



HHS Public Access

Author manuscript

Lancet Child Adolesc Health. Author manuscript; available in PMC 2023 May 10.

Published in final edited form as:

Lancet Child Adolesc Health. 2021 August ; 5(8): e28–e29. doi:10.1016/S2352-4642(21)00168-1.

Micronutrient powders and diarrhoea risk in infants and young children

Parminder S Suchdev,

Department of Pediatrics, Emory University, and Emory Global Health Institute, Atlanta, GA, USA;
Nutrition Branch, Centers for Disease Control and Prevention, Atlanta, GA, USA

Maria Elena Jefferds,

Nutrition Branch, Centers for Disease Control and Prevention, Atlanta, GA, USA

Kathryn G Dewey,

Department of Nutrition and Institute for Global Nutrition, University of California, Davis, CA, USA

Stanley Zlotkin,

Centre for Global Child Health, Hospital for Sick Children, Toronto, ON, Canada; Departments of Paediatrics, Nutritional Sciences and Public Health, University of Toronto, Toronto, ON, Canada

Victor M Aguayo,

Programme Division, Nutrition, UNICEF HQ, New York, NY, USA

Saskia de Pee,

Nutrition Division, UN World Food Programme, Rome, Italy

Klaus Kraemer,

Sight and Life, Basel, Switzerland

Alison Greig,

Nutrition International, Ottawa, ON, Canada

Mandana Arabi,

Nutrition International, Ottawa, ON, Canada

Luz Maria De-Regil

Department of Nutrition and Food Safety, WHO, Geneva, Switzerland

the Home Fortification Technical Advisory Group

Emily Keats and colleagues¹ revisited the evidence base of maternal and child nutrition interventions using updated systematic reviews. The authors recommend micronutrient powders as an effective intervention to reduce childhood anaemia and iron deficiency, in line with WHO recommendations.² Using data from a 2020 systematic review by Tam and colleagues,³ the authors reported a 30% increased risk of diarrhoea (relative risk [RR] 1.30 [95% CI 1.11–1.53]) associated with micronutrient powders. This finding contrasts with

psuchde@emory.edu .

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findings from two Cochrane reviews of micronutrient powders that found no association between micronutrient powder use and diarrhoea in children aged 6–23 months (odds ratio [OR] 1.05 [95% CI 0.82–1.35]) and 2–12 years (RR 0.97 [95% CI 0.53–1.78]).^{4,5} We raise several points to explain these differences.

First, there were differences in systematic review methodology. Tam and colleagues included children aged 1 month to 5 years in low-and-middle income countries,³ whereas the two Cochrane reviews on micronutrient powder use included children aged 6–23 months⁴ and 2–12 years⁵ in any geographical setting. The reviews included and excluded different trials. All reviews assessed the longitudinal prevalence of diarrhoea as a secondary outcome. Tam and colleagues included four trials in their diarrhoea sub-analysis. One trial used ready-to-eat fortified maize flour, not micronutrient powders, and was thus not included in the Cochrane reviews.⁶ This trial and two others that Tam and colleagues included found no differences in diarrhoea by treatment group; only one trial by Soofi and colleagues⁷ (overall weight of 92.9%) showed an increase in the proportion of days with diarrhoea. Suchdev and colleagues included five trials in their diarrhoea subanalysis, with only one trial by Soofi and colleagues in common with the Tam review. A total of four trials selected for inclusion in the review by Tam and colleagues and two trials selected for inclusion in the review by Suchdev and colleagues did not have their diarrhoea results extracted. De-Regil and colleagues included two trials, only one of which included children aged 6 months to 5 years,⁸ but this trial was not included by Tam and colleagues.

Statistical analysis procedures also differed. Tam and colleagues and De-Regil and colleagues used a Mantel-Haenszel random effects model and reported risk ratios based on diarrhoea prevalence; Suchdev and colleagues used generic inverse-variance random effects models because two trials presented pre-calculated estimates of treatment effects, and reported ORs given the overall low rates of diarrhoea.

To produce an estimate of risk of diarrhoea from micronutrient powders in children aged 6 months to 5 years using more comprehensive evidence, excluding the non-micronutrient powder trial,⁶ we did an analysis of eight trials included in these three systematic reviews in duplicate in RevMan (version 5.4) and R (version 4.0.2), including 10 335 children aged 6 months to 5 years. We found no effect of micronutrient powder use on diarrhoea prevalence (OR 0.95 [95% CI 0.72–1.25]; appendix). UNICEF reports 16 million children in 46 countries were reached with micronutrient powders in 2019.⁹ Although additional research on the safety and cost-effectiveness of iron interventions in children might be needed, identifying diarrhoea as a significant side-effect associated with micronutrient powder use, when additional evidence suggests that it might not be, could set back global goals to improve child nutrition in high burden settings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The findings and conclusions of this report are those of the authors and do not necessarily represent the official position of the US Centers for Disease Control and Prevention or WHO. The Home Fortification Technical Advisory Group (HF-TAG), hosted and chaired by Nutrition International, is a community of partners involved in home fortification, which includes micronutrient powders. The group is comprised of members from the public, private, academic and non-governmental organisation sectors with a mission to provide leadership by supporting well designed and effective home fortification interventions at scale for children and women, based on sound technical guidance and best practices. We declare no competing interests.

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