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Meeting the challenges of micronutrient malnutrition in the developing world

Zulfiqar A. Bhutta*, **Rehana A. Salam,** and **Jai K. Das**

Division of Women and Child Health, The Aga Khan University, Karachi 74800, Pakistan

Background: Malnutrition still remains one of the major public health challenges, particularly in developing countries. Major risk factors for undernutrition such as suboptimal breastfeeding and micronutrient deficiencies (vitamin A and zinc) are responsible for more than one-third of all under five child deaths and 11% of the global total disease burden.

Sources of data: Several strategies have been employed to supplement micronutrients. These include education, dietary modification, food provision, supplementation and fortification either alone or in combination.

Areas of agreement: Supplementation is the most widely practiced intervention while fortification can also be a potentially cost-effective public health intervention and target a larger population through a single strategy. Universal coverage with the full bundle of interventions including micronutrient provision, complementary foods, treatments for worms and diarrheal diseases and behavior change programs package could be the way forward in achieving the Millennium Development Goals (MDGs).

Areas of controversy: Bio-fortification and agricultural interventions including home and school gardening are relatively newer strategies and require further research as they have the potential to impact nutritional status of populations at large.

Growing points: Effectiveness of the various interventions is well recognized; however, consensus needs to be built around approaches to scale up coverage and delivery strategies to reduce disparities and provide equitable access.

Areas timely for developing research: Future studies should focus on evaluating various approaches to address malnutrition with a standard methodology and defined outcomes. This will help gauge the actual morbidity and mortality impacts of these specific interventions and the long-term viability of these programs. On a broader scale, strategies to address food insecurity and poverty alleviation are the key as these are complex sustainable development issues, linked to health through malnutrition, but also to sustainable economic development, environment and trade.

Keywords: micronutrient deficiency/undernutrition/developing countries

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**Correspondence address. Division of Women and Child Health, The Aga Khan University, Karachi 74800, Pakistan. E-mail: zulfiqar.bhutta@aku.edu*

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Background

Micronutrients play a critical role in cellular and humoral immune responses, cellular signaling and function, work capacity, reproductive health, learning and cognitive functions and even in the evolution of microbial virulence.[1,2] The body cannot synthesize micronutrients, so they must be made available through diet.[2] Micronutrient deficiencies affect people of all ages but their effects appear more devastating in pregnant women and children specially young infants.

Malnutrition, including micronutrient deficiencies, remains one of the major public health challenges, particularly in developing countries.[3] In 2011, almost 6.9 million children under 5 years of age died worldwide.[4] Suboptimal breastfeeding and micronutrient deficiencies (particularly vitamin A and zinc) (Figs 1 and 2) were responsible for more than one-third of these deaths and 11% of the global total disease burden.[4] Around 165 million children under five suffer from stunting, 101 million are underweight and 52 million wasted. Approximately 90% of these live in just 36 countries with highest prevalence in Southeast Asia and sub-Saharan Africa, and India alone contributes 36.3% to the total stunted population.[5] Prevalence of malnourished children has reduced substantially and progress has been made in the past two decades but at the current rate of progress, United Nations regional goals for reducing stunting and underweight prevalence by the year 2015 are unlikely to be achieved in all developing countries.

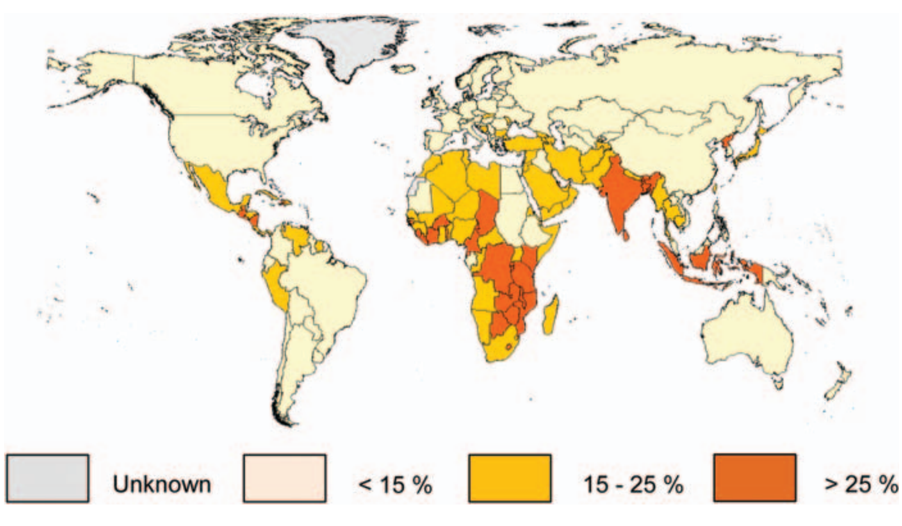

Fig. 1 Global burden of iron, iodine and vitamin A deficiencies. Source: Wessells and Brown, 2012.[52]

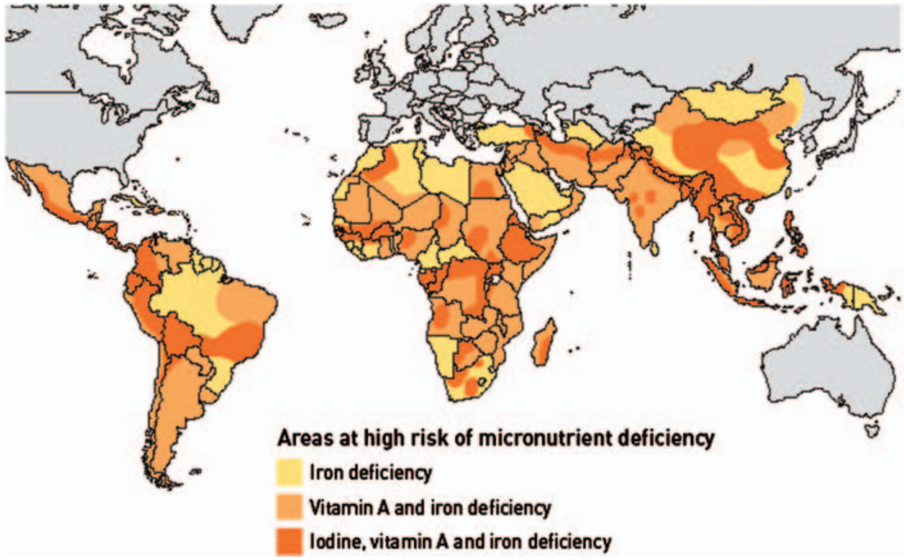

Fig. 2 Global burden of inadequate zinc intake. Source: USAID.

Global micronutrient deficiency burden

The World Health Organization (WHO) estimates that in spite of recent efforts in the prevention and control of micronutrient deficiencies, over two billion people are at risk of vitamin A, iodine and/or iron deficiency globally.[6] Other micronutrient deficiencies of public health concern include zinc, folate and the B vitamins. In many settings, more than one micronutrient deficiency coexist, suggesting the need for simple approaches that evaluate and address multiple micronutrient (MMN) malnutrition.[7]

Anemia, one of the major global nutrition concerns, is caused not only by deficiency of iron but is also associated with other nutrient deficiencies like vitamin A, B6, B-12, riboflavin and folic acid. Besides nutrient deficiencies, general infections, chronic diseases, malaria and helminthes infestation also lead to anemia.[8,9] Majority of the data for folate deficiencies are based on small, local surveys, but they suggest that the deficiency may be a public health problem affecting millions of people globally.[10] Folate and B12 deficiencies are associated with adverse pregnancy outcomes, including low birth weight (LBW) and pre-term birth.[11] Iodine deficiency (IDD) is a concern in 130 countries and affects 13% of world's population.[12] Globally about 740 million people are affected by goiter, and over two billions are considered at risk of IDD.[13] An estimated one-third of the world population lives in countries with a high prevalence of zinc deficiency. There is now increasing recognition of the importance of zinc in childhood growth and development[14] and subclinical zinc deficiency has been widely recognized as a significant limiting factor for growth among children in both developing and developed countries.[15] Clinical vitamin A deficiency (VAD) affects at least 2.80 million preschool children in over 60 countries, and sub clinical VAD is considered a problem for at least 251 million that includes school-age children and pregnant women.[16] Severe as well as marginal VAD has been shown to lead to an increased risk of morbidity and mortality in children. Delayed growth, especially stunting has also been reported in children with clinical signs of VAD.[17]

Several micronutrients such as vitamin A, beta-carotene, folic acid, vitamin B12, vitamin C, riboflavin, iron, zinc and selenium have immune-modulating functions and thus influence the susceptibility of a host to infectious diseases and the course and outcome of such diseases. Certain of these micronutrients also possess antioxidant functions that not only regulate immune homeostasis of the host, but also alter the genome of the microbes, particularly in viruses, resulting in grave consequences like resurgence of old infectious diseases or the emergence of new infections.[18] Children who are stunted or born with IUGR are also shown to complete fewer years of schooling and earn less income than adults, which hinders their cognitive growth and economic potential. Lower income, poor health and reduced access to proper nutrition then continue to impact on the health of children born into future generations, establishing a viscous cycle.

Strategies for micronutrient malnutrition

Several strategies have been employed to supplement micronutrients to women and children (Table 1).[19–23] These include education, dietary modification, food provision, agricultural interventions, supplementation and fortification either alone or in combination. Apart from these direct nutritional interventions, parallel programs have also been pursued to aid implementation of these primary interventions including provision of financial incentives at various levels, home gardening and community-based nutrition education and mobilization programs. These strategies can be delivered through the health systems, agriculture, market-based approaches or other community-based platforms.[24]

Micronutrient supplementation is the most widely practiced intervention to prevent and manage single or MMN deficiencies. Supplementation programs are currently in place to combat iron[25–31] and vitamin A deficiencies among high-risk populations.[31,32] A review on preventive vitamin A supplementation (VAS) among children under 5 years of age in community settings showed reduced all-cause mortality and diarrhea-specific mortality

Table 1 Interventions to address micronutrient deficiencies and their impacts

Interventions	Impacts
Vitamin A supplementation[33]	Reduction in all-cause mortality by 24% Reduction in diarrhea specific mortality by 28%
Iron supplementation in pregnancy[34]	69% reduction in incidence of anemia at term, 66% reduction in iron deficiency anemia at term, 20% reduction in incidence of LBW Increased mean birth weight (MD: 42.18, 95% CI: 9.27, 75.09)
Calcium supplementation during pregnancy[35]	52% reduction in the incidence of pre-eclampsia Increase in birth weight of 85 g 24% reduction in risk of pre-term birth.
MMN during pregnancy[36]	Reduced the number of LBW infants by 14% Reduced SGA by 13%
Micronutrient powders/sprinkles for children[37]	Effective in reducing anemia and iron deficiency in children 6 months to 23 months of age
Bio-fortification[42]	Increases micronutrient intake and improves micronutrient status
Salt Iodization and vitamin A fortification[40]	Improves iodine status
Food-based agricultural interventions[23]	Home gardening interventions had a positive effect on the production of the agricultural goods and consumption of food rich in protein and micronutrients. Some evidence of a positive effect on absorption of vitamin A[23]

SGA, small for gestational age.

by 24 and 28%, respectively.[33] Among pregnant women, daily iron supplementation has shown a 69% reduction in incidence of anemia at term, 66% reduction in iron deficiency anemia at term and 20% reduction in incidence of LBW.[34] Calcium supplementation during pregnancy is found to be associated with a reduction in the risk of gestational hypertensive disorders and has also shown a 52% reduction in the incidence of pre-eclampsia and a 24% reduction in pre-term birth with an increase in birth weight of 85 g.[35] A recent Cochrane review[36] shows that MMN supplementation during pregnancy significantly decreased the number of LBW infants by 14% and small for gestational age (SGA) by 13%. This review also further indicated that MMN compared with iron and folate supplementation resulted in a significant 11% decrease in the number of LBW and 13% decrease in SGA babies. While the impact on pre-term birth, miscarriage, pre-eclampsia, maternal mortality, perinatal mortality, still birth and neonatal mortality were statistically non-significant.

In the last decade point of use or home fortification of food has emerged to tackle the widespread micronutrient deficiencies. Multiple Micronutrient Powders (MNPs) or Sprinkles are powdered vitamins and minerals that can be added to the prepared food with little change in taste or texture. A review assessing the impact of MNPs among children 6–23 months of age concluded that it is effective in reducing anemia and iron deficiency,[37] while the impact on growth and other developmental outcomes are unclear.

Food fortification can also be a potentially cost-effective public health intervention and target a larger population through a single strategy. According to WHO and Food and Agricultural Organization (FAO), fortification is done to increase the content of an essential micronutrient in a food irrespective of whether the nutrients were originally in the food before processing or not, so as to improve the nutritional quality of the food supply and to provide a public health benefit with minimal risk to health.[38] Fortification programs take different forms: mass fortification involves fortifying foods that are widely consumed by the general population, targeted fortification involves fortifying a food eaten by a specific subgroup of the population that has a particular need, for example, complementary food for young children, and market-driven (or industry-driven) fortification involves the food industry choosing to fortify, within regulatory limits set by the government. Fortification has shown functional impacts by significantly increasing serum micronutrient concentrations among children. A meta-analysis of multi micronutrient fortification in children showed an increase in hemoglobin levels by 0.87 g/dl (95% CI: 0.57–1.16) and reduced risk of anemia by 57% (RR: 0.43; 95% CI 0.26–0.71). Fortification also increased vitamin A serum levels (retinol increase by 3.7 μg/dl, 95% CI: 1.3–6.1).[39] A review on mass salt fortification with vitamin A and iodine concluded that the fortified and iodized salt can improve the iodine status.[40] The evidence from developing countries, however, is scarce and these programs also need to assess the direct impact on morbidity and mortality. Key issues to ensure a sustainable program include identifying the right food (considering bioavailability, interaction with food, availability, acceptability and cost) and the target population, ensuring quality of product and consumption of sufficient quantity of the fortified food.[41]

Bio-fortification is a relatively new strategy to address micronutrient deficiencies in developing countries to improve iron, zinc and vitamin A status in low-income populations. It is the use of conventional breeding techniques and biotechnology to improve the micronutrient quality of staple crops. A review on bio-fortification concluded that it has the potential to contribute to increased micronutrient intakes and improved micronutrient status; however, this domain requires further research.[42]

Agricultural interventions including home and school gardening also have the potential for affecting nutritional status, when implemented with that objective. A review on agricultural interventions to improve nutritional status of children concluded that home gardening interventions had a positive effect on the production of the agricultural goods and consumption of food rich in protein and micronutrients. Some evidence of a positive effect on absorption of vitamin A was also observed. However, the impacts on iron absorption and anthropometric indices remained inconclusive.[23]

Multiple complimentary nutrition interventions targeted to improve nutritional status of children have also been reviewed. These include complementary and supplementary feeding programs with or without nutrition education. Dewey 2008[43] reviewed the effectiveness and efficacy of complementary feeding interventions in children aged 6–24 months in developing countries. It indicated that provision of complementary food can have a significant impact on growth under well-controlled situations. Complementary food combined with maternal education improved weight (0.35, range 0.18–0.66) and linear growth (0.17, range 0–0.32). A recent Cochrane review by Sguassero,[44] looking at the impact of supplementary feeding that covered energy protein supplementation but not other complementary feeding, found a statistically significant difference of effect for length in children aged less than 12 years (MD 0.19 cm; 95% CI: 0.07, 0.31).

Way forward

In a recent analysis for the Global Burden of Disease Study 2010,[45] burden of micronutrients has reduced compared with the previous estimates in the Lancet's Maternal and Child Undernutrition Series.[46] The deaths attributable to iron, vitamin A and zinc deficiencies have reduced from 1990 to 2010 (Table 2). However, there is a need to systematically reconsider micronutrient supplementation and the relative cost effectiveness of other nutrition interventions. It is more feasible to implement supplementation interventions for the targeted groups in developing countries. Since the systems are already in place as iron/folate supplementation is recommended for pregnant women, other micronutrient supplementation programs could be integrated at little additional cost.[47,48] In the Copenhagen consensus statement 2012,[49] it was concluded that for about $100 per child, bundle of interventions including micronutrient provision and also complementary foods, treatments for

Table 2 Trends in deaths attributable to iron, vitamin A and zinc deficiency worldwide

Micronutrient status	Deaths		Disease burden (1000 DALYs)	
	1990	2010	1990	2010
Iron deficiency	168 084 (130 444–197 085)	119 608 (93 261–139 985)	51 841 (37 477–71 202)	48 225 (33 769–67 592)
Vitamin A Deficiency	349 354 (170 504–632 149)	119 762 (61 723–191 846)	30 288 (14 884–54 488)	10 770 (5625–17 149)
Zinc deficiency	275 590 (51 274–529 451)	97 330 (17 575–190 527)	24 375 (5385–45 685)	9136 (2458–16 903)

Source: Lim.[45]

worms and diarrheal diseases and behavior change programs could reduce chronic undernutrition by 36% in developing countries. Even in very poor countries, each dollar spent reducing chronic undernutrition has at least a $30 payoff. Hence, the universal coverage with the full package of proven interventions could be the way forward in achieving the Millennium Development Goals (MDGs). The long-term sustainability of such programs, however, is hindered in developing countries because of government policies, human resource constraints, bad communication networks including roads and the fragile health system infrastructure.[50] Participants compliance and some adverse effects observed with high-dose supplements may also hinder their effectiveness.[51]

Evidence still lacks from developing countries where these interventions are mainly needed. Most of the major national level programs pertaining to mass fortification come from the developed countries. This is due to the fact that larger programs require a larger magnitude of resources, as multiple facilities need to be synchronized for the effective implementation of the program. Large production facilities are necessary to fulfill the demands of the entire population and effective logistical support is of prime importance. Additionally effective monitoring systems are necessary to monitor, regulate and evaluate the production, distribution facilities and the demands of the communities. Foremost fair and just political will and policies are essential. As the poor have limited purchasing power, funding agencies and public private partnerships are eminent in ensuring cost subsidies and cost-sharing and in ensuring that the products reach the poor who need them most. Additional demand creation and social marketing may be necessary through campaigns to ensure adequate marketing pull factors and consumption. Future studies should focus on evaluating various approaches to address malnutrition with a standard methodology and defined outcomes. This will help gauge the actual morbidity and mortality impacts of these specific interventions and the long-term viability of these programs. Effectiveness of the various interventions is well recognized; however, consensus needs to be built around approaches to scale up coverage and delivery strategies to reduce disparities and provide equitable access.

Food-based approaches are regarded as the long-term strategy for improving nutrition, which would need mega efforts and proper planning but for certain micronutrients, supplementation, be it to the general population, to high-risk groups or as an adjunct to treatment must also be considered. Given the wide prevalence of MMN deficiencies in developing countries, the challenge is to implement intervention strategies that combine appropriate infant and young child feeding with micronutrient interventions at scale. Emerging data from community intervention trials now provides evidence that this is both tangible and can lead to alleviation of undernutrition. On a broader scale, strategies to address food insecurity and poverty alleviation are the key as these are complex sustainable development issues, linked to health through malnutrition, but also to sustainable economic development, environment and trade.

References

1 Guerrant RL, Lima AAM, Davidson F. Micronutrients and infection: interactions and implications with enteric and other infections and future priorities. *J Infect Dis* 2000;**182**(Suppl 1): S134–8.

2 Kapil U, Bhavna A. Adverse effects of poor micronutrient status during childhood and adolescence. *Nutr Rev* 2008;**60**(s5):S84–90.

3 Black RE, Allen LH, Bhutta ZA, *et al*. Maternal and child undernutrition: global and regional exposures and health consequences. *Lancet* 2008;**371**:243–60.

4 UNICEF, WHO, The World Bank. Levels and trends in child mortality: report 2012. Estimates Developed by the UN Inter-agency Group for Child Mortality Estimation.

5 Bhutta ZA. Micronutrient needs of malnourished children. *Curr Opin Clin Nutr Metab Care* 2008;**11**:309–14.

6 World Health Organization. World health report, 2000. Geneva: World Health Organization, 2000.

7 Ramakrishnan U. Prevalence of micronutrient malnutrition worldwide. *Nutr Rev* 2002;**60** (5 Pt 2):S46–52.

8 Morais MB, Ferrari AA, Fisberg M. Effect of oral iron therapy on physical growth. *Rev Paul Med* 1993;**111**:439.

9 Olivares M, Walter T, Hertrampf E *et al*. Anaemia and iron deficiency disease in children. *Br Med Bull* 1999;**55**:534–43.

10 Krishnaswamy K, Lakshmi AV. Role of nutritional supplementation in reducing the levels of homocysteine. *J Assoc Physicians India* 2002;**50**:36.

11 Vollset SE, Refsum H, Irgens LM *et al*. Plasma total homocysteine, pregnancy complications, and adverse pregnancy outcomes: the Hordaland Homocysteine study. *Am J Clin Nutr* 2000;**71**:962–8.

12 Vir SC. Current status of iodine deficiency disorders (IDD) and strategy for its control in India. *Indian J Pediatr* 2002;**69**:589–96.

13 De Benoist B, Delange F. Iodine deficiency: current situation and future prospects. *Sante (Montrouge, France)* 2002;**12**:9.

14 Child Health Research Project. Zinc for Child Health: John Hopkins School of Public Health. June 1997 November 17–19, 1996.

15 Ploysangam A, Falciglia GA, Brehm BJ. Effect of marginal zinc deficiency on human growth and development. *J Trop Pediatr* 1997;**43**:192–8.

16 Stephenson LS, Latham MC, Ottesen EA. Global malnutrition. *Parasitology* 2000;**121**:5–22.

17 Chaudhary S, Verma M, Dhawan V *et al*. Plasma vitamin A, zinc and selenium concentrations in children with acute and persistent diarrhoea. *J Diarrhoeal Dis Res* 1996;**14**:190–3.

18 Bhaskaram P. Micronutrient malnutrition, infection and immunity: an overview. *Nutr Rev* 2002;**60** (5 Pt 2):S40–5 0029-6643.

19 Best C, Neufingerl N, Del Rosso JM *et al*. Can multi micronutrient food fortification improve the micronutrient status, growth, health, and cognition of schoolchildren? A systematic review. *Nutr Rev* 2011;**69**:186–204.

20 Bhutta ZA, Ahmed T, Black RE *et al*. What works? Interventions for maternal and child undernutrition and survival. *Lancet* 2008;**371**:417–40.

21 Dewey KG, Yang Z, Boy E. Systematic review and meta analysis of home fortification of complementary foods. *Matern Child Nutr* 2009;**5**:283–321.

22 Serdula M. Maximizing the impact of flour fortification to improve vitamin and mineral nutrition in populations. *Food Nutr Bull* 2010;**31**(1 Suppl):S86–93.

23 Masset E, Haddad L, Cornelius A *et al*. Effectiveness of agricultural interventions that aim to improve nutritional status of children: systematic review. *BMJ* 2012;**344**:d8222.

24 Olney D, Rawat R, Ruel M. Identifying potential programs and platforms to deliver multiple micronutrient interventions. *J Nutr* 2012;**142**:178S–85S.

25 WHO (World Health Organization). *Guideline: Use of Multiple Micronutrient Powders for Home Fortification of Foods Consumed by Infants and Children 6–23 Months of Age*. Geneva: World Health Organization, 2011.

26 Villar J, Bergsjo P. Scientific basis for the content of routine antenatal care. I. Philosophy, recent studies and power to eliminate or alleviate adverse maternal outcomes. *Acta Obstet Gynecol Scand* 1997;**76**:1–14.

27 WHO, UNICEF, UNU. *Iron Deficiency Anaemia: Assessment, Prevention, and Control. Iron Deficiency Anaemia: Assessment, Prevention, and Control*. Geneva: World Health Organization, 2001.

28 WHO. Intermittent iron supplementation for menstruating women. http://www.who.int/nutrition/publications/micronutrients/weekly˙iron˙folicacid.pdf, 2011 (7 April 2012, date last accessed).

29 WHO. *Guideline: Daily Iron and Folic Acid Supplementation in Pregnant Women*. Geneva: World Health Organization, 2011.

30 WHO. *Guideline: Intermittent Iron Supplementation in Preschool and School Age Children*. Geneva: World Health Organization, 2011.

31 WHO. *Guideline: Intermittent Iron and Folic Acid Supplementation in Non anaemic Pregnant Women*. Geneva: World Health Organization, 2011.

32 WHO. *Guideline: Vitamin A Supplementation in Infants and Children 6–59 Months of Age*. Geneva: World Health Organization, 2011.

33 Imdad A, Herzer K, Mayo-Wilson E *et al*. Vitamin A supplementation for preventing morbidity and mortality in children from 6 months to 5 years of age. *Cochrane Database Syst Rev* 2010;**12**. Art. No:CD008524.

34 Imdad A, Bhutta ZA. Routine iron/folate supplementation during pregnancy: effect on maternal anaemia and birth outcomes. *Paediatr Perinat Epidemiol* 2012;**26**(s1):168–77.

35 Imdad A, Bhutta ZA. Effects of calcium supplementation during pregnancy on maternal, fetal and birth outcomes. *Paediatr Perinat Epidemiol* 2012;**26**(s1):138–52.

36 Haider BA, Bhutta ZA. Multiple micronutrient supplementation for women during pregnancy. *The Cochrane Library* 2012.

37 De-Regil LM, Suchdev PS, Vist GE *et al*. Home fortification of foods with multiple micronutrient powders for health and nutrition in children under two years of age. *Cochrane Database Syst Rev* 2011;**9**. Art. No:CD008959.

38 Allen L, de Benoist B, Dary O *et al*. *Guidelines on Food Fortification with Micronutrients*. Geneva: World Health Organization/Food and Agriculture Organization, 2006.

39 Eichler K, Wieser S, Ruthemann I *et al*. Effects of micronutrient fortified milk and cereal food for infants and children: a systematic review. *BMC Public Health* 2012;**12**:506.

40 Ting J, Qian X. Fortified salt for preventing iodine deficiency disorders: a systematic review. *Chin J Evid-based Med* 2010;**10**:857–61.

41 Harvey PWJ, Dary O. Governments and academic institutions play vital roles in food fortification: iron as an example. *Public Health Nutr* 2012;**1**:1–5.

42 Hotz C, McClafferty B. From harvest to health: challenges for developing biofortified staple foods and determining their impact on micronutrient status. *Food & Nutrition Bulletin* 2007;**28**(Suppl 2):271S–79S.

43 Dewey KG, Adu-Afarwuah S. Systematic review of the efficacy and effectiveness of complementary feeding interventions in developing countries. *Matern Child Nutr* 2008;**4**(Suppl 1):24–85.

44 Sguassero Y, de Onis M, Bonotti AM *et al*. Community-based supplementary feeding for promoting the growth of children under five years of age in low and middle income countries. *Cochrane Database Syst Rev* 2012;**6**:CD005039.

45 Lim SS, Vos T, Flaxman AD *et al*. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the global burden of disease study 2010. *The lancet* 2013;**380**:2224–60.

46 Bhutta ZA, Ahmed T, Black RE, *et al*. What works? Interventions for maternal and child undernutrition and survival. *Lancet* (Research Support, Non-U.S. Gov't Review). 2008; **371**:417–40.

47 Black R. Micronutrients in pregnancy. *Br J Nutr* 2001;**85**(Suppl 2):S193–7.

48 Alderman H, Horton S. The economics of addressing nutritional anemia. In: Kraemer K, Zimmermann MB (eds). *Nutritional Anemia*. Basel: Sight and Life Press, 2007, 19–35.
49 Copenhegan Consensus 2012: Solving the World's Challenges.
50 Zimmermann M, Hurrell R. Nutritional iron deficiency. *Lancet* 2007;**370**:511–20.
51 Baltussen R, Knai C, Sharan M. Iron fortification and iron supplementation are cost-effective interventions to reduce iron deficiency in four subregions of the world. *J Nutr* 2004; **134**:2678–84.
52 Wessells KR, Brown KH. Estimating the global prevalence of zinc deficiency: results based on zinc availability in National Food Supplies and the prevalence of stunting. *PloS one* 2012;**7**:e50568.