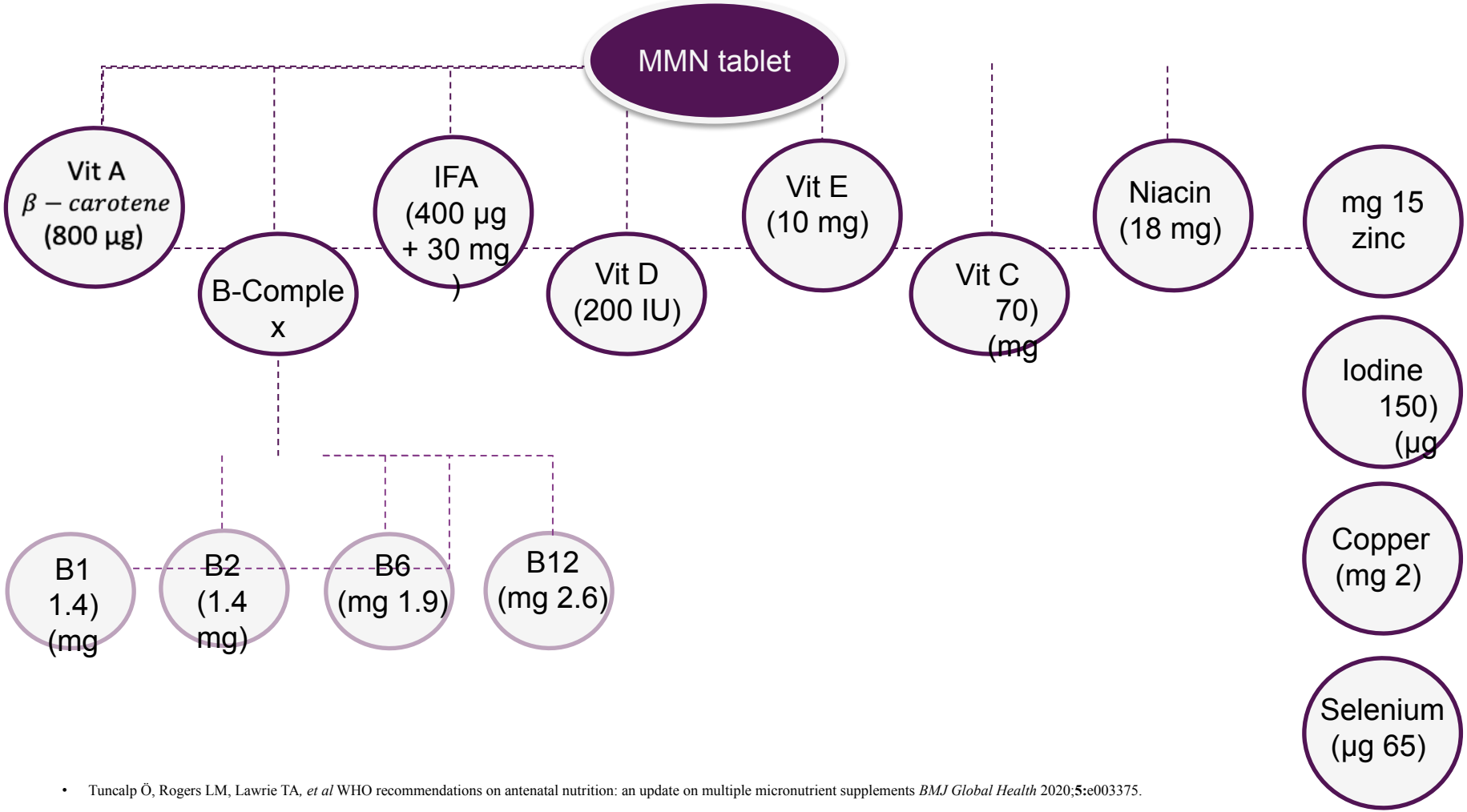
Vitamins, Micronutrients and Macronutrients	Unit	Institute of Medicine Recommended Dietary Allowance (RDA) for Pregnancy		
		14–18 Years	19–30 Years	31–50 Years
Copper	µg	1000	1000	1000
Fluoride	mg	*3*	*3*	*3*
Iodine	µg	220	220	220
Iron	mg	27	27	27
Magnesium	mg	400	350	360
Phosphorus	mg	1250	700	700
Selenium	µg	60	60	60
Zinc	mg	12	11	11
Potassium	mg	*2600*	*2900*	*2900*
Sodium	mg	*1500*	*1500*	*1500*
Chloride	g	*2.3*	*2.3*	*2.3*
Carbohydrate	g	175	175	175
Fat	g	Not determined	Not determined	Not determined
Linoleic Acid	g	*13*	*13*	*13*
α-Linoleic Acid	g	*1.4*	*1.4*	*1.4*
Protein	g	71	71	71

*Note: Adequate intakes are in *italics*.

UNIMMAP

- To address the issue of multiple, concurrent micronutrient deficiencies, the United Nations Children's Fund (UNICEF), United Nations University, and the WHO developed a multiple-micronutrient (MMN) tablet, called UNIMMAP

- UNICEF; WHO; UNU. *Composition of a Multi-Micronutrient Supplement to Be Used in Pilot Programmes among Pregnant Women in Developing Countries*; Report of a United Nations Children's Fund (UNICEF), World Health Organization (WHO), United Nations University (UNU) Workshop; UNICEF: New York, NY, USA, 1999.



- Tuncalp Ö, Rogers LM, Lawrie TA, *et al* WHO recommendations on antenatal nutrition: an update on multiple micronutrient supplements *BMJ Global Health* 2020;**5:**e003375.

Table 1. Daily Recommended Dietary Allowance for Vitamins, Micronutrients and Macronutrients for Pregnancy.

Vitamins, Micronutrients and Macronutrients	Unit	Institute of Medicine Recommended Dietary Allowance (RDA) for Pregnancy		
		14–18 Years	19–30 Years	31–50 Years
Vitamin A (retinol)	µg	750	770	770
Vitamin B1 (thiamin)	mg	1.4	1.4	1.4
Vitamin B2 (riboflavin)	mg	1.4	1.4	1.4
Vitamin B3 (niacin)	mg	18	18	18
Vitamin B5 (pantothenic acid)	mg	*6*	*6*	*6*
Vitamin B6 (pyridoxine)	mg	1.9	1.9	1.9
Vitamin B7 (biotin)	µg	*30*	*30*	*30*
Vitamin B9 (folate)	µg	600	600	600
Vitamin B12 (cobalamine)	µg	2.6	2.6	2.6
Vitamin C (ascorbate)	mg	80	85	85
Vitamin D (cholecalciferol)	IU	15	15	15
Vitamin E (tocopherol acetate)	mg	15	15	15
Vitamin K (phytomenadione)	µg	*75*	*90*	*90*
Choline	mg	*450*	*450*	*450*
Calcium	mg	1300	1000	1000
Chromium	g	*29*	*30*	*30*
Copper	µg	1000	1000	1000
Fluoride	mg	*3*	*3*	*3*
Iodine	µg	220	220	220
Iron	mg	27	27	27
Magnesium	mg	400	350	360
Phosphorus	mg	1250	700	700
Selenium	µg	60	60	60
Zinc	mg	12	11	11
Potassium	mg	*2600*	*2900*	*2900*
Sodium	mg	*1500*	*1500*	*1500*
Chloride	g	*2.3*	*2.3*	*2.3*
Carbohydrate	g	175	175	175
Fat	g	Not determined	Not determined	Not determined
Linoleic Acid	g	*13*	*13*	*13*
α-Linoleic Acid	g	*1.4*	*1.4*	*1.4*
Protein	g	71	71	71

*Note: Adequate intakes are in *italics*.

Table 1 Vitamins and minerals included in the United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP) formulation[6]

Micronutrient	Dose
Vitamin A	800 µg
Vitamin D	200 IU
Vitamin E	10 mg
Niacin	18 mg
Folic acid	400 µg (0.4 mg)
Vitamin B_1	1.4 mg
Vitamin B_2	1.4 mg
Vitamin B_6	1.9 mg
Vitamin B_{12}	2.6 µg
Vitamin C	70 mg
Zinc	15 mg
Iron	30 mg
Selenium	65 µg
Copper	2 mg
Iodine	150 µg

- lipid-based nutrient supplements (LNS) have been used to address the adverse effects of micronutrient deficiencies in mothers.
- LNS supplements typically contain the same vitamins and minerals found in MMN supplements, with the added components of protein, essential fatty acids, and energy in the form of fats (such as vegetable fat, peanut/groundnut paste, milk powder and sugar)

- Arimond, M.; Zeilani, M.; Jungjohann, S.; Brown, K.H.; Ashorn, P.; Allen, L.H.; Dewey, K.G. Considerations in developing lipid-based nutrient supplements for prevention of undernutrition: Experience from the International Lipid-Based Nutrient Supplements (iLiNS) Project. *Matern. Child Nutr.* **2015**, *11* (Suppl. 4), 31–61

Point

It is important to highlight that the WHO does not advocate MMN supplementation for pregnant women living in developed countries or for anyone who does not have deficits in order to improve maternal and perinatal outcomes.

WHO has not yet issued any guidance for LNS

- WHO. *WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience*; World Health Organization: Geneva, Switzerland, 2016.

04

Results

Vitamin A

Finding:

- ✔ Some Vitamin A precursors, such as carotenoids, produce no mutagenic, embryotoxic, or teratogenic effects and do not induce hypervitaminosis A
- ✔ β-C supplementation during pregnancy was associated with a 40% reduction in risk of pregnancy-related mortality
- ✔ High intakes of total carotenoids, β-Carotene, β-cryptoxanthin, lycopene and lutzea may be associated with a reduction in the risk of developing Preeclampsia

- Thorne-Lyman, A. L., & Fawzi, W. W. (2012). Vitamin A and carotenoids during pregnancy and maternal, neonatal and infant health outcomes: a systematic review and meta-analysis. *Paediatric and perinatal epidemiology*, *26 Suppl 1*(0 1), 36–54. https://doi.org/10.1111/j.1365-3016.2012.01284.x
- Guo, J., Li, B., Zuo, Z., Chen, M., & Wang, C. (2019). *Maternal Supplementation with β-Carotene During Pregnancy Disturbs Lipid Metabolism and Glucose Homoeostasis in F1 Female Mice. Molecular Nutrition & Food Research, 1900072*.doi:10.1002/mnfr.201900072
- Kang, T., Liu, Y., Chen, X., Huang, X., Cao, Y., Dou, W., Duan, D., Bo, Y., Traore, S. S., Zhao, X., Fu, W., Zeng, F., Liu, J., & Lyu, Q. (2022). Dietary carotenoid intake and risk of developing preeclampsia: a hospital-based case-control study. *BMC pregnancy and childbirth*, *22*(1), 427. https://doi.org/10.1186/s12884-022-04737-5

Zinc

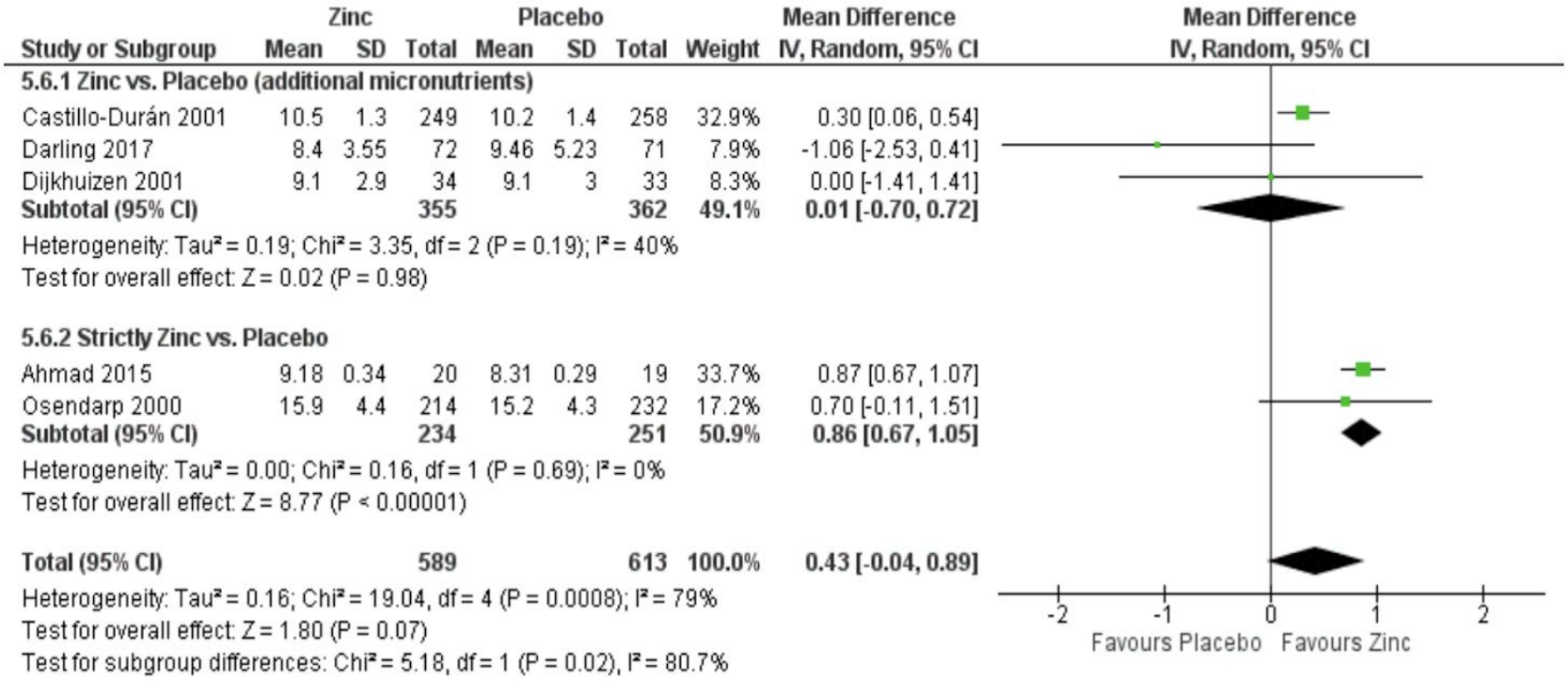


Figure 3. Forest plot for comparison zinc supplementation versus placebo/no zinc from baseline to post-intervention for maternal serum/plasma zinc concentration (umol/L).

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347
- Darling A.M., Mugusi F.M., Etheredge A.J., Gunaratna N.S., Abioye A.I., Aboud S., Duggan C., Mongi R., Spiegelman D., Roberts D., et al. Vitamin A and Zinc Supplementation Among Pregnant Women to Prevent Placental Malaria: A Randomized, Double-Blind, Placebo-Controlled Trial in Tanzania. *Am. J. Trop. Med. Hyg.* 2017;96:826–834. doi: 10.4269/ajtmh.16-0599.

Finding:

- ✔ **No impact** on the risk of having a low birthweight baby

- ✔ **No effect** on reducing the risk of pre-eclampsia/eclampsia preterm birth infants considered SGA

- ✔ May **have improved** maternal serum/plasma zinc concentrations, although the lower limit of the confidence interval just crossed the line of no effect

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

Iron

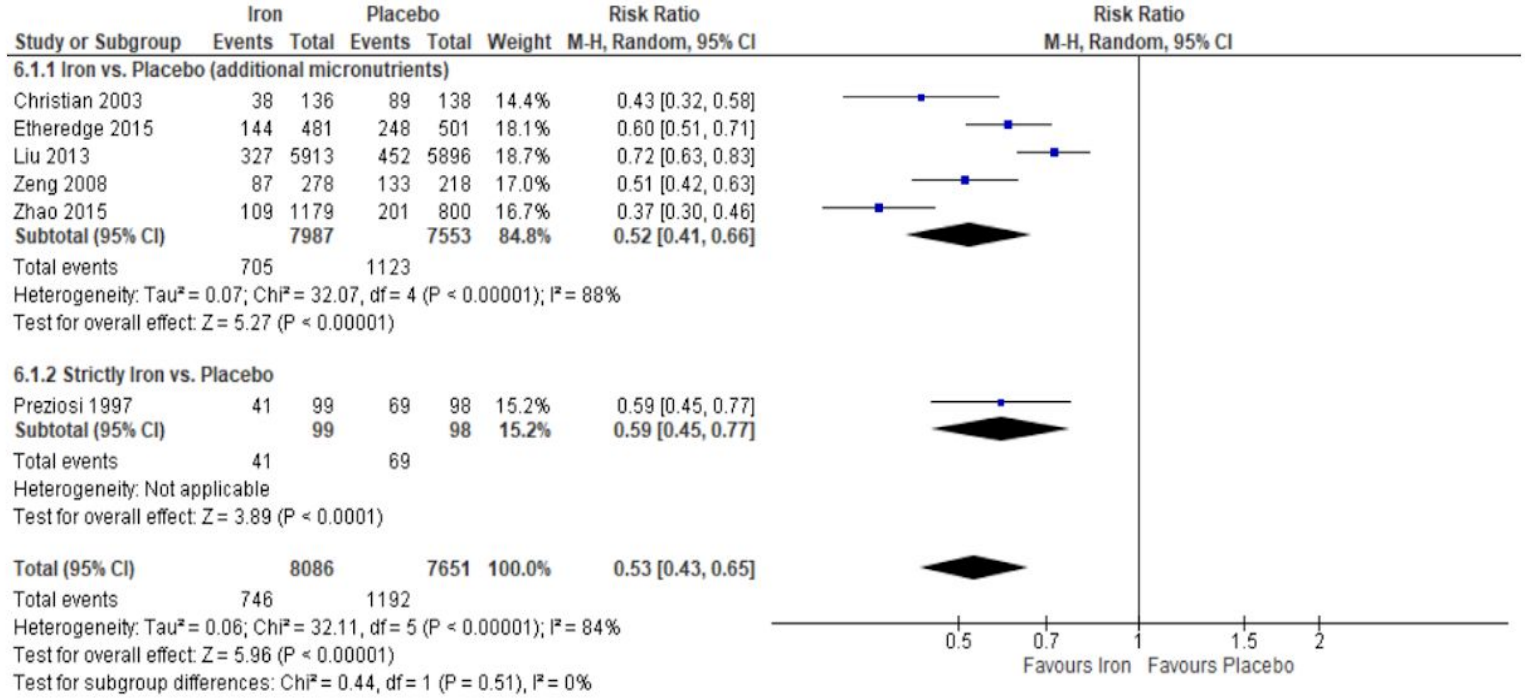


Figure 4. Forest plot for comparison iron supplementation versus placebo/no iron from baseline to post-intervention on the risk of maternal anemia.

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

- Etheredge A.J., Premji Z., Gunaratna N.S., Abioye A.I., Aboud S., Duggan C., Mongi R., Meloney L., Spiegelman D., Roberts D., et al. Iron Supplementation in Iron-Replete and Nonanemic Pregnant Women in Tanzania: A Randomized Clinical Trial. *JAMA Pediatr.* 2015;169:947–955. doi: 10.1001/jamapediatrics.2015.1480

Finding:

- ✔ For maternal anemia, a post-hoc analysis was conducted between studies that gave strictly iron supplements versus placebo and studies that provided iron supplements with other additional micronutrients, typically vitamin A or folic acid:
- ✔ **No significant** differences between subgroups were observed
- ✔ Iron supplementation **improved** maternal hemoglobin concentration, maternal serum/plasma ferritin concentrations

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

Finding:

- ✔ **No differences** were observed for maternal hemoglobin concentration between studies that provided strictly iron and studies that gave additional micronutrients

- ✔ There were **significant differences** for maternal serum/plasma ferritin concentrations

- ✔ Studies that gave iron with additional micronutrients showed a **greater effect** on ferritin concentration than studies that gave only iron

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

Finding:

- ✔ Iron supplementation **reduced** rates of iron deficiency when compared to placebo
- ✔ Iron supplementation appeared to have little effect
  - Maternal transferrin receptor concentration
  - Reducing the risk of pre-eclampsia/eclampsia
  - Infant mortality
  - Preterm births
  - And SGA infants

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

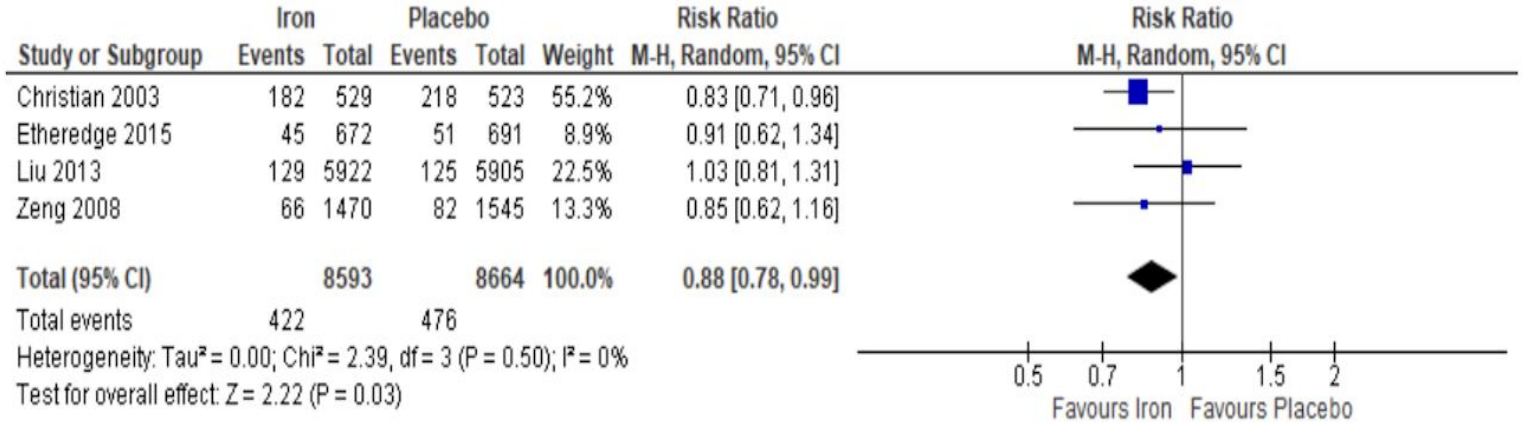


Figure 5. Forest plot for comparison iron supplementation versus placebo/no iron from baseline to post-intervention on the risk of low birthweight infants.

- ✔ Iron supplementation reduced the risk of maternal anemia by 47%
- ✔ Reduced the risk of having a low birthweight baby by 12%
- ✔ No effect of iron on the risk of perinatal mortality

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

Vitamin D

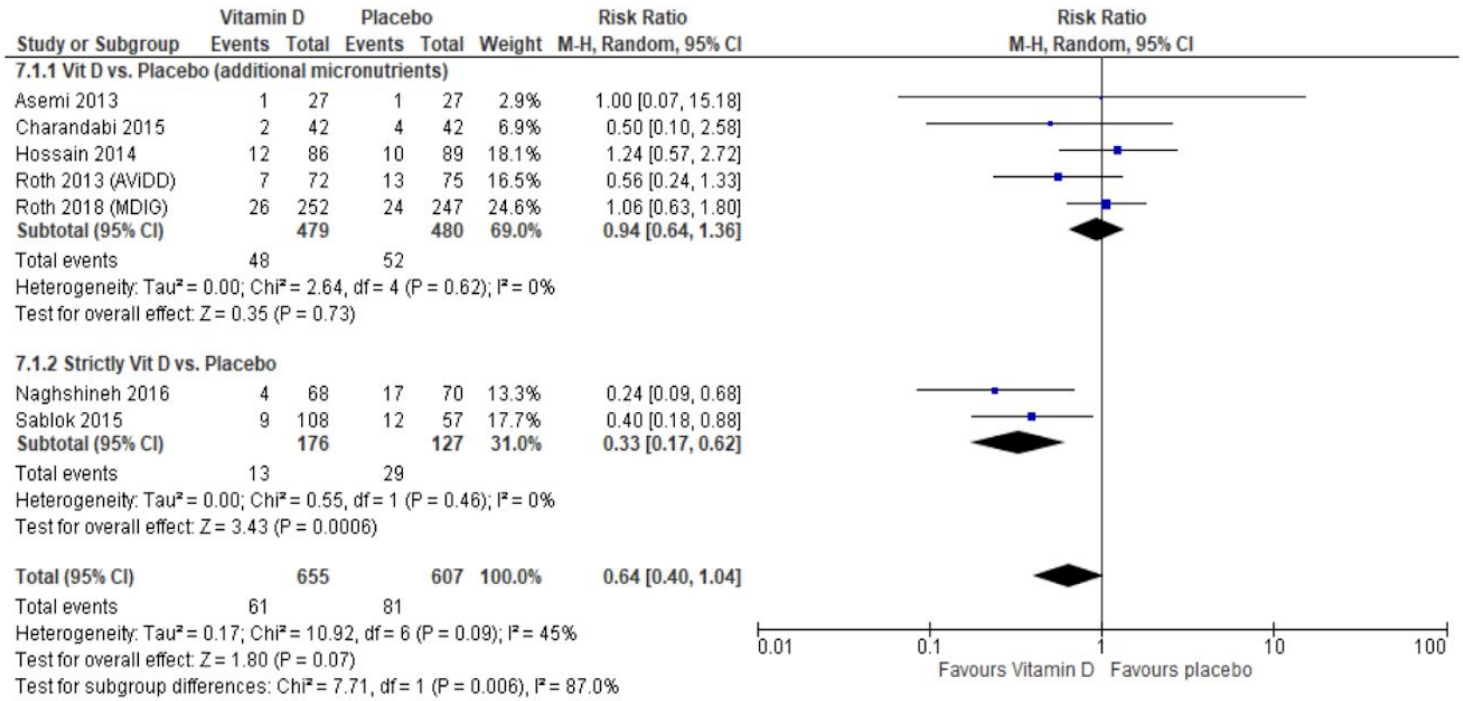


Figure 6. Forest plot for comparison vitamin D supplementation versus placebo/no vitamin D on the risk of preterm births.

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

- Etheredge A.J., Premji Z., Gunaratna N.S., Abioye A.I., Aboud S., Duggan C., Mongi R., Meloney L., Spiegelman D., Roberts D., et al. Iron Supplementation in Iron-Replete and Nonanemic Pregnant Women in Tanzania: A Randomized Clinical Trial. *JAMA Pediatr.* 2015;169:947–955. doi: 10.1001/jamapediatrics.2015.1480

Finding:

- ✔ Vitamin D supplementation may **have reduced** the risk of preterm births by 36%
- ✔ Studies that strictly gave vitamin D showed **a greater reduction** in preterm birth risk compared to studies that provided additional supplements such as iron and folic acid

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

Finding:

- ✔ Vitamin D supplementation made **no difference** on the risk of infants born SGA, the risk of having a Caesarean section as a mode of delivery or maternal serum/plasma calcium concentrations

- ✔ **BUT** did **significantly increase** the vitamin D concentrations in pregnant mothers

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

Guidelines for countrywide supplemental aid

From the onset of pregnancy until birth, all pregnant women must take 1000 IU of vitamin D every day. This vitamin may be taken alone or, after the 16th week of pregnancy, as part of a multivitamin (as long as it includes 1,000 units of vitamin D).

Drugs interactions

Drugs	Decreased absorption	Increase level of vitamin D
Prednisolone	✓	
Anticonvulsant drugs	✓	
Tuberculosis drugs	✓	
Tiazid		✓

Drugs interactions

Point

- A person who is taking an antacid must take vitamin D two hours before or four hours after taking the **antiacid**.

Drugs interactions

Point

A monthly oral dosage of 50,000 units and injectable doses of 30,000 and 500,000 units of vitamin D are **not suggested** (due to the increased risk of bone fractures associated with extremely high doses during pregnancy).

Calcium

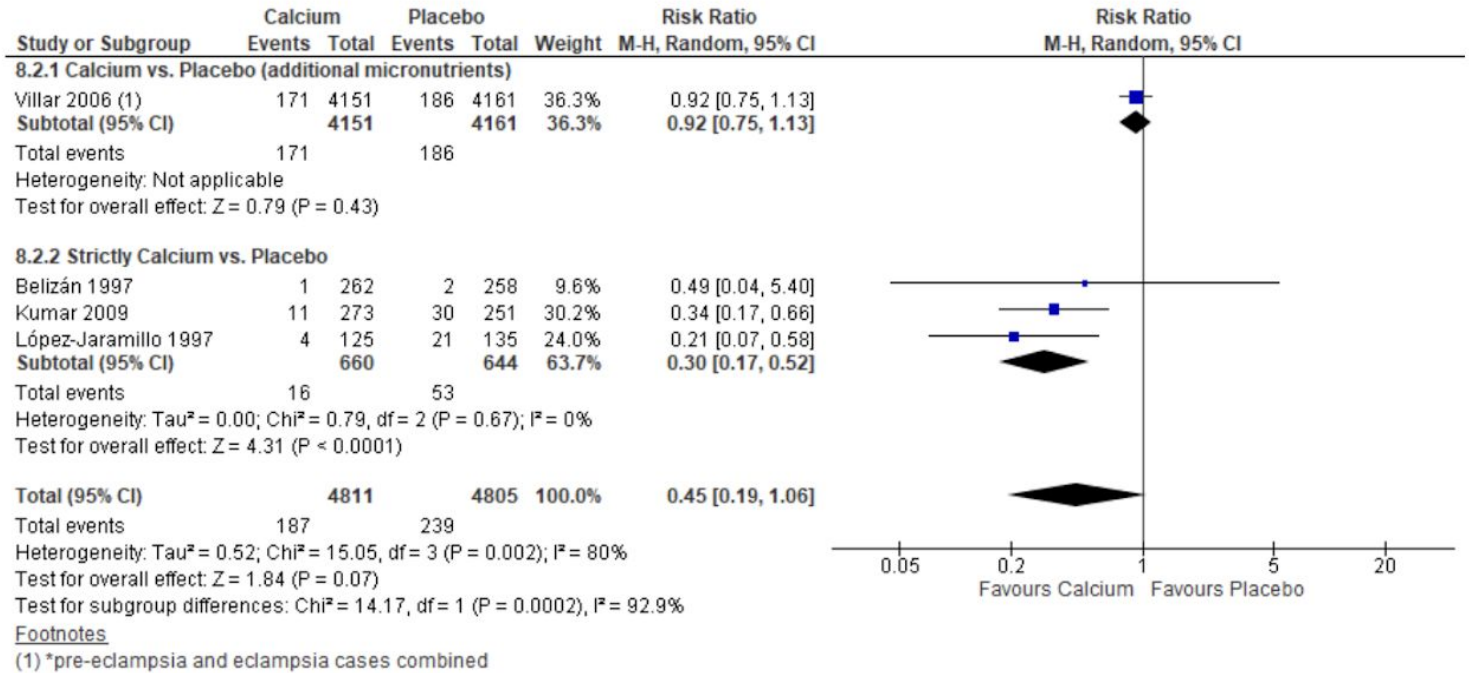


Figure 7. Forest plot for comparison calcium supplementation versus no calcium/placebo on the risk of pre-eclampsia/eclampsia in mothers during pregnancy.

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

Finding:

- ✔ Calcium supplementation, compared to placebo, **did not impact** the risk of having a low birthweight baby, stillbirths, preterm births, or Caesarean section as a mode of delivery.
- ✔ Calcium supplementation **may have improved** the risk of maternal preeclampsia/ eclampsia

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

Finding:

✔ In a post-hoc analysis, studies that provided only calcium to mothers showed a **greater reduction** in the risk of pre-eclampsia/eclampsia compared to studies that provided additional micronutrients

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

Iron-Folic Acid

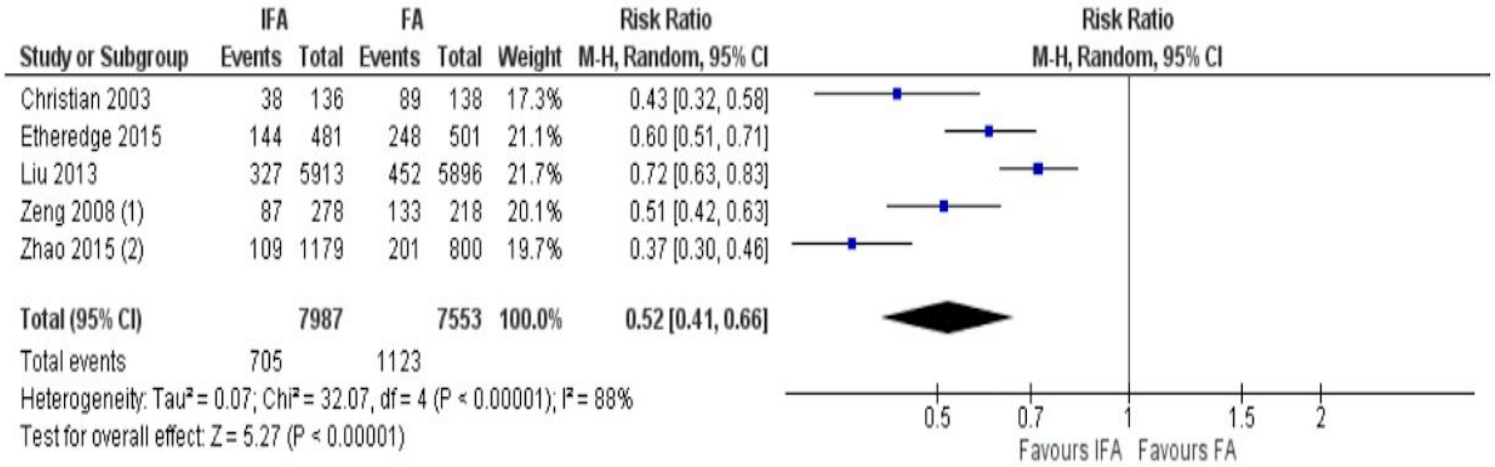


Figure 8. Forest plot of comparison Iron-Folic Acid (IFA) versus Folic Acid (FA) supplementation/placebo, from baseline to post-intervention on the risk of maternal anemia.

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

- Zhao G., Xu G., Zhou M., Jiang Y., Richards B., Clark K.M., Kaciroti N., Georgieff M.K., Zhang Z., Tardif T., et al. Prenatal Iron Supplementation Reduces Maternal Anemia, Iron Deficiency, and Iron Deficiency Anemia in a Randomized Clinical Trial in Rural China, but Iron Deficiency Remains Widespread in Mothers and Neonates. *J. Nutr.* 2015;145:1916–1923. doi: 10.3945/jn.114.208678.

Finding:

- ✔ IFA supplementation compared to FA, a **48% reduction** in the risk of maternal anemia in the third trimester of pregnancy.
- ✔ **Significant increases** with IFA supplementation were maternal hemoglobin concentration and maternal serum/plasma ferritin concentration.
- ✔ IFA supplementation **did not show significant** differences for the following outcomes: maternal serum/plasma transferrin receptor concentration, neonatal mortality, preterm births, SGA infants, and infant mortality.

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

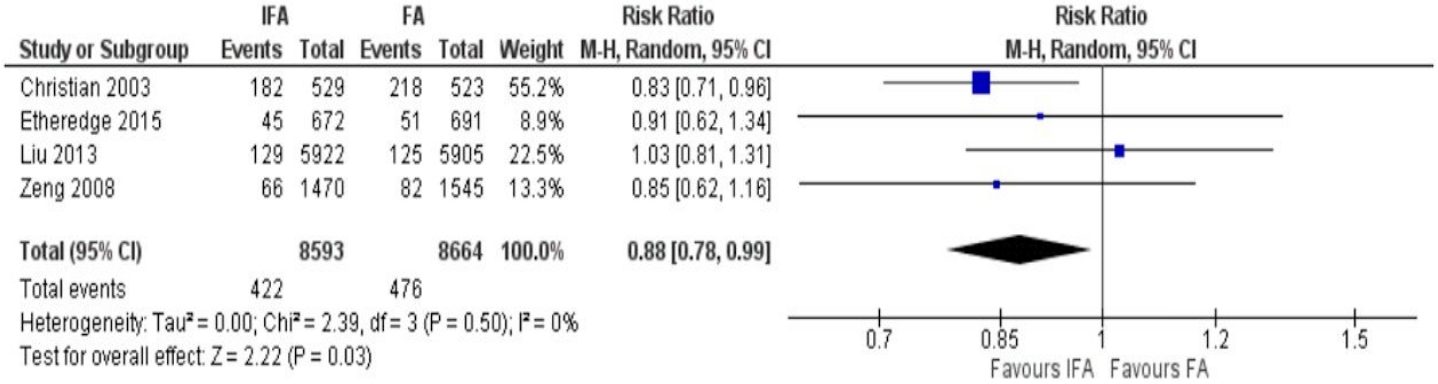


Figure 9. Forest plot of comparison IFA versus FA supplementation/placebo, from baseline to post-intervention on the risk of low birthweight infants.

- ✔ For the risk of low birthweight babies, a 12% reduction
- ✔ IFA did not reduce the risk of perinatal mortality

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

MMN AND IFA

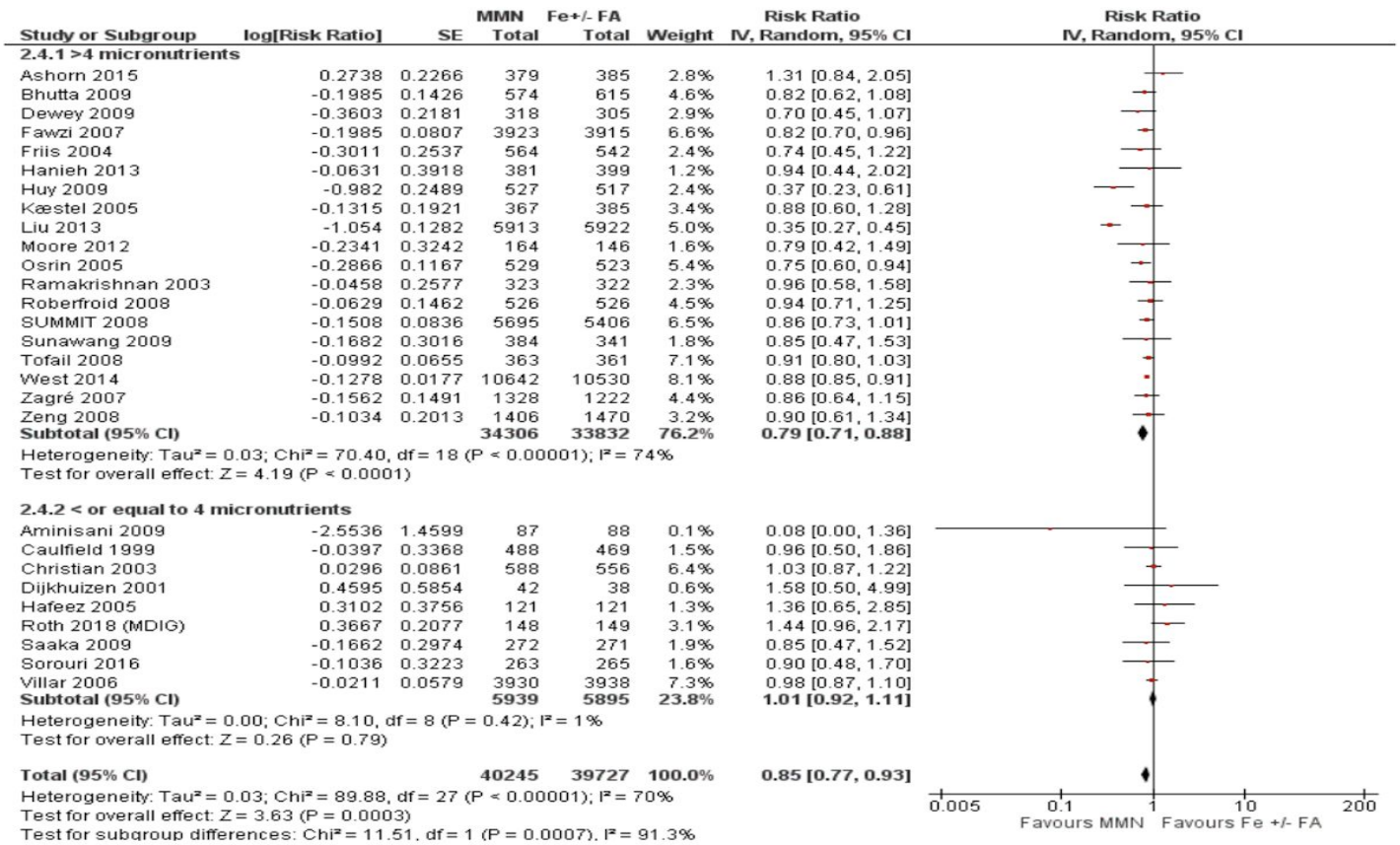


Figure 10. Forest plot of comparison MMN versus IFA supplementation, from baseline to post-intervention, on the risk of low birthweight infants.

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

- Ashorn P., Alho L., Ashorn U., Cheung Y.B., Dewey K.G., Gondwe A., Harjunmaa U., Lartey A., Phiri N., Phiri T.E., et al. Supplementation of Maternal Diets during Pregnancy and for 6 Months Postpartum and Infant Diets Thereafter with Small-Quantity Lipid-Based Nutrient Supplements Does Not Promote Child Growth by 18 Months of Age in Rural Malawi: A Randomized Controlled Trial. *J. Nutr.* 2015;145:1345–1353. doi: 10.3945/jn.114.207225

Finding:

- ✔ Compared to iron supplementation with or without folic acid, MMN supplementation demonstrated **no impact** on maternal mortality; perinatal mortality; maternal anemia; and iron deficiency anemia
- ✔ MMN supplementation showed a **15% reduction** in the risk of delivering a low birthweight when compared to iron with or without folic acid
- ✔ A post-hoc analysis revealed a **greater reduction** in the risk of LBW in studies whose MMN formulation contained > 4 micronutrients, compared to studies whose MMN supplement contained only 3 or 4 components

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

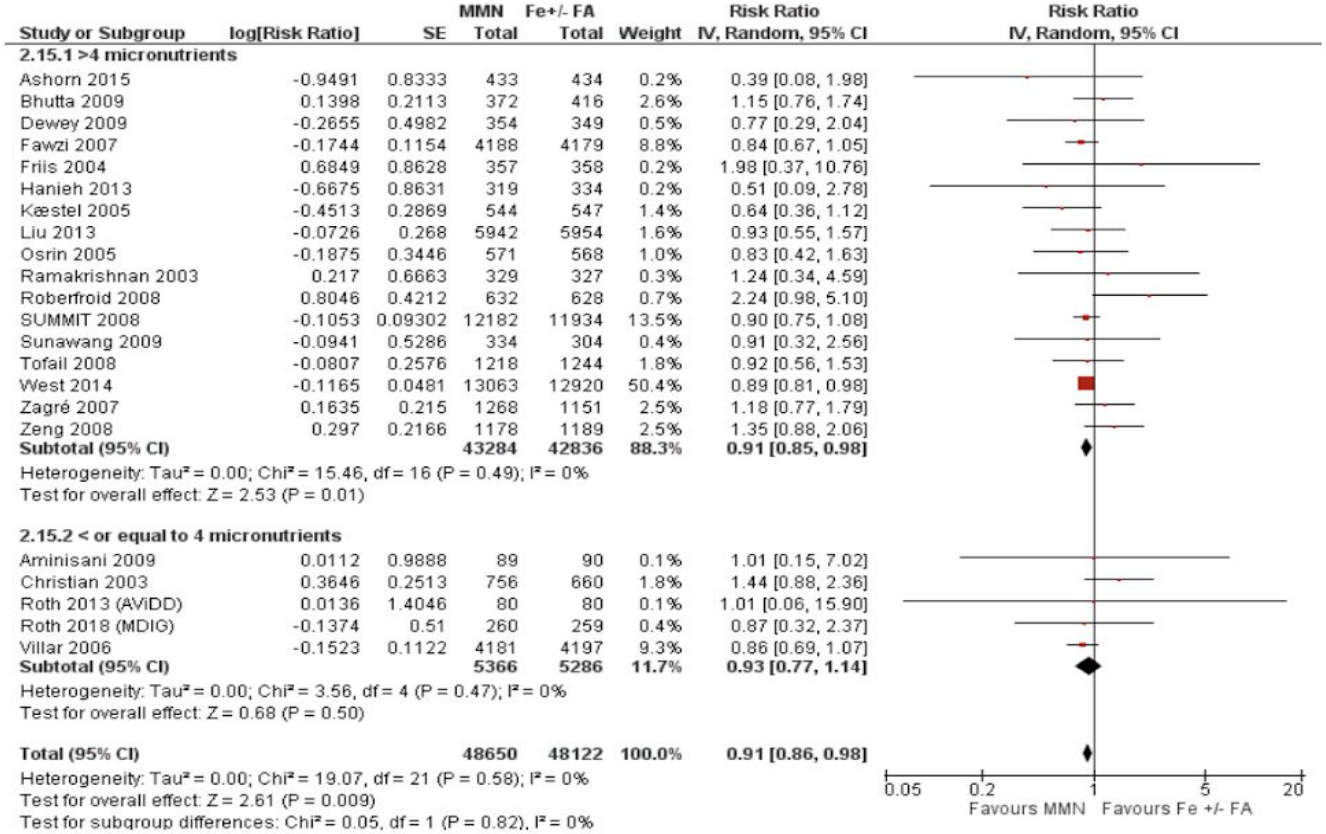


Figure 11. Forest plot of comparison MMN versus IFA supplementation, from baseline to post-intervention, on the risk of stillbirths.

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

- Ashorn P., Alho L., Ashorn U., Cheung Y.B., Dewey K.G., Gondwe A., Harjunmaa U., Lartey A., Phiri N., Phiri T.E., et al. Supplementation of Maternal Diets during Pregnancy and for 6 Months Postpartum and Infant Diets Thereafter with Small-Quantity Lipid-Based Nutrient Supplements Does Not Promote Child Growth by 18 Months of Age in Rural Malawi: A Randomized Controlled Trial. *J. Nutr.* 2015;145:1345–1353. doi: 10.3945/jn.114.207225

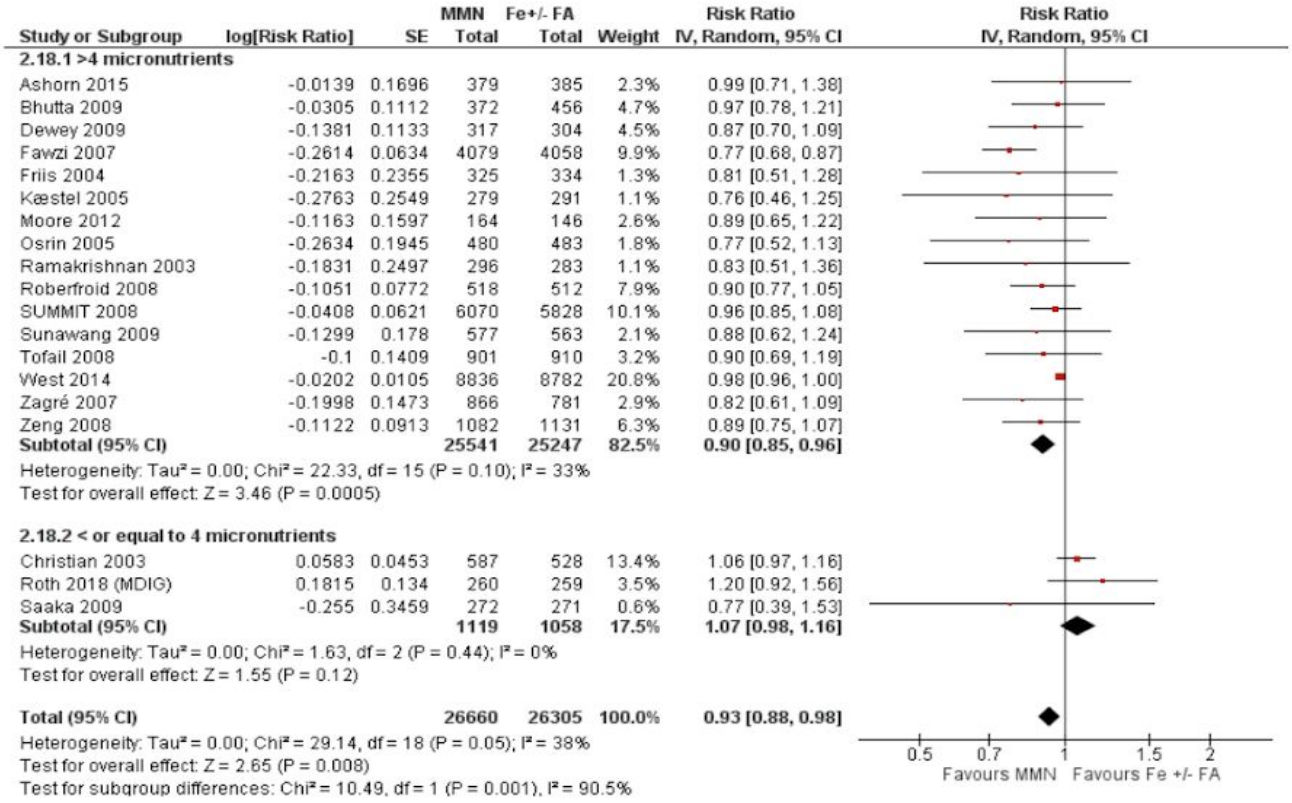


Figure 12. Forest plot of comparison MMN versus IFA supplementation, from baseline to post-intervention, on the risk of small-for-gestational-age (SGA) infants.

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

- Ashorn P., Alho L., Ashorn U., Cheung Y.B., Dewey K.G., Gondwe A., Harjunmaa U., Lartey A., Phiri N., Phiri T.E., et al. Supplementation of Maternal Diets during Pregnancy and for 6 Months Postpartum and Infant Diets Thereafter with Small-Quantity Lipid-Based Nutrient Supplements Does Not Promote Child Growth by 18 Months of Age in Rural Malawi: A Randomized Controlled Trial. *J. Nutr.* 2015;145:1345–1353. doi: 10.3945/jn.114.207225

Finding:

- ✔ A **7% reduction** in the risk of SGA infants
- ✔ For SGA infants:
  - A post-hoc analysis showed a **greater reductive** effect among studies that used MMN supplements with > 4 micronutrients compared to studies whose supplements had 3 or 4 components

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

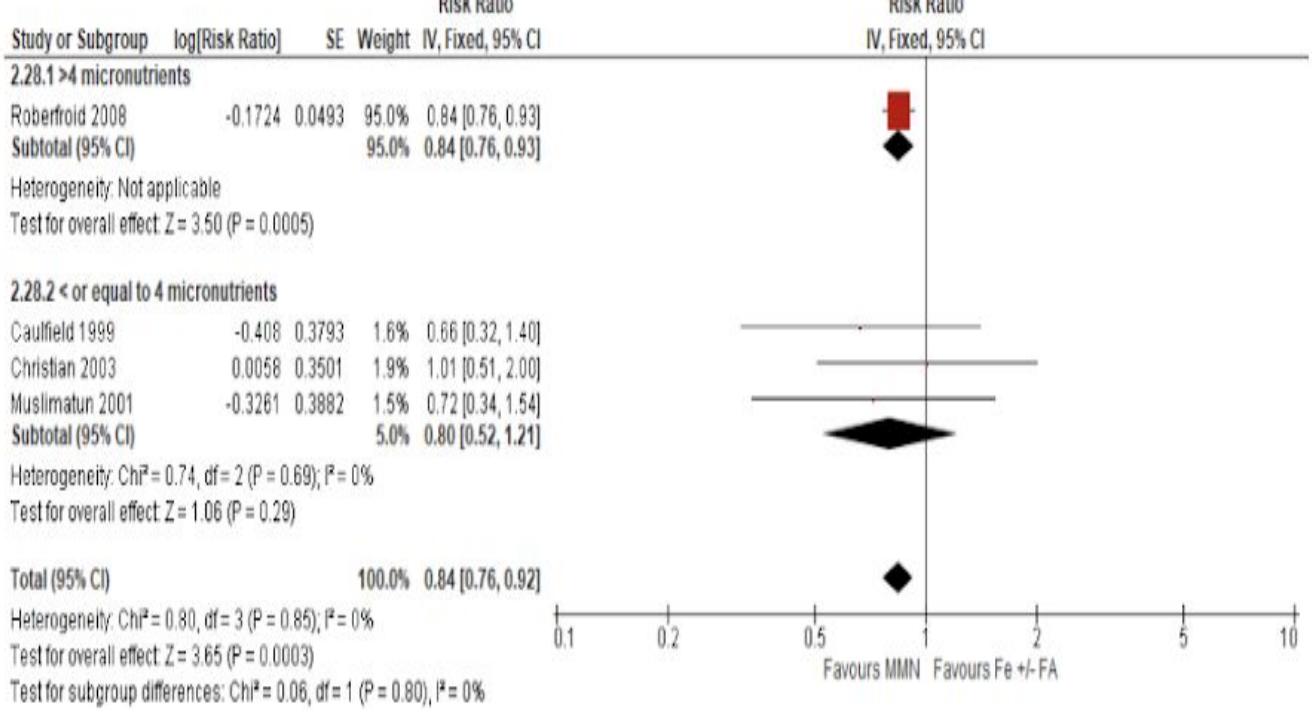


Figure 13. Forest plot of comparison MMN versus IFA supplementation, from baseline to post-intervention, on the risk of diarrhea in children.

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

Finding:

- ✔ antenatal MMN supplementation showed a **16% reduction** in the risk of diarrhea among children ages 6 months to under-five, when compared to IFA
- ✔ MMN supplementation showed a **slight improvement** in child serum/plasma retinol concentration
- ✔ MMN supplementation showed **no effect** on hemoglobin concentration, zinc serum/plasma concentration or anemia in children.

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

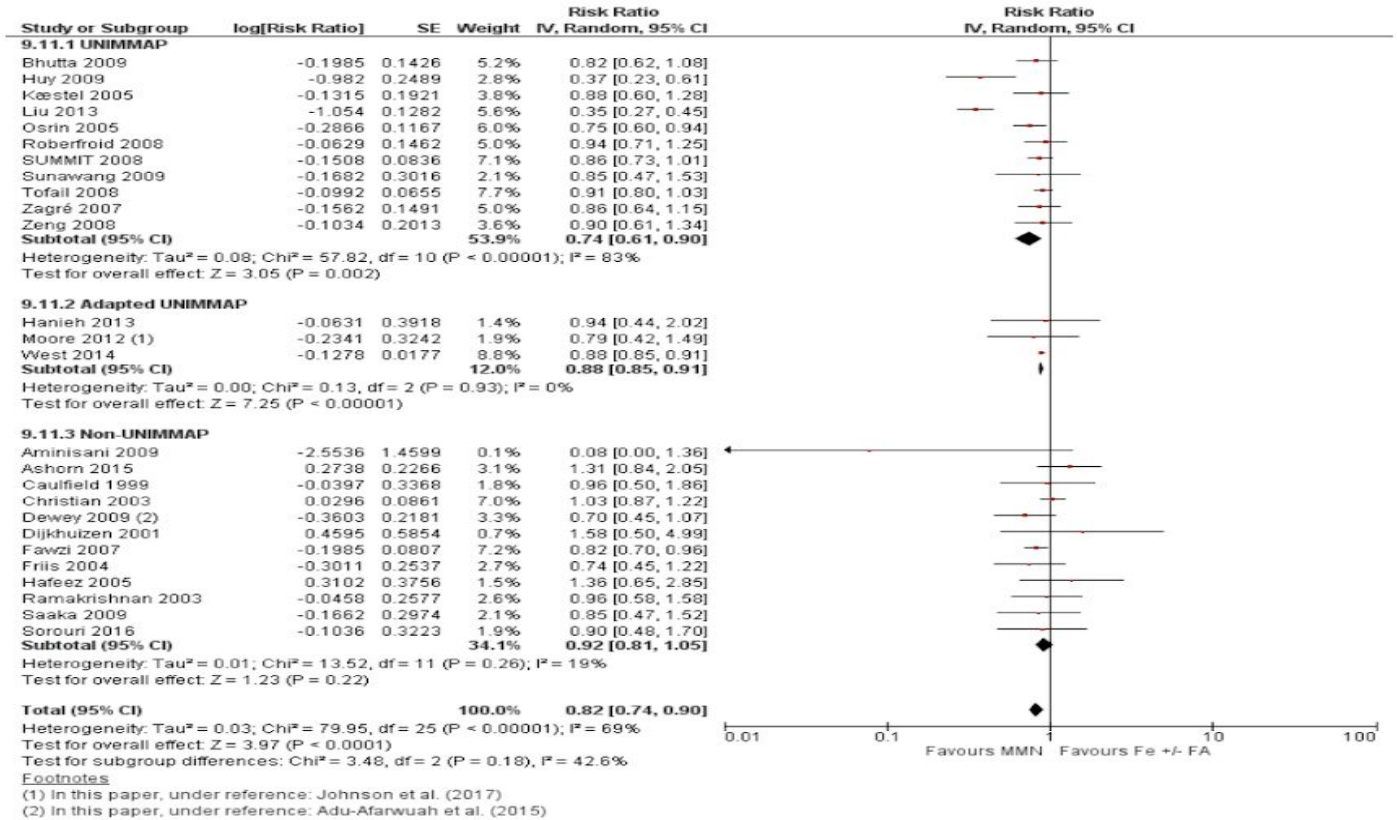


Figure 14. Forest plot of MMN versus IFA supplementation, a subgroup analysis of the risk of low birthweight infants by multiple micronutrient formulation (UNIMMAP versus adapted-UNIMMAP versus non-UNNIMAP).

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

- West K.P., Shamim A.A., Mehra S., Labrique A.B., Ali H., Shaikh S., Klemm R.D.W., Wu L.S.F., Mitra M., Haque R., et al. Effect of Maternal Multiple Micronutrient vs Iron–Folic Acid Supplementation on Infant Mortality and Adverse Birth Outcomes in Rural Bangladesh. *JAMA.* 2014;312:2649. doi: 10.1001/jama.2014.16819

Finding:

- ✔ The outcome of low birthweight showed **significant differences** between groups based on MMN formulation.

- ✔ In the subgroup of women who took the UNIMMAP formulation compared to participants that used an adapted formulation or non-UNIMMAP formulation, there was a **greater reduction** in the risk of having a low birthweight baby

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

LNS AND MMN

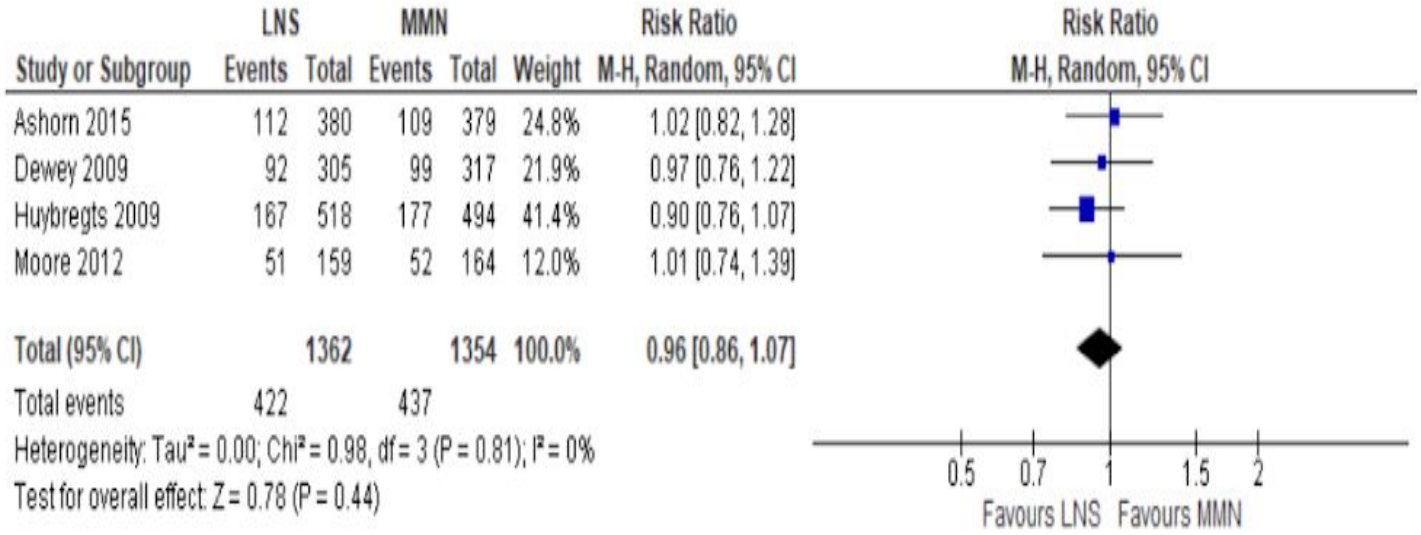


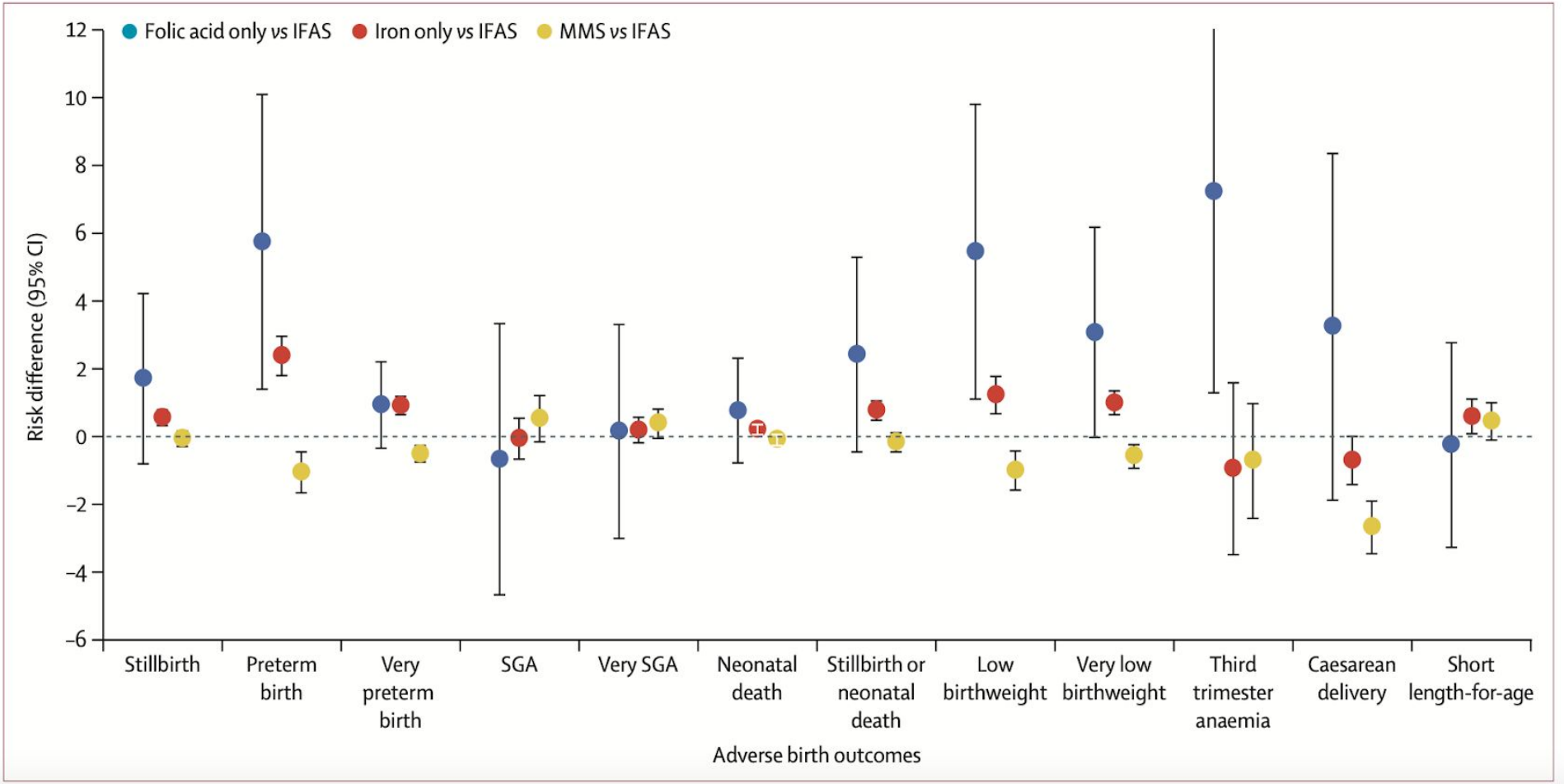
Figure 15. Forest plot for comparison LNS supplementation versus MMN from baseline to post-intervention for the risk of small-for-gestational age infants.

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347

Finding:

- ✔ Of the primary outcomes, LNS supplementation showed **no effect** on the risk of having a low birthweight baby and did **not impact** perinatal mortality
- ✔ Among the secondary outcomes examined, LNS supplementation showed **No effect** on the risk of miscarriage, neonatal mortality and preterm birth
- ✔ LNS also did **not show** an effect on the risk of SGA infants

- Oh C, Keats EC, Bhutta ZA. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. Nutrients. 2020 Feb 14;12(2):491. doi: 10.3390/nu12020491. PMID: 32075071; PMCID: PMC7071347



- **Iron, folic acid, and multiple micronutrient supplementation strategies during pregnancy and adverse birth outcomes in Botswana** Caniglia, Ellen C et al. The Lancet Global Health, Volume 10, Issue 6, e850 - e861

Finding:

- ✔ Compared with IFAS, the risk of stillbirth, preterm birth, very preterm birth, neonatal death, stillbirth or neonatal death, low birthweight, and very low birthweight was **greater** for women who received folic acid only or iron only supplementation

- ✔ Women initiating MMS had **lower risks** of preterm birth, very preterm birth, low birthweight, very low birthweight, and caesarean delivery compared with women initiating IFAS

- **Iron, folic acid, and multiple micronutrient supplementation strategies during pregnancy and adverse birth outcomes in Botswana** Caniglia, Ellen C et al. The Lancet Global Health, Volume 10, Issue 6, e850 - e861

Finding:

- ✔ Compared with IFAS, the risk of maternal third trimester anemia was **higher** for those who received folic acid only, and the risk of short fetal length-for-age was **larger** for those who received iron only.

- **Iron, folic acid, and multiple micronutrient supplementation strategies during pregnancy and adverse birth outcomes in Botswana** Caniglia, Ellen C et al. The Lancet Global Health, Volume 10, Issue 6, e850 - e861

05

CONCLUSIONS

- ✔ Micronutrient and vitamin supplementation is an important intervention to enhance maternal and child nutrition, health, and well-being, and it should be sustained, particularly throughout pregnancy in LMICs, regardless of maternal nutritional status.

- ✔ Specifically, this analysis suggests that MMN supplementation is preferable than IFA for conventional prenatal care, especially for stillbirths, SGA, and low birthweight babies.

- ✔ Single micronutrient and vitamin supplementation improves particular outcomes, such as calcium on pre-eclampsia/eclampsia risk and vitamin A on maternal serum/plasma retinol concentration.

- ✔ Compared to MMN, LNS supplementation has less studies in this review, suggesting the need for further study to clarify differences.

02

Lactation supplementation

Background

Maternal breast milk composition usually depends on maternal nutrition

Micronutrients and vitamins are also very important factors for the development and growth of infants.

Micronutrients and vitamins have a profound effect on the neural development of children, metabolic processes, development of soft tissues and muscles, transport of oxygen and synthesis of DNA.

Darnton-Hill, I.; Mkparu, U.C. Micronutrients in pregnancy in low- and middle-income countries. *Nutrients* **2015**, *7*, 1744–1768

Table 1. Dietary Reference Intakes (DRIs): Recommended Dietary Allowances (RDA) and Adequate Intakes (AI) of vitamins during lactation and the first six months of life. Values as established by the Food and Nutrition Board, Institute of Medicine, National Academies, USA.

Life Stage Group	Vit A (µg/day) [a]	Vit D (µg/day) [b,c]	Vit E (mg/day) [d]	Vit K (µg/day)	Vit C (mg/day)	Thiamin (mg/day)	Riboflavin (mg/day)	Niacin (mg/day) [e]	Vit B6 (mg/day)	Folate (µg/day) [f]	Vit B12 (µg/day)	Pantothenic Acid (mg/day)	Biotin (µg/day)	Choline (mg/day) [g]
Infants														
0–6 month	400 *	5 *	4 *	2.0 *	40 *	0.2 *	0.3 *	2 *	0.1 *	65 *	0.4 *	1.7 *	5 *	125 *
Lactating women														
14–18 year	1200	15	19	75 *	115	1.4	1.6	17	2.0	500	2.8	7 *	35 *	550 *
19–30 year	1300	15	19	90 *	120	1.4	1.6	17	2.0	500	2.8	7 *	35 *	550 *
31–70 year	1300	15	19	90 *	120	1.4	1.6	17	2.0	500	2.8	7 *	35 *	550 *

SOURCES: [19,32,33,34]; the table is based on DRI tables published by the Institute of Medicine; NOTE: The RDA values reflect the intake that meets the nutrient need of almost all (97–98%) individuals in a group. For healthy infants receiving human milk, the Adequate Intake (AI) of a vitamin represents the mean intake. For other life stages, the AI is believed to cover the needs of all healthy individuals in the group, but lack of data or uncertainty in the data prevent the ability to specify the percentage of individuals covered by this intake with confidence; * Adequate Intake (AI); [a] As retinol activity equivalents (RAEs). 1 RAE = 1 µg retinol, 12 µg β-carotene, 24 µg α-carotene, or 24 µg β-cryptoxanthin. The RAE for dietary provitamin A carotenoids is two-fold greater than retinol equivalents (RE), whereas the RAE for preformed vitamin A is the same as RE; [b] As cholecalciferol. 1 µg cholecalciferol = 40 IU vitamin D; [c] In the absence of adequate exposure to sunlight; [d] As α-tocopherol. α-Tocopherol includes RRRα-tocopherol, the only form of αtocopherol that occurs naturally in foods, and the 2R-stereoisomeric forms of α-tocopherol (RRR-, RSR-, RRS-, and RSS-α-tocopherol) that occur in fortified foods and supplements; [e] As niacin equivalents (NE). 1 mg of niacin = 60 mg of tryptophan; 0–6 months = preformed niacin (not NE); [f] As dietary folate equivalents (DFE) 1 DFE = 1 µg food folate = 0.6 µg of folic acid from fortified food or as a supplement consumed with food = 0.6 µg of a supplement taken on an empty stomach.; [g] Although AIs have been set for choline, there are few data to assess whether a dietary supply of choline is needed at all stages of the life cycle, and it may be that the choline requirement can be met by endogenous synthesis at some of these stages.

Vitamin A

- The mature milk of well-nourished mothers contains approximately **1.7 moles/L** vitamin A
- vitamin A content of human milk is strongly influenced by maternal nutritional status

- Soares MM, Silva MA, Garcia PPC, Silva LSD, Costa GDD, Araújo RMA, et al. Efect of vitamin a suplementation: a systematic review. Ciência & Saúde Coletiva. 2019;24(3):827–38.

Vitamin A

Randomized controlled trials evaluating the effect of postpartum maternal vitamin A supplementation indicated **a significant** improvement in maternal serum retinol, breast milk retinol and vitamin A liver stores, after single dose of vitamin A supplementation.

- Ding, Ye & Hu, Ping & Yang, Yue & Xu, Fangping & Li, Fang & Lu, Xiaolong & Xie, Zhencheng & Wang, Zhixu. (2021). Impact of Maternal Daily Oral Low-Dose Vitamin A Supplementation on the Mother–Infant Pair: A Randomised Placebo-Controlled Trial in China. Nutrients. 13. 2370. 10.3390/nu13072370. .

Vitamin A

Study design	dosage	duration
Randomized controlled trials	daily oral vitamin A and D drops (one soft capsule of 1800 IU vitamin A and 600 IU vitamin D_2	2 months

- Ding, Ye & Hu, Ping & Yang, Yue & Xu, Fangping & Li, Fang & Lu, Xiaolong & Xie, Zhencheng & Wang, Zhixu. (2021). Impact of Maternal Daily Oral Low-Dose Vitamin A Supplementation on the Mother–Infant Pair: A Randomised Placebo-Controlled Trial in China. Nutrients. 13. 2370. 10.3390/nu13072370.

Vitamin A

Result :

Daily oral low-dose vitamin A supplementation is helpful in improving maternal vitamin A status, despite having **no effect** on infant health status through breast milk.

- Ding, Ye & Hu, Ping & Yang, Yue & Xu, Fangping & Li, Fang & Lu, Xiaolong & Xie, Zhencheng & Wang, Zhixu. (2021). Impact of Maternal Daily Oral Low-Dose Vitamin A Supplementation on the Mother–Infant Pair: A Randomised Placebo-Controlled Trial in China. Nutrients. 13. 2370. 10.3390/nu13072370.

Vitamin E

Newborns are considered high-risk for vitamin E deficiency due to oxidative stress generated by postnatal transition from the intrauterine environment, relatively low in oxygen, to the extrauterine one, significantly richer in oxygen

- Melo LR, Clemente HA, Bezerra DF, Dantas RC, Ramalho HM, Dimenstein R. Effect of maternal supplementation with vitamin E on the concentration of α-tocopherol in colostrum. J Pediatr (Rio J). 2017 Jan-Feb;93(1):40-46. doi: 10.1016/j.jped.2016.03.007. Epub 2016 Jun 18. PMID: 27327566.

Vitamin E

Study design	dosage	duration
A randomized clinical trial enrolled 99 healthy adult pregnant women	400 IU of supplementary vitamin E	24 hours First time (colostrum) Second time (24 h later)

- Melo LR, Clemente HA, Bezerra DF, Dantas RC, Ramalho HM, Dimenstein R. Effect of maternal supplementation with vitamin E on the concentration of α-tocopherol in colostrum. J Pediatr (Rio J). 2017 Jan-Feb;93(1):40-46. doi: 10.1016/j.jped.2016.03.007. Epub 2016 Jun 18. PMID: 27327566.

Vitamin E

The mean concentration of α-tocopherol in colostrum			
Groups	Initial (0 hour)	After 24 h	P value
Control groups	1509.3 ± 793.7 µg/dL	1650.6 ± 968.7 µg/dL	$p > 0.05$
Supplemented groups	1452.9 ± 808.6 µg/dL	2346.9 ± 1203.2 µg/dL	$p < 0.001$

Increasing the vitamin E supply to the newborn to 9.3 mg/day.

- Melo LR, Clemente HA, Bezerra DF, Dantas RC, Ramalho HM, Dimenstein R. Effect of maternal supplementation with vitamin E on the concentration of α-tocopherol in colostrum. J Pediatr (Rio J). 2017 Jan-Feb;93(1):40-46. doi: 10.1016/j.jped.2016.03.007. Epub 2016 Jun 18. PMID: 27327566.

Vitamin E

Conclusion

Maternal vitamin E supplementation increases the supply of the vitamin to the infant by providing more than twice the Recommended Daily Intake.

- Melo LR, Clemente HA, Bezerra DF, Dantas RC, Ramalho HM, Dimenstein R. Effect of maternal supplementation with vitamin E on the concentration of α-tocopherol in colostrum. J Pediatr (Rio J). 2017 Jan-Feb;93(1):40-46. doi: 10.1016/j.jped.2016.03.007. Epub 2016 Jun 18. PMID: 27327566.

Vitamin E

Study design	dosage	duration
A randomized clinical trial on 79 lactating women	supplementation with 800 IU RRR-alpha-tocopherol	24 hours First time (30 and 90 days after delivery) Second time (next day)

- Lira LQ, Gurgel CSS, de Sousa AL, da Silva AGA, Padovam JC, Moia MN, Silva RLM, Dimenstein R. Effect of RRR-α-tocopherol supplementation on serum of breastfeeding women up to 60 days after delivery: a randomised controlled trial. J Hum Nutr Diet. 2017 Dec;30(6):771-778. doi: 10.1111/jhn.12482. Epub 2017 May 23. PMID: 28544241.

Vitamin E

Results:

In the supplemented group, the alpha-tocopherol content in serum and milk increased after supplementation ($p < 0.001$).

- Lira LQ, Gurgel CSS, de Sousa AL, da Silva AGA, Padovam JC, Moia MN, Silva RLM, Dimenstein R. Effect of RRR-α-tocopherol supplementation on serum of breastfeeding women up to 60 days after delivery: a randomised controlled trial. J Hum Nutr Diet. 2017 Dec;30(6):771-778. doi: 10.1111/jhn.12482. Epub 2017 May 23. PMID: 28544241.

Vitamin B12

Breastmilk vitamin B_{12} levels are correlated with maternal intake and blood levels.

Methylcobalamin is the major form of vitamin B_{12} in milk. **Deoxyadenosylcobalamin**, **hydroxocobalamin** and **cyanocobalamin** are minor forms.

- Drugs and Lactation Database (LactMed) [Internet]. Bethesda (MD): National Library of Medicine (US); 2006–. Vitamin B_{12}. 2021 Oct 18. PMID: 30489717.

Vitamin B12

Average milk levels in mature milk are 200 to 700 pmol/L (270 to 950 ng/L) during **the first 28 weeks postpartum** in healthy, lactating women with known or presumed adequate vitamin B_{12} status and not taking a supplement Levels are highest during the first 4 weeks postpartum and gradually decrease thereafter.

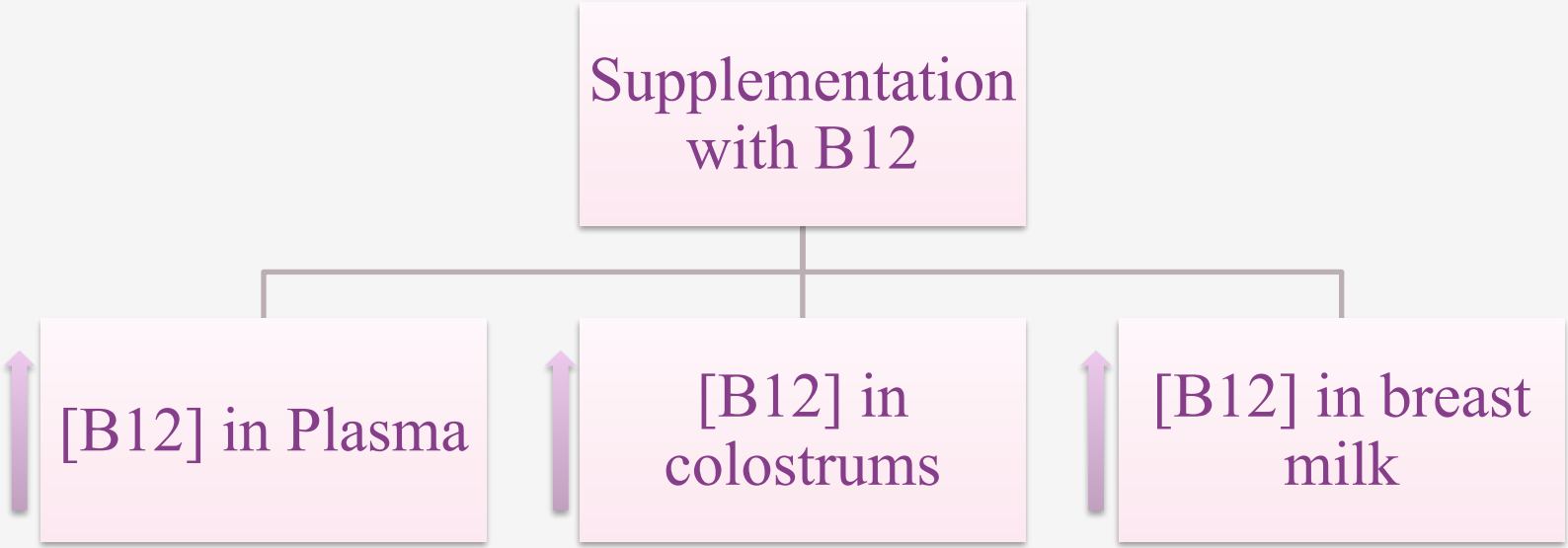
- Drugs and Lactation Database (LactMed) [Internet]. Bethesda (MD): National Library of Medicine (US); 2006–. Vitamin B_{12}. 2021 Oct 18. PMID: 30489717.

Vitamin B12

Study design	dosage	duration
A randomized clinical trial	give 250 µg/day B12 along with 60 mg iron + 400 µg folate.	through pregnancy 3- month postpartum

- Siddiqua, T.J., Ahmad, S.M., Ahsan, K.B. *et al.* Vitamin B12 supplementation during pregnancy and postpartum improves B12 status of both mothers and infants but vaccine response in mothers only: a randomized clinical trial in Bangladesh. *Eur J Nutr* **55**, 281–293 (2016). https://doi.org/10.1007/s00394-015-0845-x

Result



- Siddiqua, T.J., Ahmad, S.M., Ahsan, K.B. *et al.* Vitamin B12 supplementation during pregnancy and postpartum improves B12 status of both mothers and infants but vaccine response in mothers only: a randomized clinical trial in Bangladesh. *Eur J Nutr* **55**, 281–293 (2016). https://doi.org/10.1007/s00394-015-0845-x

Vitamin B12

Result:

Supplementation with 250 mg/day B12 during pregnancy and lactation substantially **improved** maternal, infant and breast milk B12 status.

- Siddiqua, T.J., Ahmad, S.M., Ahsan, K.B. *et al.* Vitamin B12 supplementation during pregnancy and postpartum improves B12 status of both mothers and infants but vaccine response in mothers only: a randomized clinical trial in Bangladesh. *Eur J Nutr* **55**, 281–293 (2016). https://doi.org/10.1007/s00394-015-0845-x

Vitamin D

Study design	dosage	duration
randomized controlled trial among 95 exclusively breastfeeding mother	vitamin D_3 maternal supplementation of 6000 IU/day (group 1) maternal supplementation of 600 IU/day + 400 IU for infant (group 2)	six-month post-partum

- Dawodu A, Salameh KM, Al-Janahi NS, Bener A, Elkum N. The Effect of High-Dose Postpartum Maternal Vitamin D Supplementation Alone Compared with Maternal Plus Infant Vitamin D Supplementation in Breastfeeding Infants in a High-Risk Population. A Randomized Controlled Trial. Nutrients. 2019 Jul 17;11(7):1632. doi: 10.3390/nu11071632. PMID: 31319554; PMCID: PMC6682993.

Vitamin D

The mean concentration of α-tocopherol in colostrum			
Groups	baseline	After 24 h	P value
Group 1 (mothers)	35.1 nmol/L	98 ± 35 nmol/L	$p < 0.0001$
Group 2 (mothers)	35.7 nmol/L	52 ± 20 nmol/L	$p < 0.001$

Mothers on 6000 IU vitamin D_3/day had higher human milk vitamin D content

- Dawodu A, Salameh KM, Al-Janahi NS, Bener A, Elkum N. The Effect of High-Dose Postpartum Maternal Vitamin D Supplementation Alone Compared with Maternal Plus Infant Vitamin D Supplementation in Breastfeeding Infants in a High-Risk Population. A Randomized Controlled Trial. Nutrients. 2019 Jul 17;11(7):1632. doi: 10.3390/nu11071632. PMID: 31319554; PMCID: PMC6682993.

Vitamin D

The mean concentration of α-tocopherol in colostrum			
Groups	baseline	After 24 h	P value
Group 1 (infant)	31.9 ± 21.7	92.2 ± 35.5	P=0.03
Group 2 (infant)	29.6 ± 16.1	109.1 ± 43.3	P=0.03

Infants of mothers on 600 IU and also supplemented with 400 IU vitamin D_3 had slightly higher serum 25(OH)D

- Dawodu A, Salameh KM, Al-Janahi NS, Bener A, Elkum N. The Effect of High-Dose Postpartum Maternal Vitamin D Supplementation Alone Compared with Maternal Plus Infant Vitamin D Supplementation in Breastfeeding Infants in a High-Risk Population. A Randomized Controlled Trial. Nutrients. 2019 Jul 17;11(7):1632. doi: 10.3390/nu11071632. PMID: 31319554; PMCID: PMC6682993.

Vitamin D

1

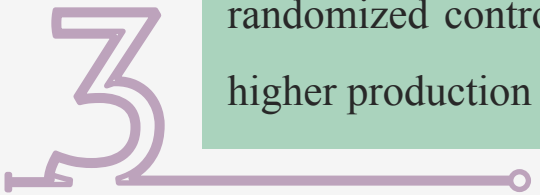
A strong positive association was demonstrated between maternal vitamin D intake during exclusive breastfeeding and infant serum 25-hydroxyvitamin D levels

2

supplementation during lactation with 4,000–6,400 IU/d of vitamin D may be needed to prevent vitamin D deficiency in the mother and her breastfed infant

- Samuel TM, Zhou Q, Giuffrida F, Munblit D, Verhasselt V, Thakkar SK. Nutritional and Non-nutritional Composition of Human Milk Is Modulated by Maternal, Infant, and Methodological Factors. Front Nutr. 2020 Sep 16;7:576133. doi: 10.3389/fnut.2020.576133. PMID: 33117843; PMCID: PMC7557356.

Vitamin D



randomized controlled study demonstrated that a single bolus led to a higher production of vitamin D, compared with a daily dose

- Samuel TM, Zhou Q, Giuffrida F, Munblit D, Verhasselt V, Thakkar SK. Nutritional and Non-nutritional Composition of Human Milk Is Modulated by Maternal, Infant, and Methodological Factors. Front Nutr. 2020 Sep 16;7:576133. doi: 10.3389/fnut.2020.576133. PMID: 33117843; PMCID: PMC7557356.

Iodine

01

Iodine supplementation (75–400 mg iodine/day) increased HM iodine concentrations.

02

lower dose (75 or 150 μg/d) through either supplementation or fortification may be insufficient to ensure adequate iodine status in women or their infants.

- Dror DK, Allen LH. Iodine in human milk: a systematic review. *Adv Nutr.* (2018) 9:347S−57S. doi: 10.1093/advances/nmy020

Iodine

03

Administering a single dose of 400 mg iodine as oral iodized oil to mothers may be an effective strategy to provide adequate iodine to their infants through HM for at least 6 months

04

iodine concentrations in HM were 1.3 and 1.7 times higher in women supplemented with 75 and 150 μg per day would also suggest a dose-response relationship

- Dror DK, Allen LH. Iodine in human milk: a systematic review. *Adv Nutr.* (2018) 9:347S−57S. doi: 10.1093/advances/nmy020

Result

A systematic review of epidemiological and clinical data suggested that a high dose as well as daily iodine supplementation were effective in increasing iodine concentrations in Human milk.

- Dror DK, Allen LH. Iodine in human milk: a systematic review. *Adv Nutr.* (2018) 9:347S−57S. doi: 10.1093/advances/nmy020

THANKS!

Do you have any questions?

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