Multimicronutrient interventions but not vitamin A or iron interventions alone improve child growth: results of 3 meta-analyses
Ramakrishnan U, Aburto N, McCabe G, Martorell R

CRD summary
This review assessed the effects of vitamin A, iron and multimicronutrients on the growth of children. The authors concluded that vitamin A and iron did not improve growth in children, but multimicronutrients increased height and may increase weight. It is difficult to comment on the reliability of these conclusions given that the review methods were not reported and the quality of the included studies was not assessed.

Authors' objectives
To assess the effects of vitamin A, iron and multimicronutrients on the growth of children.

Searching
PubMed was searched from 1966 to between August and October 2003; the search terms were stated. The reference lists of reviews were also checked.

Study selection
Study designs of evaluations included in the review
Randomised controlled studies (RCTs) with at least 8 weeks' follow-up were eligible for inclusion. The studies had to be clearly randomised.

Specific interventions included in the review
Studies that compared vitamin A, iron or multimicronutrients with controls were eligible for inclusion. The treatment groups had to differ only in the micronutrients of interest. Most of the included studies provided supplements in tablet or syrup formulations. The included studies of multimicronutrients all used formulations containing vitamin A, iron, zinc, B vitamins and folic acid. Some studies also used other supplements (details were reported). Studies of iron varied in the amount of iron provided: some provided at least 2 mg/kg body weight (the UNICEF/WHO recommended therapeutic dose), while others provided less. Many studies of iron included a deworming treatment. The duration of the included studies ranged from 8 to 52 weeks.

Participants included in the review
Studies of children aged under 18 years were eligible for inclusion. The mean age of children in the included studies ranged from 9 months to 10.5 years for vitamin A studies, and from younger than 2 to older than 5 years for iron and multimicronutrient studies.

Outcomes assessed in the review
Studies that presented sufficient data to allow the calculation of an effect size (ES) for growth were eligible for inclusion. The primary review outcomes were height and weight. The review also assessed changes in serum retinol for vitamin A interventions and in haemoglobin (Hb) for iron interventions.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

ESs and 95% confidence intervals (CIs) were calculated for each study. Some studies contributed more than one data set.

Methods of synthesis
How were the studies combined?
The studies were grouped by intervention and pooled in random-effects meta-analyses. An overall ES was estimated using the weighted mean ES and 95% CI. Weighting was by the inverse of the within-study variance.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared statistic. Meta-analysis graphs were visually inspected for outliers and meta-analyses were performed with and without outliers. A stratified analysis was used to explore the influence of age, mode of administration, dosage, duration of the intervention, and initial Hb for iron interventions and Z-scores. Weighted mean ESs were calculated for each subgroup containing two or more studies. A regression analysis was used to examine the influence of study duration, baseline weight-for-age Z-score (WAZ), height-for-age Z-score (HAZ), weight-for-height Z-score (WHZ) and Hb levels. There were insufficient data to examine the effects of baseline serum retinol levels for vitamin A studies, or for formal stratified analyses of multimicronutrient studies.

Results of the review
Fourteen RCTs (n=68,678) provided 17 data sets for the assessment of vitamin A, 21 RCTs (n=3,610) provided 28 data sets for the assessment of iron, and 5 RCTs (n=1,604) assessed multimicronutrients.

Vitamin A.
There was no significant difference between vitamin A and control for height (ES 0.08, 95% CI: -0.20, 0.36) or weight (ES -0.01, 95% CI: -0.24, 0.22). There was evidence of heterogeneity. However, the exclusion of an extreme outlier did not alter the results, while a regression analysis found no effect of the baseline characteristics on the ESs.

Iron.
There was no significant difference between iron and control for height (ES 0.09, 95% CI: -0.07, 0.24) or weight (ES 0.13, -0.05, 0.30). These ESs excluded data from an extreme outlier, but the inclusion of this outlier did not alter the results.

There was evidence of heterogeneity. The results were similar after stratifying the analysis for age, type of intervention and dose. A regression analysis found no effect of the baseline characteristics on the ESs.

Iron significantly increased Hb compared with the control; the ES (16 RCTs providing 21 data sets with 2,542 children) was 1.49 (95% CI: 0.46, 2.51).

Multimicronutrients.

Multimicronutrients significantly increased height (ES 0.28, 95% CI: 0.16, 0.41), but did not significantly increase weight (ES 0.28, -0.07, 0.63), compared with the control. There was evidence of statistical heterogeneity for height.

There was no significant correlation between ES for either height or weight for baseline HAZ, WAZ, WHZ, Hb or study duration.

Authors' conclusions
Vitamin A and iron did not improve growth in children, whereas multimicronutrients increased height and may increase
The review question was clear in terms of the study design, intervention, participants and outcomes. Only one database was searched and this might have resulted in the omission of other relevant studies. No attempt to locate unpublished studies was reported, thus raising the possibility of publication bias. It was unclear whether any language restrictions had been applied. The methods used to select studies and extract the data were not described, so it is not known whether any efforts were made to reduce errors and bias. Only RCTs were included but the quality of the included studies was not assessed.

The studies were combined in meta-analyses. Significant heterogeneity was found and the authors explored several potential reasons for this. However, the heterogeneity remained unexplained and potential reasons why results from some identified outliers differed from the majority were not discussed. Since the quality of the included studies and the methods used to conduct the review were not reported, it is difficult to comment on the strength of the evidence underpinning the authors' conclusions.

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

**Practice:** The authors stated that more sustainable food-based approaches to supplementation should be pursued.

**Research:** The authors did not state any implications for further research.

**Funding**

World Bank, National Institutes of Health grant number HD-34531-05; Woodruff Health Sciences, Emory University.

**Bibliographic details**


**PubMedID**

15465753

**Original Paper URL**

http://jn.nutrition.org

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Africa; Asia; Body Height /drug effects; Child; Child, Preschool; Databases, Factual; Growth /drug effects; Humans; Infant; Iron /pharmacology; Micronutrients /pharmacology; Randomized Controlled Trials as Topic; Vitamin A /pharmacology; Weight Gain /drug effects

**AccessionNumber**

12004006784

**Date bibliographic record published**

31/03/2006

**Date abstract record published**

31/03/2006
Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.