Maternal and Child Undernutrition 3

What works? Interventions for maternal and child undernutrition and survival

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We reviewed interventions that affect maternal and child undernutrition and nutrition-related outcomes. These interventions included promotion of breastfeeding; strategies to promote complementary feeding, with or without provision of food supplements; micronutrient interventions; general supportive strategies to improve family and community nutrition; and reduction of disease burden (promotion of handwashing and strategies to reduce the burden of malaria in pregnancy). We showed that although strategies for breastfeeding promotion have a large effect on survival, their effect on stunting is small. In populations with sufficient food, education about complementary feeding increased height-for-age *Z* score by 0·25 (95% CI 0·01–0·49), whereas provision of food supplements (with or without education) in populations with insufficient food increased the height-for-age *Z* score by 0·41 (0·05–0·76). Management of severe acute malnutrition according to WHO guidelines reduced the case-fatality rate by 55% (risk ratio 0·45, 0·32–0·62), and recent studies suggest that newer commodities, such as ready-to-use therapeutic foods, can be used to manage severe acute malnutrition in community settings. Effective micronutrient interventions for pregnant women included supplementation with iron folate (which increased haemoglobin at term by 12 g/L, 2·93–21·07) and micronutrients (which reduced the risk of low birthweight at term by 16% (relative risk 0·84, 0·74–0·95). Recommended micronutrient interventions for children included strategies for supplementation of vitamin A (in the neonatal period and late infancy), preventive zinc supplements, iron supplements for children in areas where malaria is not endemic, and universal promotion of iodised salt. We used a cohort model to assess the potential effect of these interventions on mothers and children in the 36 countries that have 90% of children with stunted linear growth. The model showed that existing interventions that were designed to improve nutrition and prevent related disease could reduce stunting at 36 months by 36%; mortality between birth and 36 months by about 25%; and disability-adjusted life-years associated with stunting, severe wasting, intrauterine growth restriction, and micronutrient deficiencies by about 25%. To eliminate stunting in the longer term, these interventions should be supplemented by improvements in the underlying determinants of undernutrition, such as poverty, poor education, disease burden, and lack of women's empowerment.

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This is the third in a **Series** of five papers about maternal and child undernutrition

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Introduction

Of an estimated 178 million children aged younger than 5 years who are stunted (ie, have a height-for-age *Z* score of less than –2),[1] most live in sub-Saharan Africa and south-central Asia. 160 million (90%) stunted children live in just 36 countries, and make up 46% of the 348 million children in those countries. About 55 million children are wasted (ie, have a weight-for-height *Z* score of less than –2), of whom 19 million have severe wasting (weight-for-height *Z* score of less than –3) or severe acute malnutrition (weight-for-height *Z* score of –3 or lower or associated oedema).

Although the prevalence of maternal undernutrition—assessed by low body-mass index—varies, fetal undernutrition or intrauterine growth restriction is common, with the highest prevalence in south-central Asia.[1] The association between undernutrition and child mortality is strong,[2] but evidence for the contribution of intrauterine growth restriction to mortality of neonates and children younger than 5 years has been less robust.[3]

Key messages

- Effective interventions are available to reduce stunting, micronutrient deficiencies, and child deaths. If implemented at sufficient scale, they would reduce DALYs (all child deaths) by about a quarter in the short term
- Of available interventions, counselling about breastfeeding and fortification or supplementation with vitamin A and zinc have the greatest potential to reduce the burden of child morbidity and mortality
- Improvement of complementary feeding through strategies such as counselling about nutrition for food-secure populations and nutrition counselling, food supplements, conditional cash transfers, or a combination of these, in food-insecure populations could substantially reduce stunting and related burden of disease
- Interventions for maternal nutrition (supplements of iron folate, multiple micronutrients, calcium, and balanced energy and protein) can improve outcomes for maternal health and births, but few have been assessed at sufficient scale
- Although available interventions can make a clear difference in the short term, elimination of stunting will also require long-term investments to improve education, economic status, and empowerment of women

Search strategy and selection criteria

Estimates of the efficacy or effectiveness of interventions either were taken from the most recent meta-analysis, or were calculated by the authors. We searched for both published and unpublished literature. We searched electronic reference libraries including the Cochrane library, ExtraMed, WHO Reproductive Health Library, Food and Nutrition Library, and PubMed. To retrieve reports of controlled trials, we searched for: "(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR ("clinical trial" [tw]) OR ((singl* [tw] OR doubl* [tw] OR trebl* [tw] OR tripl* [tw]) AND (mask* [tw] OR blind* [tw])) OR ("latin square" [tw]) OR placebos [mh] OR placebo* [tw] OR random* [tw] OR research design [mh:noexp] OR comparative study [mh] OR evaluation studies [mh] OR follow-up studies [mh] OR prospective studies [mh] OR cross-over studies [mh] OR control* [tw] OR prospectiv* [tw] OR volunteer* [tw]) NOT (animal [mh] NOT human [mh])".

We reviewed evidence from randomised controlled trials, where available, but supplemented these with non-randomised and observational studies. Review groups assessed each study on a standardised rating scale according to its study design, size, execution, and data quality.[6] We identified unpublished literature by contacting experts and agencies that work on undernutrition and searching available information on agency websites. We also included studies from the bibliographies of retrieved publications. Two different reviewers independently rated large-scale nutrition programmes. Criteria included external assessment of the programme, adequacy of the description of the intervention and its implementation, presentation of methods in sufficient detail, appropriateness of the assessment design for the nature of the intervention, adequacy of the sample size, and appropriateness of the statistical analyses for the type of outcome measures and clustering. Other criteria included plausibility, alternative explanations for discarded results, peer review, and design or analytic strategies used to rule out or minimise selection bias.

We have therefore aimed in this Series[1] to estimate the effects of undernutrition, including intrauterine growth restriction, on childhood death and disability outcomes. We have also investigated the effects of intrauterine growth restriction and patterns of growth in early childhood on disease and human capital in adulthood.[4]

Sufficient evidence for implementation in all 36 countries	Evidence for implementation in specific, situational contexts
Maternal and birth outcomes	
Iron folate supplementation	Maternal supplements of balanced energy and protein
Maternal supplements of multiple micronutrients	Maternal iodine supplements
Maternal iodine through iodisation of salt	Maternal deworming in pregnancy
Maternal calcium supplementation	Intermittent preventive treatment for malaria
Interventions to reduce tobacco consumption or indoor air pollution	Insecticide-treated bednets
Newborn babies	
Promotion of breastfeeding (individual and group counselling)	Neonatal vitamin A supplementation
	Delayed cord clamping
Infants and children	
Promotion of breastfeeding (individual and group counselling)	Conditional cash transfer programmes (with nutritional education)
Behaviour change communication for improved complementary feeding*	
Zinc supplementation	Deworming
Zinc in management of diarrhoea	Iron fortification and supplementation programmes
Vitamin A fortification or supplementation	Insecticide-treated bednets
Universal salt iodisation	
Handwashing or hygiene interventions	
Treatment of severe acute malnutrition	

*Additional food supplements in food-insecure populations.

Table 1: **Interventions that affect maternal and child undernutrition**

In addition to these anthropometric measures of undernutrition, globally 10% of deaths and disability-adjusted life-years (DALYs) in children younger than 5 years are attributable to micronutrient deficiencies, with nearly all this burden due to deficiencies of vitamin A and zinc. These calculations incorporate the documented effects of undernutrition on maternal and child mortality and morbidity, but do not include the possible contribution of intrauterine growth restriction or altered growth in early childhood to obesity and non-communicable diseases in adults.[4]

We aimed to estimate the reduction in deaths related to stunting and lost DALYs that could result from implementation of interventions in the 36 countries in which 90% of the world's stunted children live. We also estimated the effects of these interventions on maternal deaths and DALYs in the same countries. We reviewed all nutrition-related interventions that could affect selected nutritional outcomes or survival in mothers and children, and used a cohort model to determine the potential effect of delivering the selected interventions at high coverage to populations in need in these 36 countries.

We selected interventions on the basis of the conceptual framework outlined in the first paper in this Series.[1] We excluded several important interventions that might have broad and long-term benefits, such as education, untargeted economic strategies or those for poverty alleviation, agricultural modifications, farming subsidies, structural adjustments, social and political changes, and land reform. Although the well-known associations between humanitarian emergencies, conflict and population displacement, and undernutrition[5] underlie the burden of undernutrition in some of the 36 countries, we aimed to discuss possible intervention effects in national populations, rather than those in special circumstances of crisis.

We selected interventions that principally affect nutrition outcomes or affect morbidity and mortality through a nutritional pathway (see search strategy).[6] For major nutritional and related interventions we did primary reviews of intervention studies and undertook meta-analyses of the evidence whenever possible. We used any relevant and recent systematic reviews that were available, to estimate effects. We reviewed evidence for specific interventions that might improve maternal and child nutritional status, including breastfeeding, complementary feeding, provision of food supplements, micronutrient interventions, supportive nutrition strategies, and large-scale nutrition programmes. We also reviewed and analysed large-scale nutrition programmes, to derive estimates of population effect, achievable coverage levels, and sustainability. We developed a consensus evaluation matrix, and two independent investigators assessed effects and achievable coverage rates for all programmes on a rating scale.

Global review of interventions

Table 1 summarises the evidence for effectiveness of the interventions and feasibility of their implementation. For one group of interventions, evidence was sufficiently robust to recommend their use in most countries with high burdens of undernutrition; the rest will be relevant in some but not all contexts. Table 2 lists other interventions that we either judged to be outside the scope of our review or for which evidence was lacking. Webtables 1–3 show interventions that have been shown to affect stunting, and other nutrition-related interventions that are not mediated through stunting reduction but that do affect maternal and child health outcomes. Tables 3, 4, 5, and 6 present evidence for interventions that increase nutrient intake in general, specifically address micronutrient intake, reduce the burden of infections (and hence affect nutritional status), or are general nutritional supportive measures,, respectively. Tables 7, 8, 9, and 10 show the effects of these interventions on target age-groups.

Interventions to improve general nutrient intake (quality and quantity)

Balanced energy and protein supplements during pregnancy

We reviewed 13 studies and a systematic review[7] which included six studies with information on size at birth (table 3 and table 7). The systematic review was heavily weighted towards a large Gambian study that targeted pregnant women of low body-mass index with supplements of more than 700 kcal per day.[31] The pooled estimate showed that this strategy reduced the risk of a small-for-gestational age baby (which we took to indicate intrauterine growth restriction) by 32% (relative risk 0·68, 95% CI 0·56–0·84).

Breastfeeding promotion

Breastfeeding has already been shown to reduce mortality in infants and young children.[1,32,33] We used estimates of the effect of breastfeeding on mortality risk from this Series.[1] Since initiation of breastfeeding was almost universal in our target countries, we excluded interventions that aimed to achieve this. Epidemiological evidence suggests that beginning breastfeeding within the first day after birth lowers mortality even in exclusively breastfed infants.[34] We have not investigated improvements in the timing of initiation, since just one study had data on delayed timing, and we did not identify any evidence for interventions to improve timing.

See Online for webtables 1–3

We assessed the effect of promotion strategies on exclusive breastfeeding rates for infants younger than 6 months and on continued breastfeeding up to 12 months of age. A Cochrane review[8] that analysed 34 trials (with 29 385 mother–infant pairs from 14 countries) showed that

Interventions with insufficient or variable evidence of effectiveness	Interventions for which evidence showed little or no effect	Interventions that were not reviewed
Maternal and birth outcomes		
Maternal vitamin A supplements	Nutritional education and advice	Unconditional cash transfers and microcredit programmes
Fortification of water with iodine	Zinc supplements in pregnancy	Agricultural subsidies and land reform
Maternal mental-health interventions	Pyridoxine supplements in pregnancy	Rest during pregnancy
Family-planning interventions to promote birth spacing	Fish oil supplements	Food-for-work programmes and generalised food subsidies
Dietary diversification strategies	Maternal vitamin D supplements	
Newborn babies		
Neonatal vitamin K dosing	Mass-media promotion of breastfeeding	
Baby-friendly hospital initiatives		
Infants and children		
Dietary diversification strategies, small animal husbandry, and home gardening	Growth monitoring	
Iodine supplements	Vitamin D supplements	
Cooking in iron pots	Preschool feeding programmes	

Table 2: **Interventions that might affect maternal and child undernutrition**

	Evidence reviewed	Estimates used to model effect on DALYs	Interventions
Balanced supplements of energy and protein in pregnancy	Systematic review of RCTs[7]	National implementation in urban or rural locations, in which >10% of pregnant women have a body-mass index <18·5 kg/m², assumed to reduce the risk of term intrauterine growth restriction by 32% (RR 0·68)	Optional
Educational and promotional strategies for breastfeeding	RCTs and one systematic review[8] for effect on breastfeeding patterns (webappendices 1 and 2) Observational studies for effect of breastfeeding on mortality	Universal implementation assumed to improve breastfeeding practices up to 12 months of age and reduce risk of death; to increase odds of exclusive breastfeeding under 1 month of age (OR 4·0); increase odds of exclusive breastfeeding between 1 and 6 months of age (OR 3·5) increase odds of breastfeeding between 6 and 12 months of age (OR 1·6); and cause no change beyond 12 months	Core
Complementary feeding support and educational strategies, without food supplements or conditional cash transfers	Systematic review of RCTs (webappendices 3 and 4)	Implementation in populations with sufficient food assumed to increase linear growth (and thus reduce odds of stunting and subsequent risk of death) and, if between age 6 and 18 months, to increase height by 1·14 (SE 0·56) cm at 18 months	Core
Complementary feeding support, including education, with food supplements or conditional cash transfers	Systematic review of RCTs (webappendices 3 and 4)	Implementation in populations with insufficient food assumed to increase linear growth (and thus reduce odds of stunting and subsequent risk of death) and, if between age 6 and 36 months, to increase height by 3·6 (SE 1·11) cm at 36 months	Core
WHO-recommended case management of severe acute malnutrition	RCTs and observational studies (webappendix 5)	Assumed to reduce deaths due to severe acute malnutrition by 55% with facility-based management of malnutrition	Core

RCT=randomised controlled trial. RR=relative risk. OR=odds ratio. DALYs=disability-adjusted life-years.

Table 3: **Evidence for interventions to increase general nutrient intake (quality and quantity, including food supplements) (see webappendices 1–5)**

	Evidence reviewed	Estimates used to model effect on DALYs	Interventions
Food fortification strategies and programmes (including iodised salt, iodisation of water, and fortification with iron and vitamin A)	Few RCTs, many observational studies (webappendices 6 and 7)	Iodised salt assumed to reduce the risk of iodine deficiency and the DALYs associated with iodine deficiency by 41% in children. Iron fortification assumed to reduce the odds of iron-deficiency anaemia in children by 28% (OR 0·72) and thus a similar relative reduction in years of life lived with disability but no effect on mortality (years of life lost)	Optional
Supplementation with iron folate or iron	Systematic review of RCTs[9,10] (webappendix 8)	Assumed to reduce the risk of anaemia, and hence to reduce risk of maternal death by 23%	Optional
Multiple micronutrient supplements in pregnancy	Systematic review and recent studies (nine RCTs)	Assumed to reduce intrauterine growth restriction by 14%, and hence modelled	Optional
Dispersible micronutrient preparations for home fortification	Systematic review of RCTs and observational studies (webappendix 9)	Not modelled at present	Optional
Vitamin A supplementation	Systematic review of RCTs (webappendices 10 and 11)	Assumed to have no effect on stunting but to reduce the risk of mortality by 12% (one dose) and 22% (two doses) in children aged 6–59 months; neonatal supplementation of children in Asia assumed to reduce mortality by 21% between 2 days and 6 months	Core
Zinc supplementation (preventive and therapeutic)	Four systematic reviews[11–14] (webappendix 12)	Preventive zinc supplementation assumed to reduce both stunting and mortality directly from 6 months onwards, to reduce mortality risk by 9%, and to reduce the odds of stunting by 15% in each age-group	Core
Maternal calcium supplementation	One systematic review[15]	Potential maternal intervention which might impact health outcomes	Core
Delayed cord clamping	Three systematic reviews[16–18]	Implementation as part of the anaemia-reduction package to address iron-deficiency anaemia in infancy; not modelled at present	Optional
Cooking in iron pots	Three RCTs and one systematic review[19–23]	Possible implementation as part of the anaemia-reduction package to address iron-deficiency anaemia where fortification is not possible; not modelled at present	Optional

RCT=randomised controlled trial. OR=odds ratio. DALYs=disability-adjusted life-years.

Table 4: **Evidence for vitamin and mineral interventions (see webappendices 6–12)**

See Online for webappendices 1–12

all forms of extra support increased the duration of "any breastfeeding" (including partial and exclusive breastfeeding); the relative risk (RR) for stopping any breastfeeding before 6 months was 0·91 (95% CI 0·86–0·96). All forms of extra support together affected the duration of exclusive breastfeeding more strongly than the likelihood of any breastfeeding (RR 0·81, 0·74–0·89). Lay and professional support together extended the duration of any breastfeeding (RR before 4–6 weeks 0·65, 0·51–0·82; RR before 2 months 0·74, 0·66–0·83). We also reviewed specific breastfeeding promotion studies (table 3), and showed that, with individual counselling, the odds of exclusive breastfeeding were substantially increased in the neonatal period (15 studies; odds ratio [OR] 3·45, 95% CI 2·20–5·42, p<0·0001; random effects) and at 6 months of age (nine studies; 1·93, 1·18–3·15, p<0·0001).[35–55] Group counselling increased the odds of exclusive breastfeeding in the neonatal period, (six studies; 3·88, 2·09–7·22, p<0·0001; random effects) and at 6 months of age (five studies; 5·19, 1·90–14·15, p<0·00001; random effects).[55–63] An assessment of a national mass-media campaign in Honduras reported that it increased exclusive breastfeeding from 48% to 70% at 1 month, from 24% to 31% at 4 months, and from 7% to 12% at 6 months of age.[64] Although our

	Evidence reviewed	Estimates used to model effect on DALYs	Interventions
Malaria prophylaxis and intermittent preventive treatment for malaria in pregnancy and children	A systematic review of RCTs[24]	Assumed to reduce the risk of term intrauterine growth restriction by 43% in babies born to the first or second pregnancy of women in areas where malaria is endemic	Optional
Insecticide-treated bednets	A systematic review of RCTs[25]	Implementation for all pregnant women in malaria-endemic areas. We did not model effects other than intermittent preventive treatment	Core
Hygiene interventions (hand washing, water quality treatment, sanitation and hygiene)	Three systematic reviews[26–28] (webappendix 13)	Assumed to reduce the incidence of diarrhoea by 30% and hence to reduce the odds of stunting, with each additional episode of diarrhoea assumed to increase the odds of stunting by 4% (OR 1·04). The direct effect of hand washing on preventing deaths due to diarrhoea was not modelled	Core
Deworming in pregnancy and childhood	Three studies (webappendix 14) and a systematic review of RCTs[29]	Implementation in areas with high rates of soil helminths; effect not modelled	Optional
Probiotics	One systematic review[30] (Unpublished data from REB and colleagues, 2007)	Not modelled since corrected pooled effect estimates were not significant. Potential future intervention for reduction of diarrhoea burden	Optional

RCT=randomised controlled trial. OR=odds ratio. DALYs=disability-adjusted life-years.

Table 5: **Evidence for disease prevention strategies (see webappendices 13 and 14)**

	Evidence reviewed	Estimates used to model effect on DALYs	Interventions
Conditional cash transfers	Six case studies, mostly observational data were reviewed (webappendix 15)	Modelled as a support for complementary feeding interventions in food insecure populations; maternal effects not modelled	Optional
Dietary diversification strategies including home gardening, livestock and dietary modifications	29 studies and two systematic reviews (webappendix 16)	Not modelled; potential intervention in appropriate settings	Optional

RCT=randomised controlled trial. OR=odds ratio. DALYs=disability-adjusted life-years.

Table 6: **Evidence for general nutrition strategies (see webappendices 15 and 16)**

search did not return any trials of the effectiveness of additional strategies, such as the baby-friendly hospital initiative, community-based strategies for breastfeeding promotion should be integrated with such additional health-system support strategies.

Despite the large number of studies of the effect of interventions to promote breastfeeding on rates of breastfeeding, the few that assessed nutritional status did not prove that they increased the weight or length of infants (table 3). The exclusively breastfed children in the WHO Growth Reference Study were, on average, 360 g and 100 g heavier at 4 and 6 months than were the predominantly non-breastfed children on whom the US National Center for Health Statistics growth curves were based.[65] Non-breastfed children gain more weight than do breastfed children at 6 months and older, although their median length gains are similar.

Evidence has shown that HIV-free survival at 7 months does not differ for HIV-exposed infants who were breastfed and those who were fed formula from birth,[66,67] and that exclusive breastfeeding reduces HIV transmission compared with partial breastfeeding.[66,68] Therefore, we have included exclusive breastfeeding as an essential intervention for infants younger than 5·9 months across all populations, with continued breastfeeding thereafter. Studies are underway to find out whether HIV-positive mothers of uninfected infants should stop breastfeeding early to prevent late postnatal transmission. Preliminary results from a randomised trial have shown that HIV-free survival did not differ in infants who were HIV-negative at 4 months and were abruptly weaned or continued to be breastfed.[69]

See Online for webappendices 13–16

Complementary-feeding support nutritional education

A previous review of complementary-feeding strategies concluded that appropriately designed interventions can have a positive effect on feeding practices.[70] We reviewed the effect of complementary-feeding strategies on growth and micronutrient status and did additional meta-analyses on linear growth at various ages (table 3). Of the 307 studies, 42 met our inclusion criteria. We analysed ten studies that had measured similar outcomes, and pooled data according to whether or not the target population had an average income of more than US$1 per day per person (as a measure of food security). In three studies, nutritional education in food-secure populations[71–73] produced an increase in height-for-age *Z* score of 0·25 (95% CI 0·01–0·49), compared with the control group. Pooled analysis of seven studies in food-insecure populations showed that height-for-age *Z* score increased by a weighted mean difference of 0·41 (0·05–0·76) in the group given food supplements (with or without education) compared with controls.[74–80] However, concerns about the overall effect size and very high energy intake in one supplementation trial have been raised.[80] Although these studies were in diverse populations, and with age-groups and follow-up periods that varied, they showed that education strategies alone

	Prenatal and antenatal*	Neonates (0–1 month)†	Infants (1–12 months)	Children (12–59 months)
Balanced energy protein supplementation in pregnancy	32% reduction in term intrauterine growth restriction births (RR 0·68, 95% CI 0·56–0·84). 45% reduction in the risk of stillbirths (RR 0·55, 0·31–0·97)			
Educational and promotional strategies for breastfeeding		Exclusive breastfeeding in the neonatal period· Group counselling increased odds of exclusive breastfeeding in the neonatal period by a factor of 3·88 compared with routine care (95% CI 2·09–7·22, p<0·0001; random effects). Individual counselling increased odds of exclusive breastfeeding in the neonatal period by a factor of 3·45 compared with routine care (2·20–5·42, p<0·00001; random effects). An assessment of national mass-media campaign in Honduras reported that exclusive breastfeeding increased from 48% to 70% at 1 month	Effect of breastfeeding on growth negligible at 6 months. Group counselling increased odds of breastfeeding by a factor of 5·19 compared with routine care (95% CI 1·90–14·15, p<0·00001; random effects). Individual counselling increased odds of breastfeeding by a factor of 1·93 at 6 months compared to routine care (1·18–3·15, p<0·00001) random effects. An assessment of national mass-media campaign in Honduras reported that breastfeeding increased from 24% to 31% at 4 months and from 7% to 12% at 6 months	Effects on growth negligible. No evidence of effect of breastfeeding promotion on rates of breastfeeding beyond 12 months
Complementary feeding support and educational strategies, without food supplements or conditional cash transfers			Reduced stunting. In food-secure populations educational intervention vs control: height-for-age *Z* score WMD 0·25 (95% CI 0·01–0·49; random effects)	
Complementary feeding support, including education with food supplements or conditional cash transfers			Reduced stunting. In food-insecure populations, provision of complementary food with or without education: height-for-age *Z* score WMD 0·41 (0·05–0·76; random effects)	
WHO-recommended case management of severe acute malnutrition			Reduced mortality (case-fatality rate RR 0·45, 0·32·0·62; random effects)	

*Includes interventions focusing on mothers and their effects on maternal and child health. †Includes interventions in the neonatal period of life. WMD=weighted mean difference.

Table 7: **Effect of interventions to increase general nutrient intake on target age-groups**

were of most benefit in populations that had sufficient means to procure appropriate food.[71–73] In populations without this security, educational interventions were of benefit when combined with food supplements.[74–80] In food-secure populations, the strongest evidence of effect was seen from the interventions in China[71] and Peru.[72] The benefits on growth from food supplementation in food-insecure populations were consistent with those seen with large-scale conditional cash transfer programmes in similar populations in Mexico and Nicaragua.[81,82] These programmes combined cash transfers and nutritional education, and one also included a supplementary food fortified with multiple micronutrients.[81] We thus estimated the effect of complementary feeding strategies in various contexts and age-groups by combining the information from the pooled analysis of experimental studies and the assessment of the *Progresa* programme in Mexico.[81]

Management of childhood severe acute malnutrition

Of 276 articles on the management of severe acute malnutrition, 21 studies had appropriate experimental designs and outcomes (table 3). To assess the efficacy of the WHO guidelines for facility-based management of children with severe acute malnutrition, we were able to pool nine studies, which gave a summary risk ratio of 0·45 (95% CI 0·32–0·62; random effects) compared with conventional treatment.[83–89] Community management of severe acute malnutrition with ready-to-use therapeutic foods has been shown to induce weight gain in emergency settings and has been recommended by WHO, UNICEF, and the UN World Food Programme.[90] We could not find any randomised trials that had investigated the effect of ready-to-use therapeutic foods on mortality. However, observational data from field programmes suggest that management of severe malnutrition at home with preprepared balanced food can achieve high coverage and low case fatality (table 7). The overall case-fatality rate in 23 511 unselected severely malnourished children treated in 21 programmes of community-based therapeutic care in Malawi, Ethiopia, and Sudan, between 2001 and 2005, was 4·1%, with a recovery rate of 79·4% and default of 11·0%.[91,92] This compares favourably with case-fatality rates that are typically achieved with facility-based management. However, this comparison must be interpreted cautiously since the severity of cases in the facility-based trials and the community-based observational studies might differ. In view of the association of severe acute malnutrition with HIV infection, infected children must also be given antiretroviral therapy. These preventive strategies for

	Prenatal and antenatal*	Neonates (0–1 month)†	Infants (1–12 months)	Children (12–59 months)
Food fortification strategies and programmes (including iodised salt, iodisation of water, and fortification with iron and vitamin A)	Improved micronutrient status (haemoglobin concentration weighted mean difference in women of child bearing age 5·70 g/L, 95% CI 0·02–11·38). In pregnant women, 6·90 g/L higher compared with no fortification (WMD 6·90, 2·74–11·06). Programmes for universal iodisation of salt decreased goitre prevalence by 19–64%. Rate of goitre reduced by 51–89% by iodisation of water	Neonatal mortality reduced by 65·7% after iodisation of water	Improved micronutrient status (haemoglobin concentration WMD 7·36 g/L, 2·88–11·84). Infant mortality decreased 56·5% after iodisation of water	Improved micronutrient status (haemoglobin WMD 7·36 g/L, 2·88–11·84). After 24 months of age, use of fortified foods including milk has improved micronutrient status (WMD 10·33 from a meta-analysis of studies). Additional reduction in diarrhoea morbidity noted in one study. Fortified milk reduced odds for days with severe illnesses by 15% (5–24%), the incidence of diarrhoea by 18% (7–27%), and the incidence of acute lower respiratory illness by 26% (3–43%)
Supplementation with iron folate or iron	Improved micronutrient status (haemoglobin WMD 12 g/L, 2·93–21·07)	Improved micronutrient status (haemoglobin concentration WMD 7.4 g/L, 6·1–8·7) Potential increased risk of death in malarial areas so only recommended for non-malarial areas as a treatment strategy		
Multiple micronutrient supplements in pregnancy	Multiple micronutrient supplementation (defined as supplementation with three or more micronutrients) was associated with 39% reduction in maternal anaemia compared with placebo or two or less micronutrients (relative risk 0·61, 95% CI 0·52–0·71)	Multiple micronutrient supplementation *vs* iron folate results in a significant reduction in the risk of low birthweight births (relative risk 0·84, 0·74–0·95)	A recent study in Indonesia of multiple micronutrient supplementation versus iron-folate tablets in over 31 000 women was also associated with a 22% reduction in infant mortality (relative risk 0·78, 0·64–0·95)	
Dispersible micronutrient preparations for home fortification			Use in untargeted children results in a significant effect on haemoglobin level (WMD 5·68, 1·78–9·57) and iron-deficiency anaemia (relative risk 0·54, 0·42–0·70) random effects compared with placebo	
Vitamin A supplementation	No effect on low birthweight in HIV-negative populations, some effect in HIV-positive populations	Reduced mortality between 0–6 months (relative risk 0·80, 0·66–0·96)	Reduced disease burden (reduction in persistent diarrhoea rate ratio 0·45, 0·21–0·94). Reduced mortality (relative risk 0·76, 0·69–0·84). Effect usually between 6–11 months of age	
Zinc supplementation (preventive and therapeutic)	No evidence of benefit except for small reduction in prematurity rates	No evidence of benefit	No evidence of benefit of therapeutic zinc supplementation under 6 months of age. For older children, fewer episodes of diarrhoea (rate ratio 0·86, 0·79–0·93), severe diarrhoea or dysentery (0·85, 0·75–0·95), persistent diarrhea (0·75, 0·57–0·98). Reduced stunting (weighted average effect size for change in height 0·35, 0·19–0·51). Reduced mortality (risk ratio 0·91, 0·82–0·99)	
Maternal calcium supplementation	Reduced risk of pre-eclampsia (relative risk 0·48, 0·33–0·69). The effect was greatest for high-risk women (0·22, 0·12–0·42), and those with low baseline calcium intake (0·36, 0·18–0·70). The composite outcome maternal death or serious morbidity was reduced (0·80, 0·65–0·97)			
Delayed cord clamping		Improved iron status (mean neonatal packed-cell volume at 24–48 h WMD 10·01%; 4·10–15·92). Anaemia at 24–48 h after birth (relative risk 0·20, 0·06–0·66)	Anaemia at 2–3 months (relative risk 0·53, 0·40–0·70)	
Cooking in iron pots				Iron pot group (after 8–12 months) had higher haemoglobin (13 g/L) than non-iron pot group (p<0·05)

*Includes interventions focusing on mothers and their effects on maternal and child health. †Includes interventions in the neonatal period of life. WMD=weighted mean difference.

Table 8: **Effect of vitamin and mineral interventions on target age-groups**

severe acute malnutrition ought to be formally assessed in representative populations. Observational studies show that use of preprepared balanced foods such as spreads and ready-to-use supplementary foods is feasible in community settings.

Micronutrient interventions

Although several of the interventions we reviewed affect food choice, nutritional quality, and micronutrient intake, we separately reviewed other interventions that specifically target micronutrient intake and status (table 4 and table 8).

Food fortification with micronutrients

In addition to information provided by the Micronutrient Initiative (Mannar V, Micronutrient Initiative, Ottawa, personal communication, 2006), and a review of zinc-fortification strategies (Hess SY and Brown KH, International Zinc Nutrition Consultative Group, Dakar, Senegal, personal communication, 2007), we assessed the evidence for food-fortification strategies (table 3). This work was complemented with the results from a forthcoming meta-analysis of 21 studies of iron-fortification strategies (HPS and colleagues).

	Prenatal and antenatal*	Neonates (0–1 month)†	Infants (1–12 months)	Children (12–59 months)
Malaria prophylaxis and IPT for malaria in pregnancy and children	Women in their first or second pregnancy, mean birthweight was higher in those in the two-dose IPT with SP group (WMD 108·60 g; 55·67–161·54), and low birthweight births were reduced (relative risk 0·63, 0·47–0·84). Maternal anaemia during third trimester or at delivery reduced by 12% (0·88; 0·84–0·93)		IPT results in 46% reduction in risk of severe anaemia (relative risk 0·54, 0·42–0·68). IPT results in 48% reduction in risk of clinical malaria, from the age of 2 months (0·52, 0·35–0·77; random effects)	
Insecticide-treated bednets	Pooled estimates indicated a 23% reduction in risk of delivering a low birthweight infant (relative risk 0·77, 0·61–0·98), equivalent to a reduction in odds of term low birthweight of 43%			
Hygiene interventions (hand washing, water quality treatment, sanitation, and hygiene)			Significant decrease in diarrhoea (hand washing *vs* control: relative risk 0·70, 0·56–0·89; random effects). Multiple interventions also had similar effects on diarrhoea (0·67, 0·59–0·76), severe diarrhoea and dysentery (0·68, 0·62–0·74)	
Deworming in pregnancy and childhood	Improved micronutrient status (mean decline in haemoglobin between first and third trimester was 6·6 g/L less compared with placebo)		Improved micronutrient status (haemoglobin WMD 1·71 g/L, 0·70–2·73). Increase in height with a single dose was 0·14 cm (0·04–0·23). A single dose was associated with an average 0·24 kg increase in weight (0·15–0·32). For multiple doses, the increase was 0·10 kg (0·04–0·17) for up to 1 year of follow-up. 5–10% reduction in rates of anaemia in populations with high rates of intestinal helminthiasis	
Probiotics			Probiotics led to 57% reduction in the risk of diarrhoea in children, (risk ratio 0·43, 95% CI 0·29–0·65). Corrected proportional effect RR 0·8 (95% CI 0·64–1·01)	

*Includes interventions focusing on mothers and their effects on maternal and child health. †Includes interventions in the neonatal period of life. IPT=intermittent preventive treatment. SP=sulphadoxine-pyrimethamine. WMD=weighted mean difference.

Table 9: **Effect of disease prevention strategies on target age-groups**

	Prenatal and antenatal*	Neonates (0–1 month)†	Infants (1–59 months)
Conditional cash transfers	No effect estimates available	No effect estimates available	Reduced stunting. Increase in height on average 0·44 cm for children aged 0–12 months (*PFA* in Colombia). An increase of 16 % in mean growth rate per year corresponding to 1 cm increase in height per year. Reduced prevalence of stunting by 10% in 12–36 months age group (*Progresa* in Mexico). Decline in stunting from 41·9% to 37·1% over 2 years (*Red de Protección Social* in Nicaragua)
Dietary diversification strategies including home gardening, livestock, and dietary modifications	No effect estimates available	No effect estimates available	Improved haemoglobin concentration (107 *vs* 102 g/L; p<0·01). Improved serum retinol WMD 0·12 (95% CI 0·07–0·17)

*Includes interventions focusing on mothers and their effects on maternal and child health. †Includes interventions in the neonatal period of life. WMD=weighted mean difference. *PFA*=*Programa Familias en Acción*.

Table 10: **Effect of general nutrition support strategies on target age-groups**

22 studies assessed the effect of fortification of various commodities, such as condiments, milk, and commercial foods, with iron alone or with other micronutrients. Of these studies, only six assessed iron as a single micronutrient supplement. Two studies assessed iron fortification as a single micronutrient intervention in women of childbearing age[93,94] and showed that it increased haemoglobin concentrations, with a weighted mean difference of 5·70 (95% CI 0·02–11·38) g/L. The only study[95] to assess iron fortification in pregnant women also showed a 6·90 (2·74–11·06) g/L increase in haemoglobin. No studies investigated iron fortification in children younger than 5 years, but we estimated that haemoglobin concentrations were 7·36 (2·88–11·84) g/L higher in the intervention group than in the control group from three studies that assessed iron-only fortification in school-aged children, together with a 70% reduction in the prevalence of anaemia (two studies; relative risk 0·30, 95% CI 0·17–0·51).[96–98] Beyond 12 months of age the use of foods fortified with micronutrients (generally iron and other micronutrients including zinc) has shown benefits[99] (eg, the *Progresa* programme in Mexico[81] showed reduced anaemia rates in toddlers). A recent study in India also showed that milk fortified with zinc and iron reduced the odds for days with severe illnesses by 15% (95% CI 5–24), for the incidence of diarrhoea by 18% (7–27), and for the incidence of acute lower respiratory illness by 26% (range 3–43).[100]

Fortification of various commodities, including sugar, cooking oils, and monosodium glutamate with vitamin A has been tried in an effort to increase intake. A randomised controlled trial of commercially marketed fortified monosodium glutamate[101] showed that mortality in children aged 6–49 months was reduced by about 30%; these results were consistent with findings from other trials that used capsules.[102] Evidence for the effectiveness of these efforts is scarce, apart from large-scale sugar fortification programmes in Central America, where assessments have shown high rates of coverage (eg, fortified sugar contributes over half the daily intake of vitamin A in toddlers in Guatemala).[103,104]

Available data on salt iodisation programmes included several historical studies and survey data; eight studies of salt iodisation from seven countries and one supranational region (of 13 countries); and eight studies on water iodisation interventions (table 4). Although data specific to women of reproductive age and to children were not available, large-scale use of iodised salt was associated with a reduction of 19–64% in the occurrence of goitre.[105–112] Four studies of water iodisation showed that the occurrence of goitre was reduced by 51–89%.[113–116]

With the exception of iodised salt, the evidence for benefits of fortification strategies on micronutrient status in young children is weak; there are very few studies in children younger than 36 months. An assessment of fortification of maize with high-dose sodium iron edetic acid in children aged 3–8 years in Kenya[117] reported an 89% reduction in iron-deficiency anaemia (95% CI 49–97).

Supplementation with iron folate or iron

A pooled analysis of data from eight studies of iron-folate supplementation during pregnancy suggested an increase of 12 g/L (95% CI 2·93–21·07, random effects) in haemoglobin at term and a 73% reduction in the risk of anaemia at term (relative risk 0·27, 95% CI 0·12–0·56).[9] Of a potential 147 studies on the effect of iron supplementation on haemoglobin concentration in children, we included 55 (table 4).[10] Iron supplementation was seen to result in a haemoglobin concentration that was 7·4 g/L higher than in children who had no supplementation (weighted mean difference 7·4 g/L, 95% CI 6·1–8·7; random effects). Reductions in the occurrence of anaemia with iron supplementation alone ranged from 38% to 62% in non-malarial regions and 6% to 32% in malarial hyperendemic areas. The incidence of diarrhoea was increased in the iron-supplemented group (incidence rate ratio 1·11, 95% CI 1·01–1·23; random effects), and overall we noted no benefit of iron supplementation on growth. A study in Zanzibar was stopped prematurely because of increased rates of hospital admission and death in children who were given iron, although severe adverse events (mostly hospital admissions) were reduced by 49% when iron was provided together with adequate management of malaria.[118] A recommendation that untargeted iron supplementation should not be given to children in malaria-endemic areas was prompted by this trial and others that showed that iron supplementation has adverse effects with regard to infectious diseases.[119]

Dispersible micronutrient preparations

An alternative strategy for providing dispersible micronutrients is through sachets that contain iron and other micronutrients in microencapsulated form, which can be added to prepared food as a form of home fortification (table 4). An analysis of studies of these dispersible micronutrient preparations [120–126] showed that, in children younger than 2 years,[123,124] haemoglobin concentrations increased by 5·68 (95% CI 1·78–9·57) g/L and iron-deficiency anaemia was reduced compared with controls (relative risk 0·54, 95% CI 0·42–0·70).

Vitamin A supplementation in mothers and children

Results from trials of vitamin A and betacarotene in pregnancy in Nepal[127] and Bangladesh[128] were inconsistent with respect to their effect on maternal mortality (table 4).[129] However, vitamin A supplementation reduced childhood mortality in children aged 6–59 months,[102,130] with a pooled estimate that showed a 24% reduction in the risk of all-cause mortality (relative risk 0·76, 95% CI 0·69–0·84). Vitamin A supplementation did not affect morbidity from infectious diseases[131–134] or anthropometric measures.

We identified three reported trials of vitamin A supplementation in the neonatal period in low-income countries; they showed a 20% reduction in mortality in babies younger than 6 months (relative risk 0·80, 95% CI 0·66–0·96).[135–137] Recently, another large trial of neonatal vitamin A supplementation in Bangladesh has also been reported.[138] A pooled analysis of all studies from south Asia indicated that neonatal vitamin A supplementation was associated with a 21% reduction in mortality in babies younger than 6 months (random effects relative risk 0·79, 95% CI 0·65–0·96, R Klemm and Keith West; John Hopkins University, USA; personal communication 2007). However, because this beneficial effect has only been shown in Asian populations, we included neonatal vitamin A supplementation as an intervention for that region only.

Zinc supplementation

Although maternal zinc supplementation is associated with reduced prematurity rates (relative risk 0·86, 95% CI 0·76–0·98), it does not affect maternal health indicators, weight gain, or intrauterine growth restriction.[11] The positive effect of zinc supplementation on growth in children has been reviewed elsewhere.[12] A pooled analysis of zinc-supplementation studies in children showed a weighted average effect size for change in height of 0·35 (95% CI 0·19–0·51) and for change in weight of 0·31 (0·18–0·44).

Compared with children given placebo, those who received preventive zinc supplementation had fewer episodes of diarrhoea (rate ratio 0·86, 95% CI 0·79–0·93), severe diarrhoea or dysentery (0·85, 0·75–0·95), persistent diarrhoea (0·75, 0·57–0·98), and lower respiratory

Panel 1: **Cohort model of child mortality and stunting**

To estimate the effect of nutrition-related interventions on the health of children, we modelled the survival and linear growth status of the annual birth cohort of children from birth until 3 years of age in 36 countries with 90% of the global burden of stunted children. Stunting was defined as a height or length-for-age *Z* score of less than –2, according to WHO standards.[182] The first 3 years of life were divided into discrete age-groups between birth and 1, 6, 12, 18, 24, and 36 months. For each age-group we then modelled two outcomes: the risk of death during that period and the odds that a surviving child would be stunted at the end of the period (figure 1).

Within the cohort, the risk of death and odds of stunting were allowed to vary according to the levels of different risk factors (eg, zinc deficiency, non-breastfeeding), one of which was stunting itself. Thus, as well as being an outcome in the model, stunting is a risk factor: being stunted at the end of an age-group increases a child's risk of death during the next age-group or, if they survive, their odds of stunting at the end of the next age-group. We assumed that, within each country and age-group, these exposures could occur independently of each other. In our multiplicative model, this assumption will result in conservative estimates of the effects of interventions. We then arbitrarily chose a baseline group of children (those with a combination of risk factors that put them at lowest risk of death or odds of stunting) and, with data on the current overall risk of death,[183] current odds of stunting (MdO, personal communication), and current prevalence of exposures,[1] we estimated the risk of death and odds of stunting in this baseline group for each country and for each age-group. To model the effect of an intervention from birth to 36 months we reran the model and altered the distribution of the relevant risk factor in the population to reflect the effect of the intervention. From the model outputs we computed the number of deaths averted between birth and age 3 years and the change in the number of surviving children aged 3 years who were stunted. We then calculated the proportion of DALYs averted by the intervention(s), from the assumption that each death of a child represents, on average, about 33·3 DALYs and that each child who survives to 3 years of age but is stunted represents on average 0·23 DALYs.

Tables 11 and 12 detail the mortality risk ratios and stunting odds ratios used in the model. Since a large proportion of neonatal mortality occurs very early, the effects of breastfeeding and neonatal vitamin A supplementation were applied to only 50% of neonatal deaths. We assumed that current coverage of some interventions was close to zero: individual or group counselling on exclusive breastfeeding and continued breastfeeding beyond 6 months, zinc supplementation, neonatal vitamin A supplementation, balanced energy protein supplementation in pregnancy, and individual or group counselling on hygiene practices. We used coverage data for vitamin A supplementation in children aged 6 months and older from UNICEF.

Effects of complementary feeding strategies

We estimated the effect of complementary feeding education strategies in food-secure populations in each of two age-groups: 6–11·9 and 12–17·9 months. No data were available on the effectiveness of such a strategy at older ages. Similarly, we estimated the effect of combined strategies (supplementation with or without education) for food-insecure populations in the same age-group. No data from randomised trials were available for children older than 18 months. However, data from *Progresa* indicated an effect on linear growth of 1 cm per year across the age range 12–36 months.[81] Thus we assumed that beyond 18 months of age (18–36 months of age) such interventions would further increase children's height by 1·5 cm (ie, 1·0 cm per year). Assuming that in national food-secure and food-insecure populations the SD in height-for-age *Z* scores was around 1·4, we converted increases measured in cm to increases in height-for-age *Z* score and hence into reductions in the odds of stunting.

Effect of interventions to improve iron status

We assumed that iron fortification increased children's haemoglobin concentrations by 3·4 g/L. We further assumed, on the basis of data from Demographic and Health Surveys,[184] that the SD of children's haemoglobin concentrations at the national level was about 1·7 g/L. With this SD, an increase in mean haemoglobin of 3·4 g/L would reduce the odds of anaemia by about 28% (odds ratio 0·72). Assuming a current coverage of zero, we calculated the reduction in the prevalence of childhood anaemia that would be achieved by varying levels of fortification coverage, by use of anaemia prevalence estimates provided by WHO (C Mather, personal communication). We applied the relative reduction in anaemia prevalence to the number of under-5 years lived with disability due to iron deficiency to calculate the number of years lived with disability and hence DALYs that could be averted. Note that we assumed no effect on deaths due to iron deficiency in children.
We also assumed that iron and folate supplementation in pregnant women would increase haemoglobin by 12 g/L. From the analysis of Stoltzfus and colleagues,[185] we estimated an increase in haemoglobin of 12 g/L would be associated with a 23% reduction in the risk of maternal mortality (risk ratio 0·77). Taking account of current coverage of interventions to supplement iron and folate and assuming that the effect would increase linearly with coverage, we estimated how many maternal deaths and hence how many DALYs might be averted by increasing coverage with iron and folate supplementation to 70%, 90%, or 99% in all 36 countries.

Effect of interventions to improve iodine status

On the basis of the estimated effect of salt iodisation on goitre prevalence, we assumed that salt iodisation would reduce childhood DALYs due to iodine deficiency by 41%. Taking account of current coverage levels with iodised salt and assuming that the effect would increase linearly with coverage, we estimated how many child DALYs due to iodine deficiency might be averted by increasing coverage with iodised salt to 70%, 90%, or 99% in all 36 countries.

Effect of improved case management of children with severe acute malnutrition

In the absence of data on the effect of community-based management on case-fatality rates and on the effect of other interventions on severe acute malnutrition, we were only able to estimate the effect of applying the WHO protocol for management of severe acute malnutrition. We assumed that implementation of WHO guidelines on hospital-based management of severe acute malnutrition would reduce case fatality by 55% (risk ratio 0·45).

infections (0·80, 0·70–0·92).[13,14] A pooled estimate from meta-analysis of zinc supplementation studies on child mortality[139–144] indicated a 9% reduction in child mortality (0·91, 0·82–0·99, fixed effects). Although studies of zinc in treatment of diarrhoea show a 15–24% reduction in the duration of diarrhoea,[145] the number of episodes of

	Age-group (months)		
	<1	1–5·9	6–35·9
Term low birthweight			
Normal	1·0		
Low birthweight	2·84		
Stunting			
No		1·0	
Yes		2·4	
Breastfeeding			
Exclusive	1·0		
Predominant	1·48		1·0
Partial	2·85		
None	14·4		2·3
Neonatal vitamin A			
Supplemented	1·0		
Not supplemented	1·25		
Post-neonatal vitamin A			
Two doses a year			1·0
One dose a year			1·14
No doses			1·28
Zinc			
Supplemented			1·0
Not supplemented			1·1

Three interventions have an effect on risk of term low birthweight. Balanced energy protein supplementation during pregnancy is assumed to reduce the risk of term low birthweight by 32%. Intermittent preventive treatment (with or without insecticide-treated bednets) is assumed to reduce the risk of term low birthweight by 37% in unprotected women in their first or second pregnancy. Multiple micronutrient supplementation is assumed to reduce the risk of term low birthweight by 16%. The protective effect of breastfeeding is assumed to cease when the child reaches 2 years of age. In children aged 6–23 months the baseline breastfeeding category is breastfed (RR 1·0) vs non-breastfed (RR 2·3). We assume that breastfeeding promotion can increase the odds of exclusive breastfeeding by a factor of 4·0 (OR 4) during the first month of life, and by a factor of 3·5 during months 1–5·9. Between months 6 and 11·9, breastfeeding promotion can increase the odds of breastfeeding by a factor of 1·6. We assume no effect of breastfeeding promotion beyond 12 months of age.

***Table 11:* Mortality risk ratios used in the cohort model of mortality and stunting**

	Age-groups (months)					
	<1	1–5·9	6–11·9	12–17·9	18–23·9	24–35·9
Term low birthweight						
Normal	1·0					
Low birthweight	21·6					
Stunting						
No		1·0	1·0	1·0	1·0	1·0
Yes		12·4	21·4	30·3	41·0	54·1
Feeding						
Secure with promotion			1·0	1·0	NA	NA
Secure without promotion			1·43	1·16	1·0	1·0
Insecure with intervention			1·60	1·16	1·40	1·24
Insecure without intervention			2·39	1·94	1·67	1·67
Diarrhoea						
Effect per episode		1·04				
Zinc						
Supplemented			1·0			
Not supplemented			1·18			

Three interventions have an effect on risk of term low birthweight. Balanced energy protein supplementation during pregnancy is assumed to reduce the risk of term low birthweight by 32%. Intermittent preventive treatment (with or without insecticide-treated bednets) is assumed to reduce the risk of term low birthweight by 37% in unprotected women in their first or second pregnancy. Multiple micronutrient supplementation is assumed to reduce the risk of term low birthweight by 16%. Each episode of diarrhoea is assumed to increase a child's odds of stunting by a factor of 1·04. We assume that hygiene promotion can reduce the incidence of diarrhoea by 30%. NA=not applicable.

***Table 12:* Stunting odds ratios used in the cohort model of mortality and stunting**

diarrhoea, and the rate of lower respiratory infection and deaths, few studies have assessed the benefits of zinc supplementation on nutrition outcomes.

Iodine supplementation

Of 11 trials of iodine supplementation in pregnant women, only two reported our outcomes of interest (table 4).[146,147] These showed that iodine supplements for pregnant mothers reduced deaths during infancy and early childhood by 29% (RR 0·71, 95% CI 0·56–0·90) and decreased the risk of endemic congenital hypothyrodism at age 4 years (0·27, 0·12–0·60). One study of oral iodised oil[148] showed that this intervention was associated with reduced mortality in infants in West Java during the first 2 months of follow-up (0·28, 0·09–0·82, p=0·018). However, we did not include iodine supplementation as a core intervention because epidemiological or individual evidence of severe iodine deficiency in pregnancy is lacking and because universal salt iodisation has largely replaced this intervention in areas of endemic deficiency.

Multiple micronutrient supplementation in pregnancy

To assess the effect of multiple micronutrient supplementation during pregnancy, we did a systematic review and meta-analysis.[149] Supplementation with three or more micronutrients was associated with a 39% reduction in maternal anaemia compared with placebo or with two micronutrients or fewer (relative risk 0·61, 95% CI 0·52–0·71). Multiple micronutrient supplementation also resulted in a decrease in the risk of low-birthweight babies (0·83, 0·76–0·91) and small-for-gestational-age babies (0·92, 0·86–0·99). However, multiple micronutrient supplementation did not differ from iron and folic acid supplementation in terms of rates of low birthweight babies (0·94, 0·8–1.06), or of those who were small for gestational age (1·04, 0·93–1·17). A meta-analysis of trials of supplementation with a specific multiple micronutrient formulation for pregnant women[150] compared with iron and folic acid reported a small increase in birthweight (pooled effect 21·2 g, 95% CI 8·0–34·5). A recent study from Indonesia that compared multiple micronutrients with iron-folate tablets in more than 31 000 women showed that they reduced infant mortality by 22% (relative risk 0·78, 95% CI 0·64–0·95).[151] Two additional trials of multiple micronutrient supplements in pregnancy in India[152] and Tanzania[153] also showed that this intervention reduced the rate of low-birthweight babies. A pooled

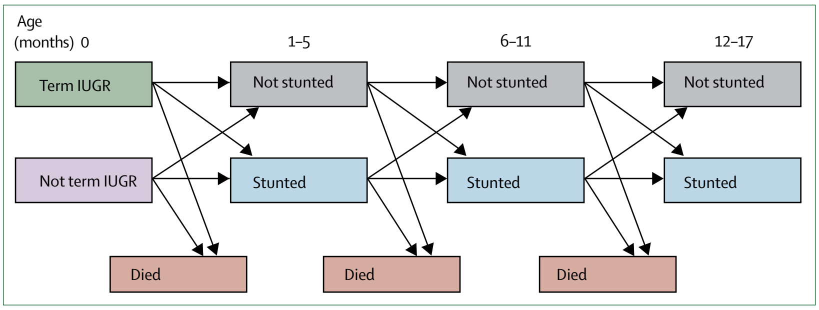

Figure 1: **Schematic presentation of the cohort model of child survival and anthropometric status**
IUGR=intrauterine growth restriction.

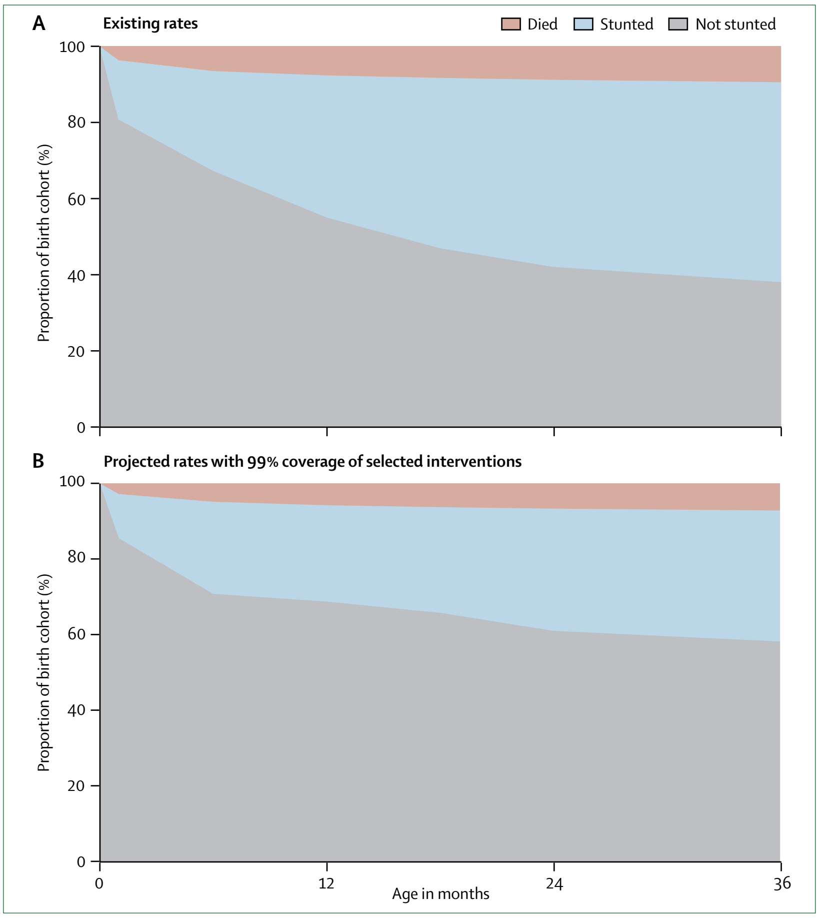

Figure 2: **Mortality and stunting rates (A) from birth to age 3 years in 36 countries, and projected mortality and stunting rates (B) with 99% coverage of selected interventions**

analysis of these data with the results of the Cochrane review showed that multiple micronutrient supplements in pregnancy can reduce the risk of low birthweight by 0·84 (0·74–0·95).

Calcium supplementation in pregnancy

A systematic review[15] of 12 trials, with more than 15 000 participants, that investigated calcium administration in pregnancy reported a reduction in the risk of pre-eclampsia (relative risk 0·48, 95% CI 0·33–0·69). The effect was greatest for women at high risk for hypertensive disorders of pregnancy (five trials, 587 women; 0·22, 0·12–0·42), and those with low baseline calcium intake (seven trials, 10 154 women; 0·36, 0·18–0·70). The composite outcome maternal death or serious morbidity was also reduced (four trials, 9732 women; 0·80, 0·65–0·97).

Delayed umbilical cord clamping

Early cord clamping could cause reduced placental transfusion and hence affect a child's subsequent iron status. Three systematic reviews,[16–18] which included 15 studies, assessed the effect of delayed cord clamping in neonates, as did two more recent studies.[154,155] Most trials defined early cord clamping as clamping immediately after or within 10 s of birth, and delayed clamping as that soon after cessation of cord pulsations or at 3 min after birth. We could not pool data from all trials because of variations in the outcomes measured. Mean neonatal packed-cell volume was higher in neonates with delayed cord clamping at 24–48 h after birth (four trials; weighted mean difference 10·01%, 95% CI 4·10–15·92) and at 5 days (four trials; 11·97%, 8·50–15·45). No evidence of a difference was seen at ages 2–3 months. Risk of anaemia was reduced by 80% at 24–48 h after birth (one study; relative risk 0·20, 95% CI 0·06–0·66) and by 47% at 2–3 months (two trials; 0·53, 0·40–0·70).

Disease prevention strategies

To model the association between infectious diseases and stunting and related DALYs, we focused on interventions that reduce the burden of malaria in pregnancy, and reduce intestinal helminthiasis and diarrhoea during childhood (table 5). Although recurrent respiratory infections could potentially affect growth, we could not find any intervention studies that had assessed this link. Neither did we include the effects of HIV/AIDS, although antiretroviral therapy can dramatically improve growth and nutritional status in affected children.[156,157] Although other chronic disorders, such as asthma and subclinical infections, are also known to cause growth faltering,[158,159] we did not include specific strategies for disease management or treatment strategies because few robust studies have prospectively assessed their effects on nutrition outcomes.

Intermittent preventive treatment for malaria in pregnancy

Four trials compared standard two-dose intermittent preventive treatment (with sulphadoxine-pyrimethamine) with case management or placebo in pregnant women.[24] For women in their first or second pregnancies, mean birthweight was highest for those given intermittent preventive treatment (weighted mean difference 108·60 g, 95% CI 55·67–161·54), and the risk of low birthweight births was also lower (relative risk 0·63, 95% CI 0·47–0·84). Analysis also showed a reduction of 12% in maternal anaemia during the third trimester or at delivery (0·88, 0·84–0·93).

Use of insecticide-treated bednets during pregnancy

Eight studies assessed the use of insecticide-treated bednets during pregnancy[25] and two reported on low birthweight as an outcome.[160,161] Pooled summary estimates indicated that use of insecticide-treated bednets was associated with a 23% reduction in the risk of delivering a baby with low birthweight (relative risk 0·77, 95% CI 0·61–0·98). Although we recognise that this outcome is important, we did not include any additional effect of intermittent preventive treatment on perinatal mortality operating through reduction in rates of prematurity.

Hygiene and sanitation measures

Three reviews assessed the effect of hygiene interventions (eg, handwashing, water quality treatment, sanitation, and health education).[26–28] A pooled analysis of several concurrent interventions, which included data from seven studies[27] in children younger than 5 years suggested a decrease in diarrhoea episodes (pooled estimate of relative risk 0·67, 95% CI 0·59–0·76; random effects). Multiple interventions had similar effects on severe diarrhoea and dysentery (pooled estimate of relative risk 0·68, 0·62–0·74). Pooled analysis of six studies of handwashing counselling (for individuals or groups) suggested a 30% reduction in the risk of diarrhoea (0·70, 0·56–0·89).

Deworming and use of helminthics during pregnancy

Two studies assessed the effect of deworming interventions during pregnancy and reported outcomes of interest (table 5).[162,163] The mean fall in haemoglobin concentration between first and third trimester in women who received albendazole was 6·6 g/L less than in women who received placebo (p=0·003). In a systematic review of 25 studies that assessed the nutritional effect of deworming in children,[29] analysis of growth outcomes in children aged 1–16 years suggested that one dose was associated with an average 0·24 (95% CI 0·15–0·32) kg increase in weight. For several doses, the increase was 0·10 (0·04–0·17) kg for up to 1 year of follow-up. The pooled estimate for increase in height was 0·14 (0·04–0·23) cm for one dose and 0·07 (0·01–0·15) cm for multiple doses up to 1 year of follow-up. Because these effects on linear growth are very small, we did not attempt to model the effects of this intervention. Another systematic review of deworming assessed the effect on haemoglobin and anaemia rates.[164] The pooled weighted mean difference (random effects model) of the change in haemoglobin was 1·71 (0·70–2·73) g/L (p<0·001) and the average estimated reduction in frequency of anaemia ranged from 1·1% to 12·4% in adults and from 4·4% to 21·0% in children. These effects, although small, could translate into a 5–10% reduction in rates of anaemia in populations with high rates of intestinal helminthiasis.

General nutrition support strategies

We assessed interventions that affect dietary quality through improved purchasing power for families and dietary diversification strategies through home gardening and livestock farming (table 6). Available evidence on growth monitoring[165–167] was not sufficient to support its use alone (without adequate nutrition counselling and referrals) as an essential nutrition support. Although the effects of family planning and birth spacing on maternal health[168] and child survival have been recognised,[169] rigorous assessment of the evidence revealed many confounding factors.[170] Observational studies of birth spacing[171] suggest that interpregnancy intervals of less than 6 months are associated with increases in the risk of small-for-gestational-age births (adjusted OR 1·26, 95% CI 1·18–1·33), but we did not include this intervention in our repertoire. In populations with high fertility rates, repeated pregnancies might cause maternal undernutrition and morbidity[172] and although objective data from intervention studies are scarce, family planning could help to reduce maternal undernutrition and intrauterine growth restriction.

Conditional cash transfers

We assessed six programmes, mainly from Latin American countries, that paid families in return for an action such as vaccination of children.[81,82,173–175] Overall, the programmes showed an improvement in care seeking and an associated increase in the value of total household consumption of goods and services (table 6). In Mexico, the *Progresa* programme, which combined conditional cash transfers with nutritional education and micronutrient-fortified food supplements,[81] resulted in an extra 1 cm increase in height per year, which translated into a 10% reduction in the prevalence of

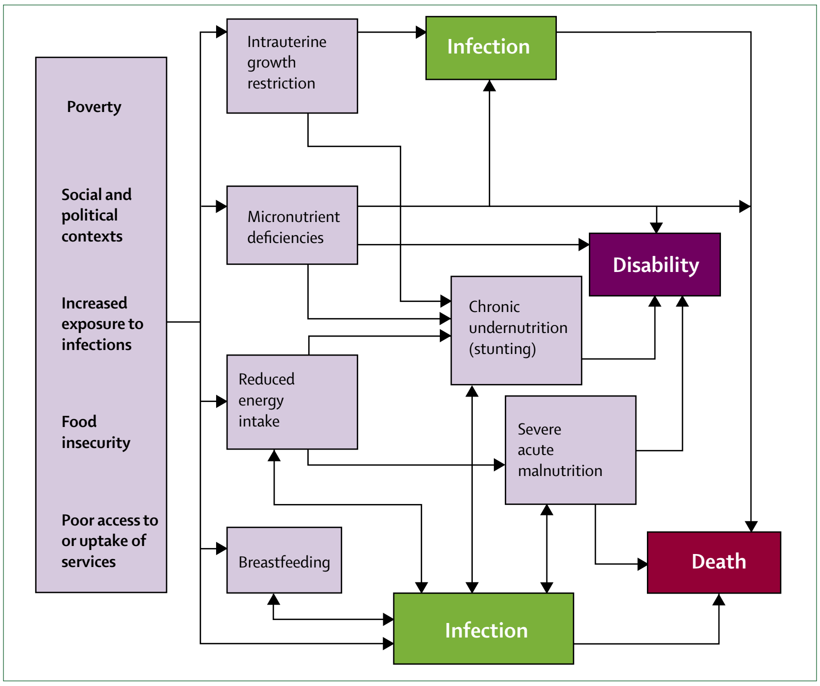

Figure 3: **Conceptual model of pathways to death and disability**

stunting in children aged 12–36 months (table 10). The *Programa Familias en Acción* in Colombia[174] reported an increase of 0·44 cm in height in children aged 0–12 months, whereas *Red de Proteccion Social* in Nicaragua[82] recorded a small decrease in the prevalence of stunting, from 41·9% to 37·1%, and that of underweight from 15·3% to 10·4% over 2 years.

Dietary diversification strategies

Interventions to diversify diets by enhancement of agriculture and small-animal production (eg, home gardening, livestock rearing, and dietary modifications) are potentially promising and culturally relevant, but in general, have only been implemented at a small scale, and have not been adequately assessed (table 6).[176–178] Dietary modification techniques (eg, germination, fermentation, and malting), have been shown in small studies to improve children's intakes of micronutrients and their micronutrient status.[179,180] Although some promising multidisciplinary nutrition interventions have been implemented,[181] dietary diversification strategies have not been proven to affect nutritional status or micronutrient indicators on a large scale. In view of the weak evidence for the effects of these interventions on human nutrition, we did not attempt to estimate their effects.

See Online for webappendix 17

Modelling the effect of interventions

Panel 1 shows the method for estimating the effects of various interventions. We used estimates of the prevalence of stunting at various ages and our own estimates of the effect of each intervention for various age-groups (tables 11 and 12).

Effect of interventions on stunting and mortality in 36 countries

About 77·5 million children are born each year in the 36 countries with the highest burden of undernutrition, of whom some 7·4 million die before the age of 3 years and a further 0·6 million die between the ages of 36 and 59 months. (Mortality for children younger than 5 years is 103 deaths per 1000 livebirths.) These deaths represent about 280 million DALYs, of which 243 million occur before 36 months of age. The prevalence of stunting in survivors increases rapidly during the first 2 years of life, reaching about 40% by 12 months of age and 54% by 24 months. The frequency of stunting increases to 58% at 36 months of age (figure 2), but remains fairly stable thereafter, and is 55% by 5 years of age. Stunting in survivors beyond 36 months contributes about 9·4 million DALYs. Because most children who will become stunted have done so by 36 months, we did not attempt to model the effect of interventions on stunting after that age. Figure 3 shows the overall conceptual model for nutrition and related disease-prevention interventions, together with pathways that affect disability and mortality.

For some interventions—eg, preventive zinc treatment, balanced intake of energy and protein in pregnancy, and individual or group counselling about handwashing—there was little or no information on coverage rates from the 36 countries, so we assumed that coverage was zero. Our review of large-scale nutrition programmes (webappendix 17) suggested that many programmes had achieved coverage levels of 70% and greater; we thus used this level as the minimum target for many interventions; and also estimated incremental gains after reaching 90% and 99% coverage.

Table 13 shows the effect of individual interventions on stunting, mortality, and DALYs up to age 36 months. Note that the deaths prevented by hygiene interventions are only those deaths prevented through a nutritional pathway (stunting). We did not include deaths due to diarrhoea, which would be prevented directly. In terms of DALYs, the largest effects are from breastfeeding promotion, vitamin A supplementation, and zinc supplementation. Tables 14 and 15 show the effects of combinations of interventions, grouped by type. Universal coverage with general nutrition interventions could prevent one in eight child deaths under the age of 36 months and prevent 10–15% of stunting. Since post-neonatal vitamin A coverage is already high in many countries, micronutrient

	Proportional reduction in deaths before			Relative reduction in prevalence of stunting at			Millions (%) of DALYs averted at
	12 months	24 months	36 months	12 months	24 months	36 months	36 months
99% coverage with balanced energy protein supplementation	3·6%	3·1%	2·9%	1·9%	0·5%	0·3%	7·1 (2·8%)
99% coverage with intermittent preventive treatment	2·4%	2·1%	1·9%	1·4%	0·3%	0·1%	4·8 (1·9%)
99% coverage with multiple micronutrient supplementation in pregnancy	2·0%	1·7%	1·6%	0·9%	0·3%	0·1%	4·0 (1·5%)
99% coverage with breastfeeding promotion and support	11·6%	9·9%	9·1%	0%	0%	0%	21·9 (8·6%)
99% coverage with feeding interventions (promotion of complementary feeding and other supportive strategies)	0%	1·1%	1·5%	19·8%	17·2%	15·0%	5·5 (2·1%)
99% coverage with vitamin A (including neonatal in Asia)	6·9%	7·1%	7·2%	0%	0%	0%	17·6 (6·9%)
99% coverage with zinc supplementation	1·3%	2·8%	3·6%	9·1%	15·5%	17·0%	10·8 (4·2%)
99% coverage with hygiene interventions	0%	0·1%	0·2%	1·9%	2·4%	2·4%	0·7 (0·2%)

Table 13: **Effect of nutrition-related interventions on mortality and stunting in 36 countries**

	Proportional reduction in deaths before			Relative reduction in prevalence of stunting at			Millions (%) of DALYs averted at
	12 months	24 months	36 months	12 months	24 months	36 months	36 months
General nutrition interventions	14·8%	13·9%	13·4%	21·7%	17·8%	15·5%	33·8 (13·3%)
Micronutrient interventions	10·0%	11·3%	12·1%	10·3%	15·9%	17·4%	31·3 (12·3%)
Disease control interventions	3·0%	2·7%	2·6%	3·7%	2·9%	2·7%	6·6 (2·6%)

Table 14: **Effect of combinations of nutrition-related interventions on mortality and stunting in 36 countries (99% coverage)**

	Proportional reduction in deaths before			Relative reduction in prevalence of stunting at			Millions (%) of DALYs averted at
	12 months	24 months	36 months	12 months	24 months	36 months	36 months
99% coverage with all interventions	24·0%	24·4%	24·7%	33·1%	35·8%	35·5%	63·4 (25·1%)
90% coverage with all interventions	22·0%	22·2%	22·4%	31·1%	32·4%	32·1%	57·5 (22·7%)
70% coverage with all interventions	17·3%	17·3%	17·3%	22·7%	24·1%	23·6%	44·3 (17·5%)

Table 15: **Effect of all nutrition-related interventions on mortality and stunting in 36 countries, by coverage level**

interventions have a slightly smaller additional effect on deaths but a larger effect (17%) on stunting, entirely due to zinc. Universal coverage with all interventions could prevent about a quarter of child deaths under 36 months of age and reduce the prevalence of stunting at 36 months by about a third, averting some 60 million DALYs. Lower coverage (70%) would avert over 40 million DALYs.

Effect of the WHO protocol for facility-based management of severe acute malnutrition

An estimated 276 000 children who are younger than 5 years die each year of causes associated with severe acute malnutrition in the 36 focus countries, resulting in some 9·2 million DALYs. Application of the WHO protocol for management of severe acute malnutrition could reduce the number of deaths by 55%, and prevent 152 000 deaths in hospitals or health facilities—on the assumption that current coverage is negligible. This is equivalent to 5 million DALYs. To achieve this reduction, all children at high risk of death from severe acute malnutrition would need to reach a health facility capable of delivering the WHO protocol. However, community and home-based management of severe acute malnutrition with ready-to-use therapeutic foods is now possible and has been recommended.[88,186]

Effect of strategies to reduce iron-deficiency anaemia

Iron-deficiency anaemia is estimated to cause 1·6 million DALYs in children under the age of 5 years in the 36 focus countries, and contributes to maternal deaths (447 000 deaths equate to 12·9 million DALYs). Table 16 indicates that universal iron and folate supplementation for pregnant women could avert an estimated 84 000 maternal deaths and 2·5 million DALYs. At present, routine iron supplementation is not recommended for children living in areas at risk of malaria caused by *Plasmodium falciparum*—ie, most of our 36 focus countries. Fortification of food or staples with iron could prevent an estimated 123 000 DALYs (8%) in children. Dispersible micronutrient preparations could have a greater effect, but proof that use is safe in malaria-endemic areas would be needed before they could be recommended as a universal strategy. Other strategies, including cooking in iron pots, deworming, and delayed cord clamping, could also help to reduce the burden of iron-deficiency anaemia, but there are no data on any additional effects that these strategies would have when added to supplementation or fortification delivered at full coverage.

Effect of strategies to reduce iodine deficiency

Iodine deficiency is estimated to cause 1·8 million DALYs in children younger than 5 years in the 36 focus countries. We estimate that universal salt iodisation could reduce this burden by almost a quarter (table 17). This estimate is affected by the fact that salt iodisation is already widespread and has already prevented some of the disease burden.

Effect of calcium and zinc supplementation in pregnancy

Calcium supplementation reduces the incidence of pre-eclampsia by 48%.[15] If we assume that this intervention has a similar effect on deaths due to hypertensive disorders, on the basis of the proportion of maternal deaths estimated to be due to hypertensive disorders,[187] we could expect universal calcium supplementation to prevent some 21 500 maternal deaths and reduce DALYs by 620 000. Although zinc supplements during pregnancy have not been shown to benefit mothers, the 14% reduction in prematurity rates could improve neonatal and child survival. Despite its potential effect on child mortality, we did not model this intervention, since few data that link prematurity with subsequent stunting are available.

Discussion

We have shown that existing interventions for nutrition and disease prevention can reduce stunting at 36 months by about a third; mortality between birth and 36 months by about a quarter; and DALYs associated with stunting, severe wasting, intrauterine growth restriction, and child mortality associated with micronutrient deficiencies by about a quarter. Although the repertoire of maternal nutrition interventions is small, universal supplementation with calcium, iron, and folic acid during pregnancy could prevent 105 500 maternal deaths (23·6% of all maternal deaths) and 3·12 million DALYs.

As the historical evidence of improvement of nutrition in various developed countries has shown, stature, living standards, disease exposure, and education are linked,[188] and virtually all stunting is avertable. However, in the past most reports and assessments of nutrition programmes have focused on weight gain rather than linear growth.[189] In general, stunting and linear-growth retardation are regarded as difficult to change. Our findings show that, in the 36 most important countries, only about a third of stunting could be averted with available interventions in the short term. This finding could indicate that maternal and antenatal factors make an important contribution to stunting that cannot be altered without first addressing the intergenerational effects of undernutrition.[190,191]

Because stunting is especially difficult to reverse after 36 months of age, we need to focus attention on interventions in pregnancy and in young children, especially those under 24 months of age. Supplementary feeding interventions beyond 36 months of age would probably not reduce stunting and might be inadvisable, since rapid weight gain in later childhood is associated with adverse long-term outcomes.[4] Data from a large programmatic intervention in Haiti also suggested that a preventive strategy of behaviour-change communication and food supplements for all children aged 6–23 months reduced numbers who were underweight or stunted more than did a targeted recuperative and food-support strategy that focused on underweight children (under 5 years).[192] These findings should be considered in conjunction with the content and timing of existing nutritional interventions, such as preschool and school-age supplementary feeding programmes. A Cochrane review of school feeding strategies in older children[193] suggests that the effect could lead to an increase in body-mass index rather than a substantial effect on stunting.

Our figures for reduction of mortality are much more conservative than those suggested in our previous reviews.[33,194] Several important differences in the methods used in this exercise must be considered for comparison of our results with previous estimates. First, the effect estimates for interventions used in previous reviews were largely derived from efficacy data, with few findings from effectiveness studies and large-scale programmes; for this review, we used evidence from effectiveness studies whenever possible. Previously no distinction was drawn between public-health interventions and personal behaviours. Thus, although exclusive breastfeeding is an individual decision, promotion of breastfeeding is a public-health intervention and universal coverage of breastfeeding promotion is not the same as universal coverage of exclusive breastfeeding. In this review we modelled the effect of universal breastfeeding promotion. The previous modelling of intervention effects[10,187] also did not assess delivery strategies or targeting to specific population groups at risk, whereas we did for this review. Lastly, previous attempts at modelling intervention effects largely relied on cross-sectional models across a

	Effect estimates (95% CI)	Coverage	DALYs averted	Reduction in DALYs*
Food fortification with iron				
Pregnancy	6·90 g/L increase in haemoglobin (2·74–11·06)			
Childhood	3·4 g/L increase in haemoglobin (0·49–6·27)	70%	87 000	6%
		90%	112 000	7%
		99%	123 000	8%
Iron (and folate) supplementation				
Pregnancy	12 g/L increase in haemoglobin at term (2·93–21·07)	70%	1 600 000	12%
		90%	2 200 000	17%
		99%	2 500 000	19%*
Childhood	Supplementation not recommended for children in areas at risk of *P falciparum* malaria. Sprinkles are associated with an increase in haemoglobin of 5·95 g/L (3·73–8·16) and 21% reduction in the risk of anaemia			
Deworming				
Pregnancy	Mean decline in haemoglobin between first and third trimester in albendazole group was 6·6 g/L less than in placebo (p=0·0034)			
Childhood	The pooled weighted mean difference (random-effects model) of the change in haemoglobin was 0·93 (0·10–1·77) g/L			
Delayed cord clamping				
At delivery	47% reduction in risk of anaemia at 2 to 3 months (RR 0·53, 0·40–0·70)			

*Proportions for DALYs in pregnant women are percentage of all DALYs attributable to maternal deaths.

Table 16: **Estimates of the effect of interventions to prevent iron-deficiency anaemia at different periods**

	Effect estimates	Coverage	DALYs averted (millions)	Reduction in DALYs
Universal iodised salt use and iodine fortification of water in high-risk areas	Goitre prevalence decreased by 19–64%	70%	0·16	8·6%
	Rate of goitre reduced by 51–89% by iodisation of water	90%	0·32	17·7%
	Overall effect estimate used 41%	99%	0·40	22·3%
Specific iodine supplementation as injectable iodine (antenatal) in areas if severe iodine deficiency	Antenatal iodine supplementation results in 73% reduction in the risk of congenital hypothyroidism in 4-year-old survivors (RR 0·27, 95% CI 0·12–0·60). Antenatal iodine supplementation results in 29% reduction in the risk of infant and child mortality (RR 0·71, 0·56–0·90)	Uncertain proportion globally affected by severe iodine deficiency in pregnancy		

Table 17: **Strategies to reduce the burden of iodine deficiency (maternal and child interventions)**

wide age range (0–4 years of age), and did not seek to differentiate effects at various ages. Therefore we developed a longitudinal, cohort model.

Another major difference is that the estimates for the mortality attributable to stunting that we have used are lower than those that were used for mortality attributable to being underweight; however, we also examined the additional benefits through reduction of severe wasting and intrauterine growth restriction, which allows better discrimination of effects for guidance of programmes.[1] Some additional specific differences merit comment. In a previous Series on child survival,[33] an optimisation of breastfeeding practices achieved a reduction of 13% in child mortality. By contrast, on the basis that the effects of various breastfeeding promotion strategies on breastfeeding practices would differ in different age-groups, we estimated that child mortality would be reduced by 8%. Another major difference was the mortality reduction attributed to appropriate complementary feeding strategies, which had previously been estimated at 6%;[33,68] we showed that this reduction would be only 1%. In previous calculations we had assumed that interventions could achieve an increase of 0·35 in weight-for-age *Z* scores, whereas for this exercise we assessed programme effects in terms of height and length, with height-for-age *Z* scores in the range of 0·2–0·4 across various age-groups. By contrast with the current age-group-specific estimates, an SD estimate of 1 was previously used across populations. This approach might have exaggerated the effect of complementary feeding. In previous models, we did not distinguish between food-secure and food-insecure populations. Given the lack of robust population indicators of food security, our choice of GDP income per head is somewhat crude and arbitrary; however, we wanted to underscore the need for different complementary feeding interventions in the two categories.

Our calculation of the effect of interventions to promote hygiene and handwashing was also lower (<1%) than previous estimates (3%). This discrepancy was expected, since we estimated the effect moderated by stunting only and did not include the direct effect on disease-related mortality (eg, due to diarrhoea). The effect estimates for micronutrient interventions were similar to previous ones for zinc and slightly higher for vitamin A. The higher estimate for vitamin A relates to the addition of an effect of neonatal dosing of vitamin A on mortality in children younger than 6 months in Asia, and might be imprecise in that our intervention model did not estimate cause-specific reduction in mortality. Lastly, since children who receive one intervention are more likely to receive other interventions,[195] the combined effect of interventions might be lower than expected from individual interventions.

Several additional limitations must also be recognised. As indicated earlier, we included only proximal interventions that might affect nutrition through improved nutrient intake or reduction in disease burden. We also restricted this group of interventions to include mainly those that reduced the burden of diarrhoea. Other disorders, such as recurrent respiratory infections[196] and intercurrent infections[197] could also possibly worsen nutrition because of reduced dietary intake and protein diversion. Although we included the effect of handwashing and zinc administration on diarrhoea morbidity, we did not estimate their potential effects on stunting from an additional reduction in the burden of respiratory infections.[143,198] Similarly we have not included the potential effects of vaccination strategies for measles, rotavirus, *Haemophilus influenzae*, or pneumococcal disease. Furthermore, we have not estimated the effects of treatment of HIV/AIDS in children or pregnant women. These strategies might have substantial benefits through reduction of morbidity and secondary undernutrition.[143,199]

Previous reviews did not attempt to assess the benefit of interventions on the reduction of lost DALYs, which capture both the effects on short-term morbidity and mortality and the effects on disability that might be life-long. Our modelling exercise indicated that most of the effects on DALYs by nutrition interventions result from reduction in child mortality. We have used the disability weightings of maternal and child undernutrition that were established by the Global Burden of Disease project but recognise that these might be inadequate.[200] Evidence presented previously[201] and in this Series[4] has suggested that the long-term effects of stunting on cognition and earning potential are larger than previously recognised; these findings might justify a larger life-time disability weight for stunting in future estimations of disease burden.

Although we considered a wide range of nutrition interventions, reviews,[202–204] and more than 25 nutrition programmes, the evidence for many interventions and

***Panel 2:* Evidence gaps**

- The effectiveness and cost-effectiveness of nutritional interventions in national health systems need urgent assessment. Both single and packaged interventions that affect general nutrient and micronutrient intake in women and children should be assessed, for their effect on stunting rates and weight gain
- Few nutritional interventions for mothers have assessed a wide range of outcomes at sufficient scale. Although promising, interventions that target maternal macronutrient and micronutrient intake, in particular, those with multiple micronutrients and calcium, need to be assessed with long-term tracking of effect on maternal and child health
- Few studies of large-scale interventions for promotion of breastfeeding have assessed their effects on feeding patterns and growth outcomes beyond infancy. With the new growth standards, such studies are needed to assess the effectiveness of strategies for breastfeeding promotion and appropriate complementary feeding for growth and morbidity in various age-groups
- The finding that nutrition interventions do not have a significant effect beyond 36 months has huge policy implications. We need large-scale studies to verify the irreversibility of stunting in children aged 36–49 months and older
- Can the adverse effects associated with stunting (eg, cognitive impairment or risk of infectious disease) be ameliorated or reversed?
- Although the efficacy of preventive zinc supplementation is proven, studies of the effectiveness of various zinc delivery strategies (fortification, supplementation, and biofortification) are urgently needed
- Since community-based preventive and treatment strategies for severe acute malnutrition have been the subject of only a few studies, robust experiments in this area should be prioritised

key questions was weak. Despite the many randomised controlled trials that show the benefit of interventions to promote breastfeeding, few trials have assessed the importance of timing of breastfeeding, or its effect on neonatal or infant survival.[34] Similarly, evidence for the effectiveness of many large-scale nutrition programmes was variable since few programmes had robust strategies for monitoring and assessment, and only one[81] was implemented in a way that allowed prospective evaluation. Evidence about food fortification programmes and their effect on maternal and childhood micronutrient status and health is especially scarce. Despite our premise of using evidence from effectiveness trials and programme assessments, fewer than 3% of all interventions qualified. Hence, much of our intervention review still consists of efficacy estimates rather than effectiveness studies, and these might have been done in specific contexts (eg, high rates of nutritional anaemia or soil helminths that might increase effect estimates). This gap in global evidence is important, since efficacy data might overestimate potential benefits, and fail to include the reality of lower coverage and technical and logistical difficulties that hamper implementation in health systems. Panel 2 summarises some of the key evidence gaps with regard to interventions and strategies that could affect nutrition outcomes. Given the paucity of effectiveness data, strengthening of monitoring and rigorous assessment of large-scale nutrition programmes are imperative.

Some technical limitations with the prediction model must also be mentioned. We largely assumed that the interventions act on their own and calculated their effects with this in mind. In reality, however, some interventions might act synergistically, especially in populations with multiple deficiencies. For instance, the effect of iron supplementation on anaemia can be substantially increased by co-administration with vitamin A in deficient populations;[205] in addition to an effect on survival in childhood, reduction in intrauterine growth restriction might affect immunity and long-term health outcomes.[206] In a similar example, the overall effect of a programme of conditional cash transfers on stunting reduction was shown to be greater than that noted in the pilot phase.[81,207] This discrepancy could possibly be explained by additional benefits of conditional cash transfers such as improved micronutrient status through consumption of better quality foods over time, greater use of health services, and access to antibiotics. Another unmeasured benefit of conditional cash transfers could include promotion of female empowerment.[208]

We recognise that we have neither included poverty alleviation strategies for their effect on nutrition outcomes, nor assessed the cost-effectiveness of various interventions. For most of the country studies available, the effects of financial market access on calorie intake and nutritional status were not statistically significant (data not shown). The association between consumption of higher quality foods and rising incomes was a major reason for the weak marginal effect on calorie intake. Also, nutritional status results from a complex interaction between food intake, access to safe water and sanitation, nutritional knowledge of caretakers, and access to care and medical services. Higher income and ability to finance food expenditures are therefore only two of many determinants of nutritional status. The policy implication is that the provision of improved financial access to rural households needs to be complemented by services to translate higher income (generated through improved access to rural financial services) into improved nutrition. In general, most rural microfinance institutions in developing countries—with some notable exceptions, mainly non-governmental organisations—do not directly provide these complementary services. However, whether the financial institutions themselves or other specialised agencies should offer such complementary services is a much debated question. Building sustainable rural financial institutions for the poor seems to be a challenging task in itself; provision of additional services in the areas of health and nutrition will probably overburden these mostly young institutions. Although a few successful institutions manage both (eg, BRAC and the Grameen Bank in Bangladesh), to strengthen existing specialised public programmes that directly address these other important determinants of nutrition is more appropriate.

Notwithstanding these limitations, our review and intervention simulation model suggest that much can be done to improve the nutritional status of mothers and children with simple evidence-based interventions. In view of the long-term consequences of iodine-deficiency disorders,[209] iodisation of salt should be extended to full population coverage. In many instances, alternative delivery strategies could be considered. For example, the potential benefit of achieving 99% coverage with vitamin A could be achieved by various approaches. Although in some countries vitamin A supplementation programmes might be the most cost-effective and feasible way to reach large populations at risk, fortification of common food commodities in some settings might enable high rates of coverage to be achieved.

Proven nutrition-related interventions offer many possibilities for improvement of undernutrition in mothers and their children and reduction of the related burden of disease in both the short and the long term. Attention to the continuum of maternal and child undernutrition is essential to attainment of several of the Millennium Development Goals and must be prioritised globally and within countries. Countries with a high prevalence of undernutrition must decide which interventions should be given the highest priority, and ensure their effective implementation at high coverage to achieve the greatest benefit. We have shown that the evidence for benefit from nutrition interventions is convincing. What is needed is the technical expertise and the political will to combat undernutrition in the very countries that need it most.

Contributors

ZAB conceptualised the global review of nutrition interventions, obtained core funding, and wrote the first draft of the paper. All authors contributed to the writing and review process. The Series steering committee contributed to the review and writing process during meetings in Baltimore (2006), Washington DC (2006), Dubai (2006), Florence (2007), Bellagio (2006), and London (2007).

Global nutrition intervention review team

ZAB and BAH coordinated the review process and the five global intervention review teams. SC, SSM, BK, and RB contributed to assessment and synthesis of evidence. TA led a team at ICDDRB which reviewed fortification strategies, treatment of severe acute malnutrition, handwashing strategies, and evidence for large-scale nutrition programmes. EG did the review of breastfeeding strategies and growth. KD and Seth Adu Afarwuah reviewed the global evidence of complementary feeding strategies and BAH, ZAB, and SC did further meta-analysis. HPSS and S Gogia contributed the reviews of iron and vitamin A supplementation strategies. Aatekah Owais contributed to the review of conditional cash transfers. The cohort model was conceptualised and developed by SC and SM with additional inputs from ZAB, RB, BK, and Colin Mathers.

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Conflict of interest statement

We declare that we have no conflict of interest.

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References

1 Black RE, Allen LH, Bhutta ZA, et al, for the Maternal and Child Undernutrition Study Group. Maternal and child undernutrition: global and regional exposures and health consequences. *Lancet* 2008; published online Jan 17. DOI:10.1016/S0140-6736(07)61690-0
2 Caulfield LE, de Onis M, Blossner M, Black RE. Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria, and measles. *Am J Clin Nutr* 2004; **80:** 193–98.
3 Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? *Lancet* 2003; **361:** 2226–34.
4 Victora CG, Adair L, Fall C, et al, for the Maternal and Child Undernutrition Study Group. Maternal and child undernutrition: consequences for adult health and human capital. *Lancet* 2008; published online Jan 17. DOI:10.1016/S0140-6736(07)61692-4.
5 Salama P, Spiegel P, Talley L, Waldman R. Lessons learned from complex emergencies over past decade. *Lancet* 2004; **364:** 1801–13.
6 Health Development Agency. Grading evidence and recommendations for public health interventions: developing and piloting a framework. London, UK: Health Development Agency, 2005.

7 Kramer MS, Kakuma R. Energy and protein intake in pregnancy. *Cochrane Database Syst Rev* 2003; **4:** CD000032. DOI: 10.1002/14651858.

8 Britton C, McCormick FM, Renfrew MJ, Wade A, King SE. Support for breastfeeding mothers. *Cochrane Database Syst Rev* 2007; **1**: CD001141. DOI: 10.1002/14651858.CD001141.pub3.

9 Pena-Rosas JP, Viteri FE. Effects of routine oral iron supplementation with or without folic acid for women during pregnancy. *Cochrane Database Syst Rev* 2006; **3:** CD004736.

10 Gera T, Sachdev HPS, Nestel P, Sachdev SS. Effect of iron supplementation on hemoglobin response in children: systematic review of randomised controlled trials. *J Pediatr Gastroenterol Nutri* 2007; **44:** 468–86.

11 Mahomed K, Bhutta Z, Middleton P. Zinc supplementation for improving pregnancy and infant outcome. *Cochrane Database Syst Rev* 2007; **2:** CD000230.

12 Brown KH, Peerson JM, Rivera J, Allen LH. Effect of supplemental zinc on the growth and serum zinc concentrations of prepubertal children: a meta-analysis of randomized controlled trials. *Am J Clin Nutr* 2002; **75:** 1062–71.

13 Bhutta ZA, Black RE, Brown KH, et al. Prevention of diarrhea and pneumonia by zinc supplementation in children in developing countries: pooled analysis of randomized controlled trials. Zinc Investigators' Collaborative Group. *J Pediatr* 1999; **135:** 689–97.

14 Aggarwal R, Sentz J, Miller MA. Role of zinc administration in prevention of childhood diarrhea and respiratory illnesses: a meta-analysis. *Pediatrics* 2007; **119:** 1120–30.

15 Hofmeyr GJ, Atallah AN, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. *Cochrane Database Syst Rev* 2006; **3**: CD001059.

16 Van Rheenen P, Brabin BJ. Late umbilical cord-clamping as an intervention for reducing iron deficiency anaemia in term infants in developing and industrialised countries: a systematic review. *Ann Trop Paediatr* 2004; **24:** 3–16.

17 Villabona BL, Ayllon EB, Thompson MLC, Chiesa JMB. Early or late umbilical cord clamping? A systematic review of the literature. *Ann Pediatr (Barc)* 2005; **63:** 14–21.

18 Hutton EK, Hassan ES. Late vs early clamping of the umbilical cord in full-term neonates: systematic review and meta-analysis of controlled trials. *JAMA* 2007; **297:** 1257–58.

19 Geerligs PDP, Brabin BJ, Omari AAA. Food prepared in iron cooking pots as an intervention for reducing iron deficiency anaemia in developing countries: a systematic review. *J Hum Nutr Dietet* 2003; **16:** 275–81.

20 Adish AA, Esrey SA, Gyorkos TW, Jean-Baptiste J, Rojhani A. Effect of consumption of food cooked in iron pots on iron status and growth of young children: a randomised trial. *Lancet* 1999; **353:** 712–16.

21 Borigato EVM, Martinez FE. Iron nutritional status is improved in Brazilian preterm infants fed food cooked in iron pots. *J Nutr* 1998; **128:** 855–57.

22 Geerligs PDP, Brabin BJ, Mkumbwa A, Broadhead R, Cuevas LE. Acceptability of the use of iron cooking pots to reduce anaemia in developing countries. *Public Health Nutr* 2002; **5:** 619–24.

23 Geerligs PDP, Brabin BJ, Mkumbwa A, Broadhead R, Cuevas LE. The effect on haemoglobin of the use of iron cooking pots in rural Malawian households in an area with high malaria prevalence: a randomised trial. *Trop Med Int Health* 2003; **8:** 310–15.

24 ter Kuile FO, van Eijk AM, Filler SJ. Effect of sulfadoxine-pyrimethamine resistance on the efficacy of intermittent preventive therapy for malaria control during pregnancy: a systematic review. *JAMA* 2007; **297:** 2603–16.

25 Gamble C, Ekwaru JP, ter Kuile FO. Insecticide-treated nets for preventing malaria in pregnancy. *Cochrane Database Syst Rev* 2006; **2**: CD003755.pub2. DOI: 10.1002/14651858.

26 Curtis V, Cairncross S. Effect of washing hands with soap on diarrhoea risk in the community: a systematic review. *Lancet Infect Dis* 2003; **3:** 275–81.

27 Fewtrell L, Kaufmann RB, Kay D, Enanoria W, Haller L, Colford Jr JM. Water, sanitation, and hygiene interventions to reduce diarrhoea in less developed countries: a systematic review and meta-analysis. *Lancet Infect Dis* 2005; **5:** 42–52.

28 Zwane AP and Kremer M. What works in fighting diarrheal diseases in developing countries? A critical review. *CID Working Paper* No. 140. March 2007.

29 Dickson R, Awasthi S, Williamson P, Demellweek C, Paul G. Effects of treatment for intestinal helminth infection on growth and cognitive performance in children: systematic review of randomised trials. *BMJ* 2000; **320:** 1697–1701.

30 Sazawal S, Hiremath G, Dhingra U, Malik P, Deb S, Black RE. Efficacy of probiotics in prevention of acute diarrhoea: a meta-analysis of masked, randomised, placebo-controlled trials *Lancet Infect Dis* 2006; **6:** 374–82.

31 Ceesay SM, Prentice AM, Cole TJ, et al. Effects on birth weight and perinatal mortality of maternal dietary supplements in rural Gambia: 5 year randomised controlled trial. *BMJ* 1997; **315:** 786–90.

32 WHO Collaborative Study Team on the Role of Breastfeeding on the Prevention of Infant Mortality. Effect of breastfeeding on infant and child mortality due to infectious diseases in less developed countries: a pooled analysis. *Lancet* 2000; **355:** 451–55.

33 Jones G, Steketee RW, Black RE, Bhutta ZA, Morris SS. Bellagio Child Survival Study Group. How many child deaths can we prevent this year? *Lancet* 2003; **362:** 65–71.

34 Edmond KM, Zandoh C, Quigley MA, Amenga-Etego S, Owusu-Agyei S, Kirkwood BR. Delayed breastfeeding initiation increases risk of neonatal mortality. *Pediatrics* 2006; **117:** e380–86.

35 Nutrition Communication Project. Honduras national breastfeeding promotion project 1989–1993. Washington DC, USA: Academy for Educational Development, 1995.

36 Frank DA, Wirtz SJ, Sorensen JR, Heeren T. Commercial hospital discharge packs and breastfeeding counseling: effects on infant feeding practices in a randomized trial. *Pediatrics* 1987; **80:** 845–54.

37 Froozani MD, Permehzadeh K, Motlagh AR, Golestan B. Effect of breastfeeding education on the feeding pattern and health of infants in their first 4 months in the Islamic Republic of Iran. *Bull World Health Organ* 1999; **77:** 381–85.

38 Haider R, Islam A, Hamadani J, et al. Breastfeeding counseling in a diarrhoeal disease hospital. *Bull World Health Organ* 1996; **74:** 173–79.

39 Langer A. Intrapartum social support and exclusive breastfeeding in mexico. In: Wellstart International, ed. Exclusive breastfeeding promotion: a summary of findings from EPB's applied research program (1992–1996). Washington DC: Wellstart International, 1996.

40 Morrow AL, Guerrero ML, Shults J, et al. Efficacy of home-based peer counselling to promote exclusive breastfeeding: a randomised controlled trial. *Lancet* 1999; **353:** 1226–31.

41 Palti H, Valderama C, Pogrund R, Jarkoni J, Kurtzman C. Evaluation of the effectiveness of a structured breast-feeding promotion program integrated into a maternal and child health service in Jerusalem. *Isr J Med Sci* 1988; **24:** 342–48.

42 Porteous R, Kaufman K, Rush J. The effect of individualized professional support on duration of breastfeeding: a randomized controlled trial. *J Hum Lact* 2000; **16:** 303–08.

43 Rodriguez-Garcia R, Kimberly JA, Angelica R. A community-based approach to the promotion of breastfeeding in Mexico. *J Obstet Gynecol Neonatal Nurs* 1990; **19:** 431–38.

44 Vandale-Toney S, Reyes-Vázquez H, Montaño-Uscanga A, Marroquín EL, Castillo NEV. Programa de promoción de la lactancia materna en el Hospital General de México: un estudio evaluativo. *Salud Pública de México* 1992; 34: **1:** 25–35.

45 Jones DA, West RR. Lactation nurse increases duration of breastfeeding. *Arch Dis Child* 1985; **60:** 772–74.

46 Brent NB, Redd B, Dworetz A, D'Amico FD, Greenberg J. Breastfeeding in a low-income population. *Arch Pediatr Adolesc Med* 1995; **149:** 798–803.

47 Graffy J, Taylor J, Williams A, Eldridge S. Randomised controlled trial of support from volunteer counselors for mothers considering breastfeeding. *BMJ* 2004; **328:** 26.

48 Grossman LK, Harter C, Kay A. The effect of postpartum lactation counseling on the duration of breastfeeding in low income women. *Am J Dis Child* 1990; **144:** 471–74.

49 Morrell CJ, Spiby H, Stewart P, Walters S, Morgan A. Costs and effectiveness of community postnatal support workers: randomised controlled trial. *BMJ* 2000; **321:** 593–98.

50 Valdés V, Puggin E, Labbok MH, et al. A three-day lactation course can change professional practices. Santiago, Chile: Department of Pediatrics, Catholic University of Chile, 1994.

51 Anderson AK, Damio G, Young S, Chapman DJ, Pérez-Escamilla R. A randomized trial assessing the efficacy of peer counseling on exclusive breastfeeding in a predominantly Latina low-income community. *Arch Pediatr Adolesc Med* 2005; **159:** 836–41.

52 Pugh L, Milligan R, Frick K, Spatz D, Bronner Y. Breastfeeding duration, costs, and benefits of a support program for low-income breastfeeding women. *Birth* 2002; **29:** 95–100.

53 Quinlivan JA, Box H, Evans SF. Postnatal home visits in teenage mothers: a randomised controlled trial. *Lancet* 2003; **361:** 893–900.

54 Dennis CL, Hodnett E, Gallop R, Chalmers B. The effect of peer support on breastfeeding duration among primiparous women: a randomized controlled trial. *CMAJ* 2002; **166:** 21–28.

55 Chapman DJ, Damio GD, Young S, Perez-Escamilla R. Effectiveness of breastfeeding peer counseling in a low-income, predominantly Latina population. *Arch Pediatr Adolesc Med* 2004; **158:** 897–902.

56 Alvarado RM, Atalah ES, Díaz SF, Rivero SV, Labbé MD, Escudero YP. Evaluation of a breastfeeding-support programme with health promoter's participation. *Food Nutr Bull* 1996; **17:** 49–53.

57 Barros FC, Semer TC, Tonioli Filho S, et al. The impact of lactation centers on breastfeeding patterns, morbidity and growth: a birth cohort study. *Acta Paediatr* 1995; **84:** 1221–26.

58 Burkhalter BR, Marin PS. A demonstration of increased exclusive breastfeeding in Chile. *Int J Gynecol Obstet* 1991; **34:** 353–59.

59 Neyzi O, Olgun P, Kutluay T, et al. Results of an educational intervention study on promotion of breast-feeding. Istanbul, Turkey: Institute of Child Health, University of Istanbul, and Barem Research Company, 1988.

60 Rivera A, Canahuati J, Lopez C, Phillips A, Lundgren R. The promotion of the lactational amenorrhea method and child spacing through breastfeeding advocates. Washington DC, USA: Institute for Reproductive Health, Georgetown University, La Liga de Lactancia Materna de Honduras, and INOPAL II, Population Council, 1993.

61 Wiles LS. The effect of prenatal breastfeeding education on breastfeeding success and maternal perception of the infant. *J Obstet Gynecol Neonatal Nurs* 1984; **13:** 253–57.

62 Valdés V, Pérez A, Labbok M, Pugin E, Zambrano I, Catalan S. The impact of a hospital and clinic-based breastfeeding promotion programme in a middle class urban environment. *J Trop Pediatr* 1993; **39:** 142–51.

63 Bhandari N, Bahl R, Mazumdar S, et al. Effect of community-based promotion of exclusive breastfeeding on diarrhoeal illness and growth: a cluster randomised controlled trial. *Lancet* 2003; **361:** 1418–23.

64 Hernandez O, Lani M, Margaret P. Assessment of the impact of a national intervention to promote exclusive breastfeeding in Honduras. Washington DC: Academy for Educational Development, 1995.

65 Victora CG, Morris SS, Barros FC, de Onis M, Yip R. The NCHS reference and the growth of breast- and bottle-fed infants. *J Nutr* 1998; **128:** 1134–38.

66 Coovadia HM, Rollins NC, Bland RM, et al. Mother-to-child transmission of HIV-1 infection during exclusive breastfeeding in the first 6 months of life: an intervention cohort study. *Lancet* 2007; **369:** 1107–16.

67 Thior I, Lockman S, Smeaton LM, et al; Mashi Study Team. Breastfeeding plus infant zidovudine prophylaxis for 6 months *vs* formula feeding plus infant zidovudine for 1 month to reduce mother-to-child HIV transmission in Botswana: a randomized trial: the Mashi Study. *JAMA* 2006; **296:** 794–805.

68 Iliff PJ, Piwoz EG, Tavengwa NV, et al; ZVITAMBO study group. Early exclusive breastfeeding reduces the risk of postnatal HIV-1 transmission and increases HIV-free survival. *AIDS* 2005; **19:** 699–708.

69 Kuhn L, Aldrovandi GM, Sinkala M, et al. Randomized controlled trial of abrupt cessation of breastfeeding at 4 months to reduce post-natal HIV transmission and mortality among children born to HIV-infected women: the Zambia Exclusive Breastfeeding Study (ZEBS). 14th Conference on Retroviruses and Opportunistic Infections (CROI), Los Angeles, USA, 2007.

70 Caulfield LE, Huffman SL, Piwoz EG. Interventions to improve intake of complementary foods by infants 6 to 12 months of age in developing countries: Impact on growth and on the prevalence of malnutrition and potential contribution to child survival. *Food Nutr Bull* 1999; **20:** 183–200.

71 Guldan GS, Fan HC, Ma X, Ni ZZ, Xiang X, Tang MZ. Culturally appropriate nutrition education improves infant feeding and growth in rural Sichuan, China. *J Nutr* 2000; **130:** 1204–11.

72 Penny ME, Creed-Kanashiro HM, Robert RC, Narro MR, Caulfield LE, Black RE. Effectiveness of an educational intervention delivered through the health services to improve nutrition in young children: a cluster-randomised controlled trial. *Lancet* 2005; **365:** 1863–72.

73 Santos I, Victora CG, Martines J, et al. Nutrition counseling increases weight gain among Brazilian children. *J Nutr* 2001; **131:** 2866–73.

74 Oelofse A, Van Raaij JM, Benade AJ, Dhansay MA, Tolboom JJ, Hautvast JG. The effect of a micronutrient-fortified complementary food on micronutrient status, growth and development of 6- to 12-month-old disadvantaged urban South African infants. *Int J Food Sci Nutr* 2003; **54:** 399–407.

75 Adu-Afarwuah S, Lartey A, Briend A, Zlotkin S, Brown KH, Dewey KG. Randomized comparison of 3 types of micronutrient supplements for home fortification of complementary foods in Ghana: Effects on growth and motor development. *Am J Clin Nutr* 2007; **86:** 412–20.

76 Lartey A, Manu A, Brown KH, Peerson JM, Dewey KG. A randomized, community-based trial of the effects of improved, centrally processed complementary foods on growth and micronutrient status of Ghanaian infants from 6 to 12 mo of age. *Am J Clin Nutr* 1999; **70:** 391–404.

77 Schroeder DG, Pachon H, Dearden KA, et al. An integrated child nutrition intervention improved growth of younger, more malnourished children in northern Viet Nam. *Food Nutr Bull* 2002; **23:** 53–61.

78 Lutter CK, Rodriguez A, Fuenmayor G, Sempertegui F. Growth and micronutrient status among children receiving a fortified complementary food. *J Nutrition* (in press).

79 Bhandari N, Bahl R, Nayyar B, Khokhar P, Rohde JE, Bhan MK. Food supplementation with encouragement to feed it to infants from 4 to 12 months of age has a small impact on weight gain. *J Nutr* 2001; **131:** 1946–51.

80 Obatolu VA. Growth pattern of infants fed with a mixture of extruded malted maize and cowpea. *Nutrition* 2003; **19:** 174–78.

81 Behrman, J Hoddinott, J. An evaluation of the impact of PROGRESA on pre-school child height, Discussion Paper No 104. Washington DC, USA: Food Consumption and Nutrition Division, International Food Policy Research Institute (IFPRI), 2001.

82 Maluccio, J Flores R. Impact evaluation of a conditional cash transfer program: the Nicaraguan red de protección social, Research Report No 141. Washington DC, USA: International Food Policy Research Institute (IFPRI), 2005.

83 Collins S, Dent N, Binns P. Management of severe acute malnutrition in children. *Lancet* 2006; **368:** 1992–2000.

84 Ahmed T, Ali M, Ullah M, et al. Mortality in severely malnourished children with diarrhoea and use of a standardised management protocol. *Lancet* 1999; **353:** 1919–22.

85 Ashworth A, Chopra M, McCoy D, et al. WHO guidelines for management of severe malnutrition in rural South African hospitals: effect on case fatality and the influence of operational factors. *Lancet* 2004; **363:** 1110–15.

86 Deen JL, Funk M, Guevara VC, et al. Implementation of WHO guidelines on management of severe malnutrition in hospitals in Africa. *Bull World Health Org* 2003; **81:** 237–43.

87 Wilkinson D, Scrace M, Boyd N. Reduction in in-hospital mortality of children with malnutrition. *J Trop Pediatr* 1996; **42:** 114–15.

88 Falbo AR, Alves JG, Batista Filho M, Cabral-Filho JE. Implementation of World Health Organization guidelines for management of severe malnutrition in a hospital in Northeast Brazil. *Cad Saude Publica* 2006; **22:** 561–70.

89 Nu Shwe T. Logical and logistic aspects of management of a child with severe malnutrition and serious infection in hospital settings: what is new, challenges and way forward. Proceedings of the 9th Asian Congress of Nutrition, 2003. Nutrition goals for Asia—Vision 2020. Feb 23–27; Delhi, India.

90 WHO, WFP, UNSCN, UNICEF. Community-based management of severe acute malnutrition. Geneva: World Health Organisation, 2007. http://www.who.int/nutrition/topics/statement_commbased_malnutrition/en/index.html (accessed on Nov 7, 2007).

91 Ashworth A. Efficacy and effectiveness of community-based treatment of severe malnutrition. *Food Nutr Bull* 2006; **27:** 24–48.

92 Ciliberto MA, Sandige H, Ndekha MJ, et al. Comparison of home-based therapy with ready to-use therapeutic food with standard therapy in the treatment of malnourished Malawian children: a controlled, clinical eff ectiveness trial. *Am J Clin Nutr* 2005; **81:** 864–70.

93 Ballot DE, MacPhail AP, Bothwell TH, Gillooly M, Mayet FG. Fortification of curry powder with NaFe(111)EDTA in an iron-deficient population: report of a controlled iron-fortification trial. *Am J Clin Nutr*. 1989; **49:** 162–69.

94 Thuy PV, Berger J, Davidsson L, et al. Regular consumption of NaFeEDTA-fortified fish sauce improves iron status and reduces the prevalence of anemia in anemic Vietnamese women. *Am J Clin Nutr* 2003; **78:** 284–90.

95 Thuy PV, Berger J, Nakanishi Y, Khan NC, Lynch S, Dixon P. The use of NaFeEDTA-fortified fish sauce is an effective tool for controlling iron deficiency in women of childbearing age in rural Vietnam. *J Nutr* 2005; **135:** 2596–601.

96 Nadiger HA, Krishnamachari KA, Naidu AN, Rao BS, Srikantia SG. The use of common salt (sodium chloride) fortified with iron to control anaemia: results of a preliminary study. *Br J Nutr* 1980; **43:** 45–51.

97 Walter T, Hertrampf E, Pizarro F, et al. Effect of bovine-hemoglobin-fortified cookies on iron status of schoolchildren: a nationwide program in Chile. *Am J Clin Nutr* 1993; **57:** 190–94.

98 van Stuijvenberg ME, Smuts CM, Wolmarans P, Lombard CJ, Dhansay MA. The efficacy of ferrous bisglycinate and electrolytic iron as fortificants in bread in iron-deficient school children. *British J Nutr* 2006; **95:** 532–38.

99 Villalpando S, Shamah T, Rivera JA, Lara Y, Monterrubio E. Fortifying milk with ferrous gluconate and zinc oxide in a public nutrition program reduced the prevalence of anemia in toddlers. *J Nutr* 2006; **136:** 2633–37.

100 Sazawal S, Dhingra U, Dhingra P, et al. Effects of fortified milk on morbidity in young children in north India: community based, randomised, double masked placebo controlled trial. *BMJ* 2007; **334:** 140.

101 Muhilal, Permeisih D, Idjradinata YR, Muherdiyantiningsih, Karyadi D. Vitamin A-fortified monosodium glutamate and health, growth, and survival of children: a controlled field trial. *Am J Clin Nutr* 1988; **48:** 1271–76.

102 Beaton GH, Martorell R, Aronson KJ, et al. Effectiveness of vitamin A supplementation in the control of young child morbidity and mortality in developing countries. Discussion Paper No 13. Geneva, Switzerland: United Nations Administrative Committee on Coordination/Sub-Committee on Nutrition; 1993.

103 Krause VM, Delisle H, Solomons NW. Fortified foods contribute one half of recommended vitamin A intake in poor urban Guatemalan toddlers. *J Nutr* 1998; **128:** 860–64.

104 Dary O, Mora JO; International Vitamin A Consultative Group. Food fortification to reduce vitamin A deficiency: international Vitamin A Consultative Group recommendations. *J Nutr* 2002; **132:** 2927–33.

105 Zhao J, van der HF. Progress in salt iodization and improved iodine nutrition in China, 1995–99. *Food Nutr Bull* 2004; **25:** 337–43.

106 Kusic Z, Jukic T. History of endemic goiter in Croatia: from severe iodine deficiency to iodine sufficiency. *Coll Antropol* 2005; **29:** 9–16.

107 Pretell EA, Delange F, Hostalek U, et al. Iodine nutrition improves in Latin America. *Thyroid* 2004; **14:** 590–99.

108 Sebotsa ML, Dannhauser A, Jooste PL, Joubert G. Iodine status as determined by urinary iodine excretion in Lesotho two years after introducing legislation on universal salt iodization. *Nutrition* 2005; **21:** 20–24.

109 Zimmerman MB, Moretti D, Chaouki N, Torresani T. Introduction of iodized salt to severely iodine-deficient children does not provoke thyroid autoimmunity: a one-year prospective trial in Northern Morocco. *Thyroid* 2003; **13:** 199–203.

110 Temple V, Mapira P, Adeniyi K, Sims P. Iodine deficiency in Papua New Guinea (sub-clinical iodine deficiency and salt iodization in the highlands of Papua New Guinea). *J Pub Health* 2004; **27:** 45–48.

111 Golkowski F, Huszno B, Trofimiuk M. et al. Prevalence of goiter in schoolchildren—a study on the influence of adequate iodine prophylaxis in Poland. *J Endocrinol Invest* 2003; **26:** 11–15.

112 Bimenya GS, Olico O, Kaviri D, Mbona N, Byarugaba W. Monitoring the severity of iodine deficiency disorders in Uganda. *Afr Health Sci* 2002; **2:** 63–68.

113 Elnagar B, Eltom M, Karlsson FA, Bourdoux PP, Gebre-Medhin M. Control of iodine deficiency using iodination of water in a goiter endemic area. *Int J Food Sci Nutr* 1997; **48:** 119–27.

114 Squatrito S, Vigneri R, Runello F, Ermans AM, Polley RD, Ingbar SH. Prevention and treatment of endemic iodine-deficiency goiter by iodination of a municipal water supply. *J Clin Endocrinol Metab* 1986; **63:** 368–75.

115 Maberly GF, Eastman CJ, Corcoran JM. Effect of iodination of a village water-supply on goitre size and thyroid function. *Lancet* 1981; **2:** 1270–72.

116 Pichard E, Soula G, Fisch A. et al. Prevention of iodine deficiency disorders in children in the rural African zone. *Ann Pediatr* 1992; **39:** 71–78.

117 Andang'o PE, Osendarp SJ, Ayah R, et al. Efficacy of iron-fortified whole maize flour on iron status of schoolchildren in Kenya: a randomised controlled trial. *Lancet* 2007; **369:** 1799–806.

118 Sazawal S, Black RE, Ramsan M, et al. Effects of routine prophylactic supplementation with iron and folic acid on admission to hospital and mortality in preschool children in a high malaria transmission setting: community-based, randomised, placebo-controlled trial. *Lancet* 2006; **367:** 133–43.

119 Iannotti LL, Tielsch JM, Black MM, Black RE. Iron supplementation in early childhood: health benefits and risks. *Am J Clin Nutr* 2006; **84:** 1261–76.

120 Zlotkin S, Arthur P, Antwi KY, Yeung G. Treatment of anemia with microencapsulated ferrous fumarate plus ascorbic acid supplied as sprinkles to complementary (weaning) foods. *Am J Clin Nutr* 2001; **74:** 791–95.

121 Hirve S, Bhave S, Bavdekar A, et al. Low dose 'sprinkles'—an innovative approach to treat iron deficiency anemia in infants and young children. *Indian Pediatr* 2007; **44:** 91–100.

122 Christofides A, Asante KP, Schauer C, et al. Multi-micronutrient Sprinkles including a low dose of iron provided as microencapsulated ferrous fumarate improves haematologic indices in anaemic children: a randomized clinical trial. *Matern Child Nutr* 2006; **2:** 169–80.

123 Menon P, Ruel MT, Loechl CU, et al. Micronutrient Sprinkles reduce anemia among 9- to 24-mo-old children when delivered through an integrated health and nutrition program in rural Haiti. *J Nutr* 2007; **137:** 1023–30.

124 Giovannini M, Sala D, Usuelli M, et al. Double-blind, placebo-controlled trial comparing effects of supplementation with two different combinations of micronutrients delivered as sprinkles on growth, anemia, and iron deficiency in Cambodian infants. *J Pediatr Gastroenterol Nutr* 2006; **42:** 306–12.

125 Sharieff W, Yin SA, Wu M, et al. Short-term daily or weekly administration of micronutrient Sprinkles has high compliance and does not cause iron overload in Chinese schoolchildren: a cluster-randomised trial. *Public Health Nutr* 2006; **9:** 336–44.

126 Zlotkin S, Antwi KY, Schauer C, Yeung G. Use of microencapsulated iron (II) fumarate sprinkles to prevent recurrence of anaemia in infants and young children at high risk. *Bull World Health Organ* 2003; **81:** 108–15.

127 West KP Jr, Katz J, Khatry SK, et al. Double blind, cluster randomised trial of low dose supplementation with vitamin A or beta carotene on mortality related to pregnancy in Nepal. The NNIPS-2 Study Group. *BMJ* 1999; **318:** 570–75.

128 Christian P, West K Jr, Labrique A, et al. Effects of maternal vitamin A or beta-carotene supplementation on maternal and infant mortality in rural Bangladesh: The JiVitA-1 trial. In: Proceedings of the Micronutrient Forum. Consequences and control of micronutrient deficiencies: science, policy, and programs. April 16–18, 2007; Istanbul, Turkey. Washington DC, USA: US Agency for International Development, 2007: 129.

129 Van DE, Kulier R, Gulmezoglu AM, Villar J. Vitamin A supplementation during pregnancy. *Cochrane Database Syst Rev* 2002; **4:** CD001996.

130 Grotto I, Mimouni M, Gdalevich M, Mimouni D. Vitamin A supplementation and childhood morbidity from diarrhea and respiratory infections: a meta-analysis. *J Pediatr* 2003; **142:** 297–304.

131 Barreto ML, Santos LM, Assis AM, et al. Effect of vitamin A supplementation on diarrhoea and acute lower-respiratory-tract infections in young children in Brazil. *Lancet* 1994; **344:** 228–31.

132 Sempertegui F, Estrella B, Camaniero V, et al. The beneficial effects of weekly low-dose vitamin A supplementation on acute lower respiratory infections and diarrhea in Ecuadorian children. *Pediatrics* 1999; **104:** e1.

133 Villamor E, Mbise R, Spiegelman D, et al. Vitamin A supplements ameliorate the adverse effect of HIV-1, malaria, and diarrheal infections on child growth. *Pediatrics* 2002; **109:** e6.

134 Long KZ, Montoya Y, Hertzmark E, Santos JI, Rosado JL. A double-blind, randomized, clinical trial of the effect of vitamin A and zinc supplementation on diarrheal disease and respiratory tract infections in children in Mexico City, Mexico. *Am J Clin Nutr* 2006; **83:** 693–700.

135 Humphrey JH, Agoestina T, Wu L, et al. Impact of neonatal vitamin A supplementation on infant morbidity and mortality. *J Pediatr* 1996; **128:** 489–96.

136 Rahmathullah L, Tielsh JM, Thulasiraj RD, et al. Impact of vitamin A supplementation to newborns on early infant mortality: a community-based randomized trial in South India. *BMJ* 2003; **327:** 254–60.

137 Malaba LC, Iliff PJ, Nathoo KJ, et al. Effect of postpartum maternal or neonatal vitamin A supplementation on infant mortality among infants born to HIV-negative mothers in Zimbabwe. *Am J Clin Nutr* 2005; **81:** 454–60.

138 Klemm R, Labrique A, Christian P, et al. Efficacy of newborn vitamin A supplementation in reducing infant mortality in rural Bangladesh: the JiVitA-2 trial. In: Proceedings of the Micronutrient Forum. Consequences and control of micronutrient deficiencies: science, policy, and programs—defining the issues. Istanbul, Turkey. April 16–18, 2007.

139 Sazawal S, Black RE, Ramsan M, et al. Effect of zinc supplementation on mortality in children aged 1–48 months: a community-based randomised placebo-controlled trial. *Lancet* 2007; **369:** 927–34.

140 Tielsch JM, Khatry SK, Stoltzfus RJ, et al. Effect of routine prophylactic supplementation with iron and folic acid on preschool child mortality in southern Nepal: community-based, cluster-randomised, placebo-controlled trial. *Lancet* 2006; **367:** 144–52.

141 Bhandari N, Bahl R, Taneja S, et al. Substantial reduction in severe diarrheal morbidity by daily zinc supplementation in young north Indian children. *Pediatrics* 2002; **109:** e86.

142 Brooks WA, Santosham M, Naheed A, et al. Effect of weekly zinc supplements on incidence of pneumonia and diarrhoea in children younger than 2 years in an urban, low-income population in Bangladesh: randomised controlled trial. *Lancet* 2005; **366:** 999–1004.

143 Baqui AH, Black RE, El Arifeen S, et al. Effect of zinc supplementation started during diarrhoea on morbidity and mortality in Bangladeshi children: community randomised trial. *BMJ*. 2002; **325:** 1059.

144 Lira PI, Ashworth A, Morris SS. Effect of zinc supplementation on the morbidity, immune function, and growth of low-birth-weight, full-term infants in northeast Brazil. *Am J Clin Nutr* 1998; **68:** 418–24.

145 Bhutta ZA, Bird SM, Black RE, et al. Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. *Am J Clin Nutr* 2000; **72:** 1516–22.

146 Thilly CH, Delange F, Lagasse R, et al. Fetal hypothyroidism and maternal thyroid status in severe endemic goiter. *J Clin Endocrin Metabol* 1978; **47:** 354–60.

147 Pharoah POD, Connolly KJ. A controlled trial of iodinated oil for the prevention of endemic cretinism: A long term follow up. *Int J Epidemiol* 1987; **16:** 68–73.

148 Cobra C, Muhilal, Rusmil K, et al. Infant survival is improved by oral iodine supplementation. *J Nutr* 1997; **127:** 574–78.

149 Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev* 2006; **4:** CD004905.

150 UNICEF/WHO/UNU. Composition of a multi-micronutrient supplement to be used in pilot programmes among pregnant women in developing countries. New York: UNICEF, 1999.

151 The Supplementation with Multiple Micronutrients Intervention Trial (SUMMIT) Study Group. Effect of maternal multiple micronutrient supplementation on fetal loss and infant death in Indonesia: a double-blind cluster-randomised trial. *Lancet* (in press).

152 Gupta P, Ray M, Dua T, Radhakrishnan G, Kumar R, Sachdev HPS. Multimicronutrient supplementation for undernourished pregnant women and the birth size of their offspring: a double-blind, randomized, placebo-controlled trial. *Arch Pediatr Adolesc Med* 2007; **161:** 58–64.

153 Fawzi WW, Msamanga GI, Urassa W, et al. Vitamins and perinatal outcomes among HIV-negative women in Tanzania. *N Engl J Med* 2007; **356:** 1423–31.

154 van Rheenen P, de Moor L, Eschbach S, de Grooth H, Brabin B. Delayed cord clamping and hemoglobin levels in infancy: a randomised controlled trial in term babies. *Trop Med Int Health* 2007; **12:** 603–16.

155 Kugelman A, Borenstein-Levin L, Riskin A, et al. Immediate versus delayed umbilical cord clamping in premature neonates born <35 weeks: a prospective, randomized, controlled study. *Am J Perinatol* 2007; **24:** 307–15.

156 Ambrus JL Sr, Ambrus JL Jr. Nutrition and infectious diseases in developing countries and problems of acquired immunodeficiency syndrome. *Exp Biol Med* 2004; **229:** 464–72.

157 Rollins N. Toronto AIDS conference: where were the children? *Lancet* 2006; **368:** 1236–37.

158 Chang KC, Miklich DR, Barwise G, Chai H, Miles-Lawrence R. Linear growth of chronic asthmatic children: the effects of the disease and various forms of steroid therapy. *Clin Allergy* 1982; **12:** 369–78.

159 Solomons NW, Mazariegos M, Brown KH, Klasing K. The underprivileged, developing country child: environmental contamination and growth failure revisited. *Nutr Rev* 1993; **51:** 327–32.

160 Njagi JK. The effects of sulfadoxine-pyrimethamine intermittent treatment and pyrethroid impregnanted bed nets on malaria morbidity in pregnancy and birth weight in Bondo District, Kenya. PhD thesis, University of Nairobi, 2002.

161 ter Kuile FO, Terlouw DJ, Phillips-Howard PA, et al. Reduction of malaria during pregnancy by permethrin-treated bed nets in an area of intense perennial malaria transmission in western Kenya. *Am J Trop Med Hyg* 2003; **68:** 50–60.

162 Torlesse H, Hodges M. Albendazole therapy and reduced decline in Hb conc during pregnancy (Sierra Leone). *Trans R Soc Trop Med Hyg* 2001; **95:** 195–201.

163 Larocque R, Casapia M, Gotuzzo E, et al. A double-blind randomized controlled trial of antenatal mebendazole to reduce low birthweight in a hookworm-endemic area of Peru. *Trop Med Int Health* 2006; **11:** 1485–1495.

164 Gulani A, Nagpal J, Osmond C, Sachdev HP. Effect of administration of intestinal antihelmintic drugs on hemoglobin: systematic review of randomised controlled trials. *BMJ*. 2007; **334:** 1095.

165 Roberfroid D, Kolsteren P, Hoeree T, et al. Do growth monitoring and promotion programs answer the performance criteria of a screening program? A critical analysis based on a systematic review. *Trop Med Int Health* 2005; **10:** 1121–33.

166 Garner P, Panpanich R, Logan S. Is routine growth monitoring effective? A systematic review of trials. *Arch Dis Child* 2000; **82:** 197–201.

167 Ashworth A, Shrimpton R, Jamil K. Growth monitoring and promotion. Review of evidence of impact. *Matern Child Nutr* (in press).

168 Winikoff B, Castle MA. Defining maternal depletion syndrome. *Am J Public Health*. 1993 Jul; **83:** 1052.

169 Rutstein SO. Effects of preceding birth intervals on neonatal, infant and under-five years mortality and nutritional status in developing countries: evidence from the demographic and health surveys. *Int J Gynaecol Obstet* 2005 Apr; **89** (suppl 1)**:** S7–24.

170 Dewey KG, Cohen RJ. Does birth spacing affect maternal or child nutritional status? A systematic literature review. *Matern Child Nutr* 2007; **3:** 151–73.

171 Conde-Agudelo A, Rosas-Bermudez A, Kafury-Goeta AC. Birth spacing and risk of adverse perinatal outcomes: a meta-analysis. *JAMA*. 2006; **295:** 1809–23.

172 Conde-Agudelo A, Rosas-Bermudez A, Kafury-Goeta AC. Effects of birth spacing on maternal health: a systematic review. *Am J Obstet Gynecol.* 2007; **196:** 297–308.
173 Glassman A, Gaarder M, Todd J. Demand-side incentives for better health for the poor: Conditional cash transfer programms in Latin America and the Caribbean. Economic and Sector Studies Series, Inter-American Development Bank, December 2006.
174 Mesnard, A. Evaluation of the Familias en Acción Programme in Colombia: Do Conditional Subsidies Improve Education, Health and Nutritional Outcomes? Institute for Fiscal Studies, London. 2005.
175 Lagarde M, Haines A, Palmer N. Conditional cash transfers for improving uptake of health interventions in low- and middle-income countries: a systematic review. *JAMA* 2007; **298:** 1900–10.
176 Berti PR, Krasevec J, Fitzgerald S. A review of the effectiveness of agriculture interventions in improving nutrition outcomes. *Public Health Nutr* 2004; **7:** 599–609.
177 Faber M, Phungula MA, Venter SL, Dhansay MA, Benade AJ. Home gardens focusing on the production of yellow and dark-green leafy vegetables increase the serum retinol concentrations of 2–5-y-old children in South Africa. *Am J Clin Nutr* 2002; **76:** 1048–54.
178 Leroy JL, Frongillo EA. Can interventions to promote animal production ameliorate undernutrition? *J Nutr* 2007; **137:** 2311–16.
179 Gibson RS, Yeudall F, Drost N, Mtitimuni BM, Cullinan TR. Experiences of a community-based dietary intervention to enhance micronutrient adequacy of diets low in animal source foods and high in phytate: a case study in rural Malawian children. *J Nutr* 2003; **133** (suppl 2): 3992S–99S.
180 Yeudall F, Gibson RS, Cullinan TR, Mtimuni B. Efficacy of a community-based dietary intervention to enhance micronutrient adequacy of high-phytate maize-based diets of rural Malawian children. *Public Health Nutr* 2005; **8:** 826–36.
181 Sheikholeslam R, Kimiagar M, Siasi F, et al. Multidisciplinary intervention for reducing malnutrition among children in the Islamic Republic of Iran. *East Mediterr Health J* 2004; **10:** 844–52.
182 WHO. The use and interpretation of Anthropometry: report of a WHO Expert Committee. WHO Technical Report Series 854. Geneva: World Health Organization, 1999: 161–262.
183 UNICEF. State of the World's Children 2007. http://www.unicef.org/publications/index_36587.html (accessed Nov 7, 2007).
184 USAID. DHS StatCompiler. Calverton, MD, USA: Demographic and Health Surveys, 2007. www.measuredhs.com (accessed Dec 10, 2007).
185 Stoltzfus R, Mullany L, Black RE. Iron deficiency anemia. In Comparative Quantification of Health Risks. WHO 2004. http://www.who.int/publications/cra/en/ (accessed Nov 7, 2007).
186 Prudhon C, Briend A, Zita Prinzo W, Daelmans B, Mason J (guest eds). WHO, UNICEF, and SCN Informal Consultation on Community-Based Management of Severe Malnutrition Management of Severe Malnutrition in Children. SCN Nutrition Policy Paper No. 21. Food and Nutrition Bulletin, 2006; **27** (supplement): S3–108.
187 Khan KS, Wojdyla D, Say L, Gulmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: a systematic review. *Lancet* 2006; **367:** 1066–74.
188 Steckel RH. Health, nutrition and physical well-being. In: Carter S, Gartner S, Haines M, Olmstead A, Sutch R, Wright G, eds. Historical statistics of the United States: Millennial Edition. New York: Cambridge University Press, 2002.
189 Gillespie S, Mason J, Martorell R. How Nutrition Improves. ACC/SCN Nutrition Policy Discussion Paper 15, United Nations Administrative Committee on Coordination/Sub-Committee on Nutrition, Geneva. http://www.unsystem.org/scn/archives/npp15/index.htm (accessed Nov 7, 2007).
190 Ramakrishnan U, Martorell R, Schroeder DG, Flores R. Role of intergenerational effects on linear growth. *J Nutr* 1999; **129** (2S suppl): 544S–49S.
191 Stein AD, Barnhart HX, Wang M, et al. Comparison of linear growth patterns in the first three years of life across two generations in Guatemala. *Pediatrics* 2004; **113:** e270–75.
192 Ruel MT, Menon P, Habicht J-P, et al. Age-based preventive targeting of food assistance and behaviour change communication for reduction of childhood undernutrition in Haiti: a cluster randomised trial. *Lancet* (in press).
193 Kristjansson EA, Robinson V, Petticrew M, et al. School feeding for improving the physical and psychosocial health of disadvantaged elementary school children. *Cochrane Database Syst Rev* 2007; **1:** CD004676.
194 Darmstadt GL, Bhutta ZA, Cousens S, Adam T, Walker N, de Bernis L, for the Lancet Neonatal Survival Steering Team. Evidence-based, cost-effective interventions: how many newborn babies can we save? *Lancet* 2005; **365:** 977–88.
195 Victora CG, Fenn B, Bryce J, Kirkwood BR. Co-coverage of preventive interventions and implications for child-survival strategies: evidence from national surveys. *Lancet* 2005; **366:** 1460–66.
196 Sempertegui F, Estrella B, Egas J, et al. Pneumonia adversely affects growth in children. 55th Annual Meeting of the American Society of Tropical Medicine and Hygiene. Atlanta, GA Abstract 771.
197 Reid M, Forrester T, Badaloo A, Heird WC, Jahoor F. Supplementation with aromatic amino acids improves leucine kinetics but not aromatic amino acid kinetics in infants with infection, severe malnutrition, and edema. *J Nutr* 2004; **134:** 3004–10.
198 Luby SP, Agboatwalla M, Feikin DR, et al. Effect of hand washing on child health: a randomised controlled trial. *Lancet* 2005; **366:** 225–33.
199 Semba RD, de Pee S, Berger SG, Martini E, Ricks MO, Bloem MW. Malnutrition and infectious disease morbidity among children missed by the childhood immunization program in Indonesia. *Southeast Asian J Trop Med Public Health* 2007; **38:** 120–29.
200 Arnesen T, Kapiriri L. Can the value choices in DALYs influence global priority-setting? *Health Policy* 2004; **70:** 137–49.
201 Grantham-McGregor S, Cheung YB, Cueto S, Glewwe P, Richter L, Strupp B. International Child Development Steering Group. Developmental potential in the first 5 years for children in developing countries. *Lancet* 2007; **369:** 60–70.
202 Allen LH, Gillespie SR. What works? A review of the efficacy and effectiveness of nutrition interventions. ACC/SCN Nutrition Policy Paper 19; Asian Development Bank (ADB) Nutrition and Development Series 5. Geneva and Manila: United Nations Administrative Committee on Coordination/Sub-Committee on Nutrition, and the Asian Development Bank, 2001.
203 Hill Z, Kirkwood B, Edmond K. Family and community practices that promote child survival, growth and development: a review of the evidence. World Health Organization, March 2004.
204 World Bank. Repositioning nutrition as central to development. Washington DC: World Bank, 2005.
205 Zimmermann MB, Biebinger R, Rohner F, et al. Vitamin A supplementation in children with poor vitamin A and iron status increases erythropoietin and hemoglobin concentrations without changing total body iron. *Am J Clin Nutr* 2006; **84:** 580–86.
206 Moore SE, Jalil F, Ashraf R, Szu SC, Prentice AM, Hanson LA. Birth weight predicts response to vaccination in adults born in an urban slum in Lahore, Pakistan. *Am J Clin Nutr* 2004; **80:** 453–59.
207 Olaiz-Fernández G, Rivera-Dommarco J, Shamah-Levy T, et al. Encuesta nacional de salud y nutrición 2006 [National survey of health and nutrition 2006]. Cuernavaca, Mexico: Instituto Nacional de Salud Pública, 2006.
208 Adato M, Feldman S. Safety nets. 2020 Focus 6 (Empowering women to achieve food security), Brief 11 of 12, August 2001. http://www.ifpri.org/2020/focus/focus06/focus06_11.htm (accessed Nov 6, 2007).
209 Wu T, Liu GJ, Li P, Clar C. Iodised salt for preventing iodine deficiency disorders. *Cochrane Database Syst Rev* 2002; **3:** CD003204.