Micronutrients food fortification and its impact on woman and child health: a systematic review

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CRD summary
The authors concluded that fortification was potentially an effective strategy but evidence from the developing world was scarce. Programmes needed to assess the direct impact of fortification on morbidity and mortality. The authors' conclusions reflect the evidence presented and despite some acknowledged limitations in the review are likely to be reliable.

Authors' objectives
To assess the effectiveness of food fortification with single micronutrients (iron, folic acid, vitamin A, vitamin D, iodine, zinc) as well as multiple micronutrient when compared with no fortification on the health and nutrition of women and children.

Searching
Several electronic databases (including PubMed, CINAHL and The Cochrane Library) were searched without language or date restrictions for published and unpublished studies up to November 2012. Search terms were not reported. Further studies were handsearched from reference lists and bibliographies of relevant studies. Existing reviews and grey literature were searched.

Study selection
Studies such as randomised controlled trials (RCTs), quasi-experimental studies and before and after studies were eligible if: they included infants, children and adolescents under 18 years of age, women of reproductive age and postmenopausal women; food was fortified with a single, dual or multiple micronutrients; and the impact of fortification was analysed on the health outcomes and relevant biochemical indicators.

Studies were included if they measured relevant outcomes: biochemical indicators; haematologic markers; anthropometric indicators such as stunting, wasting, underweight and changes in Z scores for height for age, weight for age and weight for height; pregnancy outcomes for twinning and congenital abnormalities; and relevant morbidity and mortality. Control groups received either unfortified foods or regular diets. Types and amounts of micronutrient used for fortification and durations of the intervention period varied.

Studies focused on home fortification with micronutrient powders, food contents, intake levels, bioavailability, comparisons between different food vehicles or comparisons among compounds of the same micronutrient, comparisons between fortification and supplementation, bio-fortification and studies that evaluated sensory impacts of fortification were excluded.

Two independent reviewers identified relevant studies for inclusion. Any disagreements were resolved with a third reviewer.

Assessment of study quality
It appeared that two reviewers independently assessed the methodological quality for RCTs and quasi-experimental studies using the Cochrane Risk of Bias tool for sequence generation, allocation concealment, blinding, incomplete outcome data, selected reporting and other bias.

Data extraction
Data were extracted to calculate risk ratios, odd ratios and mean differences and their respective 95% confidence intervals. Study authors were contacted for clarification or additional information.

Two reviewers extracted data.
Methods of synthesis
Pooled risk ratios, odd ratios and standardised mean differences and their respective 95% confidence intervals were calculated using a fixed-effect model where there was no evidence heterogeneity and otherwise using a random-effects model. Heterogeneity was assessed using \( \chi^2 \) and \( I^2 \) (\( I^2 > 30 \) indicated high heterogeneity). Subgroup analyses were performed according to the different age groups, countries, population characteristics, types of food fortified and intervention durations.

The overall level of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to take into account methodological quality, directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias. Evidence was rated as high, moderate, low and very low.

Results of the review
A total of 201 studies were included in this review: 121 studies were of infants and children, 79 were of women and one study had both women and children in the study population; 125 trials were RCTs and the rest were quasi-experimental and before-after studies. For the RCTs, randomisation and allocation concealment were adequate in 41 studies, attrition rates were reported in 110 studies and blinding was adequately reported in 62 studies. The quality of evidence ranged from very low to moderate on GRADE.

Children: The analysis showed that iron fortification significantly increased haemoglobin concentration and serum ferritin levels and reduced anaemia. The analysis showed a significant impact of zinc fortification on increasing serum zinc concentration. Non-significant impacts were observed for growth, weight gain, serum alkaline phosphatase, haemoglobin levels and serum copper levels.

Pooled results showed that vitamin D fortification significantly increased serum concentration of 25-hydroxy-vitamin D3 and reduced serum parathyroid hormone concentration; vitamin A fortification had significant impacts on serum retinol concentration and haemoglobin levels. Iodine fortification had a significant effect on median urinary iodine concentrations.

The pooled analysis showed a significant impact of dual fortification (iron and iodine) on haemoglobin concentration and on reducing the prevalence of anaemia. The analysis showed a significant effect of multiple micronutrients fortification on haemoglobin levels, serum ferritin concentration and on reducing anaemia prevalence. Multiple micronutrients fortification had a non-significant impact on height for age, weight for age and weight for height.

Women: Pooled results showed that iron fortification significantly improved haemoglobin concentration, serum ferritin levels and prevalence of anaemia. Folate fortification had a significant impact in reducing neural tube defects, spina bifida and anencephaly. Iodine fortification had a significant impact on median urinary iodine concentrations and on the incidence of hypothyroidism.

The analysis showed that vitamin D and calcium fortification had a significant impact on vitamin D3 levels (increased) and serum parathyroid hormone levels in postmenopausal women but not in women of reproductive age. The pooled analysis showed that multiple micronutrients fortification significantly improved haemoglobin levels, serum ferritin, serum zinc and serum retinol.

There was a lack of evidence for the impact of fortification strategies on morbidity and mortality outcomes in women and children. Most analyses were found to have high heterogeneity.

Further subgroup analyses were reported in the review.

Authors' conclusions
Fortification was potentially an effective strategy but evidence from the developing world was scarce. Programmes needed to assess the direct impact of fortification on morbidity and mortality.

CRD commentary
The review addressed a clear question and was supported by appropriate inclusion criteria. Attempts to identify all relevant studies in any language were undertaken by searching several electronic databases and checking references and grey literatures, which minimised risks of publication and language biases. Attempts were made to minimise reviewer
errors and bias in the review process. Study quality was assessed and appropriate criteria were used to assess the quality of evidence. Appropriate methods were used for pooling data and performing subgroup analyses.

The review included a large number of studies and participants. The authors noted limitations of the review such as using different foods and concentrations of micronutrients and variations in frequency of feeding/intake and intervention duration. Despite these limitations, the authors’ conclusions reflect the evidence presented and appear likely to be reliable.

**Implications of the review for practice and research**

**Practice:** The authors stated that integration of fortification and supplementation strategies together with other mother and child health and prevention programmes may be the answer to address widespread under-nutrition and ensure sustainable benefits. Community education and promotion campaigns should be implemented parallel to the primary fortification programmes to increase awareness, acceptability and equity.

**Research:** The authors stated that although fortification was potentially an effective strategy, evidence from the developing world was scarce and future programmes needed to assess the direct impact of fortification on morbidity and mortality. Limitations identified in the review should be taken into consideration while conducting future research.

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