

Table S1. Effect of food fortification with various micronutrients on health outcomes in Children

Outcomes	Illustrative comparative risks* [95% CI]	Relative effect [95% CI]	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
Iron Fortification					
Hemoglobin Levels	The mean hemoglobin levels in the intervention groups was 0.55 standard deviations higher (0.34 to 0.76 higher)		6267 (30)	⊕⊕⊕⊖ ^{1,2} moderate	SMD: 0.55 [95% CI: 0.34, 0.76]
Serum Ferritin Levels	The mean serum ferritin in the intervention groups was 0.91 standard deviations higher (0.38 to 1.44 higher)		1507 (7)	⊕⊕⊕⊖ ^{1,2} moderate	SMD: 0.91 [95% CI: 0.38, 1.44]
Effect on Anemia	Iron fortification reduced the prevalence of anemia by 45%	RR: 0.55 [95% CI: 0.42, 0.72]	3651 (17)	⊕⊕⊕⊖ ^{1,2} moderate	
Zinc Fortification					
Serum Zinc Levels	The mean serum zinc levels in the intervention groups was 1.28 standard deviations higher (0.56 to 2.01 higher)		683 (9)	⊕⊕⊕⊖ ^{1,2} moderate	SMD: 1.28 [95% CI: 0.56, 2.01]
Hemoglobin Levels	The mean hemoglobin levels in the intervention groups was 0.11 standard deviations lower (0.52 lower to 0.31 higher)		92 (3)	⊕⊕⊖⊖ ^{1,2,4} low	SMD: -0.11 [95% CI: -0.52, 0.31]
Serum Copper Levels	The mean serum copper levels in the intervention groups was 0.57 standard deviations higher (0.91 lower to 2.06 higher)		161 (4)	⊕⊖⊖⊖ ^{1,2,4,5} very low	SMD: 0.57 [95% CI: -0.91, 2.06]
Serum Alkaline Phosphatase Levels	The mean serum alkaline phosphatase levels in the intervention groups was 0.94 standard deviations higher (0.29 lower to 2.17 higher)		119	⊕⊕⊖⊖ ^{1,2,4} low	SMD: 0.94 [95% CI: -0.29, 2.17]

	higher)		(3)	low	
Weight Gain	The mean weight gain in the intervention groups was 0.50 standard deviations higher (0.12 lower to 1.11 higher)		419 (6)	⊕⊕⊕⊖ ^{1,2} moderate	SMD: 0.50 [95% CI: -0.12, 1.11]
Height Growth	The mean height growth levels in the intervention groups was 0.52 standard deviations higher (0.01 to 1.04 higher)		451 (7)	⊕⊕⊕⊖ ^{1,2} moderate	SMD: 0.52 [95% CI: 0.01, 1.04]
Iodine Fortification					
Serum thyroxin levels	The mean serum thyroxin levels in the intervention groups was 0.45 standard deviations higher (1.15 lower to 2.06 higher)		1131 (2)	⊕⊕⊖⊖ ^{1,2,3} low	SMD: 0.45 [95% CI: -1.15, 2.06]
Urinary iodine concentrations	The mean urinary iodine concentration in the intervention groups was 6.39 standard deviations higher (2.69 to 10.08 higher)		1016 (2)	⊕⊕⊕⊖ ^{1,2} moderate	SMD: 6.39 [95% CI: 2.69, 10.08]
Vitamin A fortification					
Hemoglobin Levels	The mean serum hemoglobin levels in the intervention groups was 0.48 standard deviations higher (0.07 to 0.89 higher)		1538 (2)	⊕⊕⊖⊖ ^{3,6} low	SMD: 0.48 [95% CI: 0.07, 0.89]
Serum Vitamin A Concentration	The mean serum vitamin A concentration in the intervention groups was 0.61 standard deviations higher (0.39 to 0.83 higher)		2362 (3)	⊕⊕⊖⊖ ^{3,6} low	SMD: 0.61 [95% CI: 0.39, 0.83]
Vitamin A Deficiency	Vitamin A fortification reduced prevalence of vitamin A deficiency by 61%	RR: 0.39 [95% CI: 0.09, 1.74]	1465 (2)	⊕⊕⊕⊖ ⁶ moderate	

Calcium and Vitamin D fortification

Serum PTH Levels	The mean serum PTH levels in the intervention groups was 0.40 standard deviations lower (0.56 to 0.24 lower)	637 (2)	⊕⊕⊖⊖ ^{1,2,3} low	SMD: -0.40 [95% CI: -0.56, -0.24]
Serum Vitamin D Levels	The mean serum vitamin D concentration in the intervention groups was 1.23 standard deviations higher (0.35 to 2.11 higher)	1119 (3)	⊕⊕⊕⊖ ^{1,2} moderate	SMD: 1.23 [95% CI: 0.35, 2.11]
Serum Calcium Levels	The mean serum calcium levels in the intervention groups was 0.40 standard deviations lower (0.59 to 0.20 lower)	468 (1)	⊕⊕⊖⊖ ^{1,2,3} low	SMD: -0.40 [95% CI: -0.59, -0.20]

Multiple Micronutrient Fortification

Hemoglobin Levels	The mean hemoglobin in the intervention groups was 0.75 standard deviations higher (0.41 to 1.08 higher)	3554 (16)	⊕⊕⊕⊖ ^{1,2} moderate	SMD: 0.75 [95% CI: 0.41, 1.08]
Serum Ferritin Levels	The mean ferritin in the intervention groups was 0.37 standard deviations higher (0.13 to 0.62 higher)	2539 (9)	⊕⊕⊖⊖ ^{1,2,3} low	SMD: 0.37 [0.13, 0.62]
Serum Zinc Levels	The mean zinc in the intervention groups was 0.08 standard deviations higher (0.02 lower to 0.19 higher)	2821 (10)	⊕⊕⊕⊖ ^{1,2} moderate	SMD: 0.08 [-0.02, 0.19]
Serum Retinol Levels	The mean serum retinol in the intervention groups was 0.05 standard deviations lower (0.23 lower to 0.13 higher)	1927 (8)	⊕⊕⊖⊖ ^{1,2,3} low	SMD: -0.05 [-0.23, 0.13]

Effect on Anemia	Multiple Micronutrient fortification reduced risk of anemia by 45%	RR: 0.55 [95% CI: 0.42, 0.71]	4722 (13)	⊕⊕⊖⊖ ^{1,2,3} low	
Effect on Vitamin A deficiency	Multiple Micronutrient fortification reduced risk of vitamin A deficiency by 10%	RR: 0.90 [95% CI: 0.76, 1.06]	2036 (6)	⊕⊕⊖⊖ ^{1,2,3} low	RR: 0.90 [95% CI: 0.76, 1.06]
Height-for-age Z Score	The mean height-for-age z score in the intervention groups was 0.13 standard deviations higher (0.04 lower to 0.29 higher)		2092 (8)	⊕⊕⊖⊖ ^{1,2,3} low	SMD: 0.13 [95% CI: -0.04, 0.29]
Weight-for-Age Z score	The mean weight-for-age z score in the intervention groups was 0.12 standard deviations lower (0.43 lower to 0.2 higher)		1988 (7)	⊕⊕⊖⊖ ^{1,2,3} low	SMD: -0.12 [95% CI: -0.43, 0.20]
Weight-for-height Z Score	The mean weight-for-height z score in the intervention groups was 0.11 standard deviations lower (0.4 lower to 0.17 higher)		2098 (8)	⊕⊕⊖⊖ ^{1,2,3} low	SMD: -0.11 [95% CI: -0.40, 0.17]

CI: Confidence interval;

¹ Blinding of participants, personal and outcome assessment was not described or carried out in one or more of the studies

² Allocation concealment not carried out or discussed in one or more of the studies

³ A large confidence interval noticed in the results that may account for imprecision in results

⁴ An overall small sample size has been calculated

⁵ A large unexplained/unaccounted drop out was observed in one of the studies

⁶ A before-after study design was used

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

Table S2. Effect of food fortification with various micronutrients on health outcomes in women

Outcomes	Illustrative comparative risks* [95% CI]	Relative effect [95% CI]	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
Iron Fortification					
Hemoglobin Levels	The mean hemoglobin levels in the intervention groups was 0.62 standard deviations higher (0.36 to 0.89 higher)		3223 (11)	⊕⊕⊕⊖ ^{1,2} moderate	SMD: 0.62 [95% CI: 0.36, 0.89]
Serum Ferritin Levels	The mean serum ferritin in the intervention groups was 0.41 standard deviations higher (0.23 to 0.60 higher)		3009 (10)	⊕⊕⊖⊖ ^{1,2,4} low	SMD: 0.41 [95% CI: 0.23, 0.60]
Effect on Anemia	Iron fortification reduced the prevalence of anemia by 32%	RR: 0.68 [95% CI: 0.49, 0.93]	1316 (4)	⊕⊕⊖⊖ ^{1,2,4} low	
Folate Fortification					
Neural Tube Defect	Folate fortification reduced the incidence of neural tube defects by 33%	RR: 0.57 [95% CI: 0.45, 0.73]	62183 (8)	⊕⊕⊕⊖ ⁶ moderate	
Spina Bifida	Folate fortification reduced the incidence of Spina Bifida by 36%	RR: 0.64 [95% CI: 0.57, 0.71]	41392 (11)	⊕⊕⊕⊖ ⁶ moderate	
Anencephaly	Folate fortification reduced the incidence of anencephaly by 24%	RR: 0.76 [95% CI: 0.68, 0.85]	41261 (10)	⊕⊕⊕⊖ ⁶ moderate	

Serum Folate Levels	The mean serum alkaline phosphatase levels in the intervention groups was 1.38 standard deviations higher (0.20 lower to 2.95 higher)	1239 (3)	⊕⊕⊖⊖ ^{4,6} low	SMD: 1.38 [95% CI: -0.20, 2.95]
Iodine Fortification				
Urinary iodine concentrations	The mean urinary iodine concentration in the intervention groups was 7.16 standard deviations higher (1.00 to 13.31 higher)	2352 (4)	⊕⊕⊕⊖ ^{1,2} moderate	SMD: 7.16 [95% CI: 1.00, 13.31]
Calcium and Vitamin D fortification				
Serum PTH Levels	The mean serum PTH levels of post-menopausal women in the intervention groups was 2.53 standard deviations lower (4.42 to 0.65 lower) The mean serum PTH levels of women of reproductive age in the intervention groups was 0.01 standard deviations lower (0.32 to 0.30 lower)	398 (6)	⊕⊕⊖⊖ ^{1,2,4} low	Post-menopausal women SMD: -2.53 [95% CI: -4.42, -0.65] Women of reproductive age SMD: -0.01 [95% CI: -0.32, -0.30]
Serum Vitamin D Levels	The mean serum vitamin D concentration of post-menopausal women in the intervention groups was 0.97 standard deviations higher (0.18 lower to 2.13 higher) The mean serum vitamin D concentration of women of reproductive age in the intervention groups was 1.10 standard deviations lower (3.81 lower to 1.60 higher)	416 (5)	⊕⊕⊕⊖ ^{1,2} moderate	Post-menopausal women SMD: 0.97 [95% CI: -0.18, 2.13] Women of reproductive age SMD: -1.10 [95% CI: -3.81, 1.60]
Multiple Micronutrient Fortification				

Hemoglobin Levels	The mean hemoglobin in the intervention groups was 0.31 standard deviations higher (0.13 to 0.48 higher)		516 (1)	⊕⊕⊕⊖ ^{1,2} moderate	SMD: 0.31 [95% CI: 0.13, 0.48]
Serum Ferritin Levels	The mean ferritin in the intervention groups was 0.47 standard deviations higher (0.36 to 0.58 higher)		1214 (2)	⊕⊕⊕⊖ ^{1,2} moderate	SMD: 0.47 [95% CI: 0.36, 0.58]
Serum Zinc Levels	The mean zinc in the intervention groups was 0.50 standard deviations higher (0.38 to 0.61 higher)		1214 (2)	⊕⊕⊕⊖ ^{1,2} moderate	SMD: 0.50 [95% CI: 0.38, 0.61]
Serum Retinol Levels	The mean serum retinol in the intervention groups was 0.47 standard deviations lower (0.30 to 0.65 higher)		516 (1)	⊕⊕⊕⊖ ^{1,2} moderate	SMD: 0.47 [95% CI: 0.30, 0.65]
Effect on Anemia	Multiple micronutrient fortification reduced the prevalence of anemia by 24%	RR: 0.76 [95% CI: 0.48, 1.21]	516 (1)	⊕⊕⊕⊖ ^{1,2} moderate	

CI: Confidence interval;

¹ Blinding of participants, personal and outcome assessment was not described or carried out in one or more of the studies

² Allocation concealment not carried out or discussed in one or more of the studies

³ A large confidence interval noticed in the results that may account for imprecision in results

⁴ An overall small sample size has been calculated

⁵ A large unexplained/unaccounted drop out was observed in one of the studies

⁶ A before-after study design was used

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

