Maternal and Child Nutrition 1

Maternal and child undernutrition and overweight in low-income and middle-income countries

Robert E Black, Cesar G Victora, Susan P Walker, Zulfiqar A Bhutta, Parul Christian*, Mercedes de Onis*, Majid Ezzati*, Sally Grantham-McGregor*, Joanne Katz*, Reynaldo Martorell*, Ricardo Uauy*, and the Maternal and Child Nutrition Study Group†*

Maternal and child malnutrition in low-income and middle-income countries encompasses both undernutrition and a growing problem with overweight and obesity. Low body-mass index, indicative of maternal undernutrition, has declined somewhat in the past two decades but continues to be prevalent in Asia and Africa. Prevalence of maternal overweight has had a steady increase since 1980 and exceeds that of underweight in all regions. Prevalence of stunting of linear growth of children younger than 5 years has decreased during the past two decades, but is higher in south Asia and sub-Saharan Africa than elsewhere and globally affected at least 165 million children in 2011; wasting affected at least 52 million children. Deficiencies of vitamin A and zinc result in deaths; deficiencies of iodine and iron, together with stunting, can contribute to children not reaching their developmental potential. Maternal undernutrition contributes to fetal growth restriction, which increases the risk of neonatal deaths and, for survivors, of stunting by 2 years of age. Suboptimum breastfeeding results in an increased risk for mortality in the first 2 years of life. We estimate that undernutrition in the aggregate—including fetal growth restriction, stunting, wasting, and deficiencies of vitamin A and zinc along with suboptimum breastfeeding—is a cause of 3·1 million child deaths annually or 45% of all child deaths in 2011. Maternal overweight and obesity result in increased maternal morbidity and infant mortality. Childhood overweight is becoming an increasingly important contributor to adult obesity, diabetes, and non-communicable diseases. The high present and future disease burden caused by malnutrition in women of reproductive age, pregnancy, and children in the first 2 years of life should lead to interventions focused on these groups.

Published **Online** June 6, 2013 http://dx.doi.org/10.1016/S0140-6736(13)60937-X

This is the first in a **Series** of four papers about maternal and child nutrition

*Members listed alphabetically

†Members listed at end of paper

Johns Hopkins University, Bloomberg School of Public Health, Baltimore, MD, USA (Prof R E Black MD, Prof P Christian DrPH, Prof J Katz ScD)**; Universidade Federal de Pelotas, Pelotas, Rio Grande do Sol, Brazil** (Prof C G Victora MD)**; The University of the West Indies, Tropical Medicine Research Institute, Mona Campus, Kingston, Jamaica** (Prof S P Walker PhD)**; The Aga Khan University and Medical Center, Department of Pediatrics, Karachi, Pakistan** (Prof Z A Bhutta PhD)**; World**

Introduction

Maternal and child malnutrition, encompassing both undernutrition and overweight, are global problems with important consequences for survival, incidence of acute and chronic diseases, healthy development, and the economic productivity of individuals and societies. Maternal and child undernutrition, including stunting, wasting, and deficiencies of essential vitamins and minerals, was the subject of a Series[1–5] in *The Lancet* in 2008, which quantified their prevalence, short-term and long-term consequences, and potential for reduction through high and equitable coverage of proven nutrition interventions. The Series identified the need to focus on the crucial period of pregnancy and the first 2 years of life—the 1000 days from conception to a child's second birthday during which good nutrition and healthy growth have lasting benefits throughout life. The 2008 Series also called for greater national priority for nutrition programmes, more integration with health programmes, enhanced intersectoral approaches, and more focus and coordination in the global nutrition system of international agencies, donors, academia, civil society, and the private sector. 5 years after that series, we intend not only to reassess the problems of maternal and child undernutrition, but also to examine the growing problems of overweight and obesity for women and children and their consequences in low-income and middle-income countries (LMICs). Many of these countries are said to suffer the so-called double burden of malnutrition, with continuing stunting of growth and deficiencies of essential nutrients along with obesity in national populations and within families. We also want to assess national progress in nutrition programmes and international actions consistent with our previous recommendations.

Key messages

- Iron and calcium deficiencies contribute substantially to maternal deaths
- Maternal iron deficiency is associated with babies with low weight (<2500 g) at birth
- Maternal and child undernutrition, and unstimulating household environments, contribute to deficits in children's development and health and productivity in adulthood
- Maternal overweight and obesity are associated with maternal morbidity, preterm birth, and increased infant mortality
- Fetal growth restriction is associated with maternal short stature and underweight and causes 12% of neonatal deaths
- Stunting prevalence is slowly decreasing globally, but affected at least 165 million children younger than 5 years in 2011; wasting affected at least 52 million children
- Suboptimum breastfeeding results in more than 800 000 child deaths annually
- Undernutrition, including fetal growth restriction, suboptimum breastfeeding, stunting, wasting, and deficiencies of vitamin A and zinc, cause 45% of child deaths, resulting in 3·1 million deaths annually
- Prevalence of overweight and obesity is increasing in children younger than 5 years globally and is an important contributor to diabetes and other chronic diseases in adulthood
- Undernutrition during pregnancy, affecting fetal growth, and the first 2 years of life is a major determinant of both stunting of linear growth and subsequent obesity and non-communicable diseases in adulthood

Health Organization, Department of Nutrition for Health and Development, Geneva, Switzerland (M de Onis MD)**; Imperial College of London, St Mary's Campus, School of Public Health, MRC-HPA Centre for Environment and Health, Department of Epidemiology and Biostatistics, London, UK** (Prof M Ezzati PhD)**; Institute of Child Health, University College London, London, UK** (Prof S Grantham-McGregor FRCP)**; The University of the West Indies, Mona, Jamaica** (Prof S Grantham-McGregor)**; Emory University, Atlanta, GA, USA** (Prof R Martorell PhD)**; and London School of Hygiene and Tropical Medicine, London, UK** (Prof R Uauy PhD)

Correspondence to: Prof Robert Black, Johns Hopkins University, Bloomberg School of Public Health, Baltimore, MD 21205, USA
rblack@jhsph.edu

See Online for appendix

The present Series is guided by a framework (figure 1) that shows the means to optimum fetal and child growth and development, rather than the determinants of undernutrition as shown in the conceptual model developed by UNICEF and used in the 2008 Series.[1] This new framework shows the dietary, behavioural, and health determinants of optimum nutrition, growth, and development and how they are affected by underlying food security, caregiving resources, and environmental conditions, which are in turn shaped by economic and social conditions, national and global contexts, resources, and governance. This Series examines how these determinants can be changed to enhance growth and development. These changes include nutrition-specific interventions that address the immediate causes of suboptimum growth and development. The framework shows the potential effects of nutrition-sensitive interventions that address the underlying determinants of malnutrition and incorporate specific nutrition goals and actions. It also shows the ways that an enabling environment can be built to support interventions and programmes to enhance growth and development and their health consequences. In the first paper we assess the prevalence of nutritional conditions and their health and development consequences. We deem a life-course perspective to be essential to conceptualise the nutritional effects and benefits of interventions. The nutritional status of women at the time of conception and during pregnancy is important for fetal growth and development, and these factors, along with nutritional status in the first 2 years of life, are important determinants of both undernutrition in childhood and obesity and related diseases in adulthood. Thus, we organise this paper to consider prevalence and consequences of nutritional conditions during the life course from adolescence to pregnancy to childhood and discuss the implications for adult health. In the second paper, we describe evidence supporting nutrition-specific interventions and the health effects and costs of increasing their population coverage. In the third paper we examine nutrition-sensitive interventions and approaches and their potential to improve nutrition. In the fourth paper we examine the features of an enabling environment that are needed to provide support for nutrition programmes and how they can be favourably changed. Finally, in a Comment[6] we will examine the desired national and global response to address nutritional and developmental needs of women and children in LMICs.

Prevalence and consequences of nutritional conditions

Adolescent nutrition

Adolescent nutrition is important to the health of girls and is relevant to maternal nutrition. There are 1·2 billion adolescents (aged 10–19 years) in the world, 90% of whom live in LMICs. Adolescents make up 12% of the population in industrialised countries, compared with 19% in LMICs (appendix p 2 shows values for ten countries studied in depth).[7] Adolescence is a period of rapid growth and maturation from childhood to adulthood. Indeed, some researchers have argued that adolescence is a period with some potential for height catch-up in children with

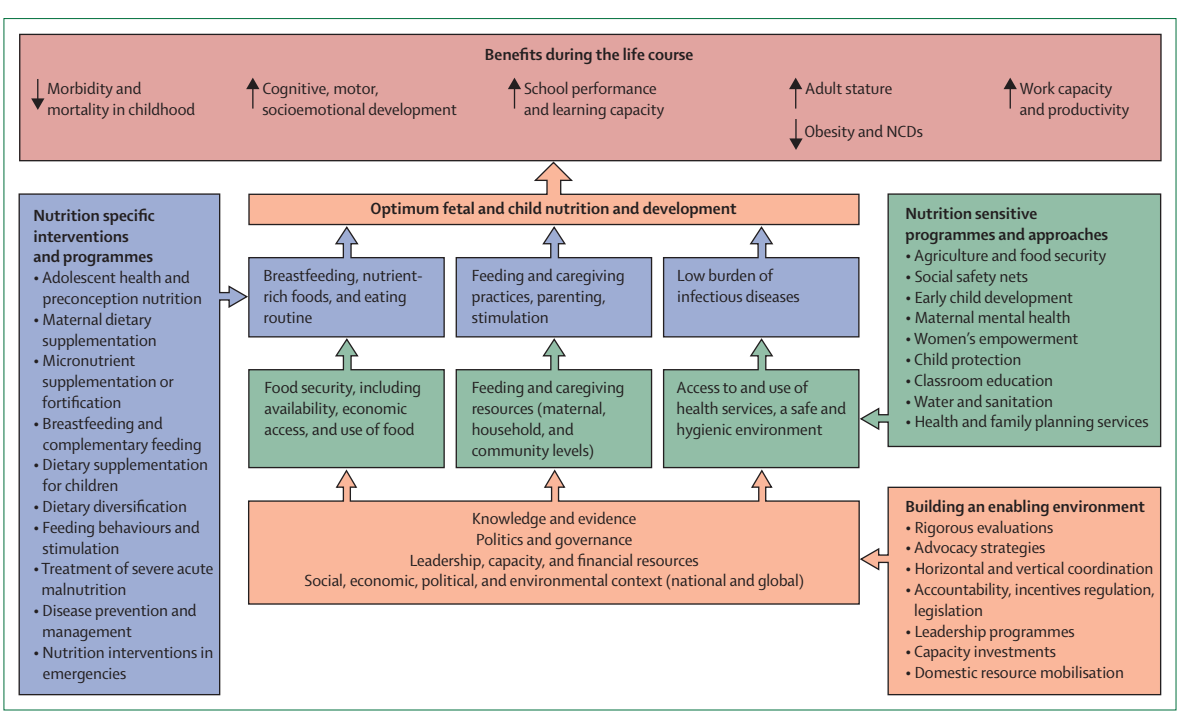

Figure 1: **Framework for actions to achieve optimum fetal and child nutrition and development**

stunting from early childhood.[8] Adolescent fertility is three times higher in LMICs than in high-income countries. Pregnancies in adolescents have a higher risk of complications and mortality in mothers[9] and children[10] and poorer birth outcomes than pregnancies in older women.[10,11] Furthermore, pregnancy in adolescence will slow and stunt a girl's growth.[12,13] In some countries, as many as half of adolescents are stunted (height-for-age *Z* score [HAZ] <–2), increasing the risk of poor perinatal outcomes in their offspring (appendix p 2). We used age-specific, low body-mass index (BMI) cutoffs (BMI *Z* score [BMIZ] <–2) from the WHO reference for children aged 5–19 years to examine ten selected countries; in these locations as many as 11% (India) of adolescent girls are thin. In these countries, prevalence of high BMI for age, defined as BMIZ >2 (obesity), is as high as 5% (Brazil; appendix p 2). Adolescents have as high a prevalence of anaemia as women aged 20–24 years. In India, for example, 55·8% of adolescents aged 15–19 years and 56·7% of women aged 20–24 years were anaemic;[14] corresponding values for Guatemala were 21·0% and 20·4 %, respectively.[15]

Maternal nutrition

Prevalence of low BMI (<18·5 kg/m²) in adult women has decreased in Africa and Asia since 1980, but remains higher than 10% in these two large developing regions (figure 2). During the same period, prevalence of overweight (BMI ≥25 kg/m²) and obesity (BMI ≥30 kg/m²) has been rising in all regions, together reaching more than 70% in the Americas and the Caribbean and more than 40% in Africa by 2008.[16,17]

Few studies have examined the risk of maternal mortality in relation to maternal anthropometry with a prospective design. In one study in Nepal[18] of about 22 000 women, mid upper arm circumference during

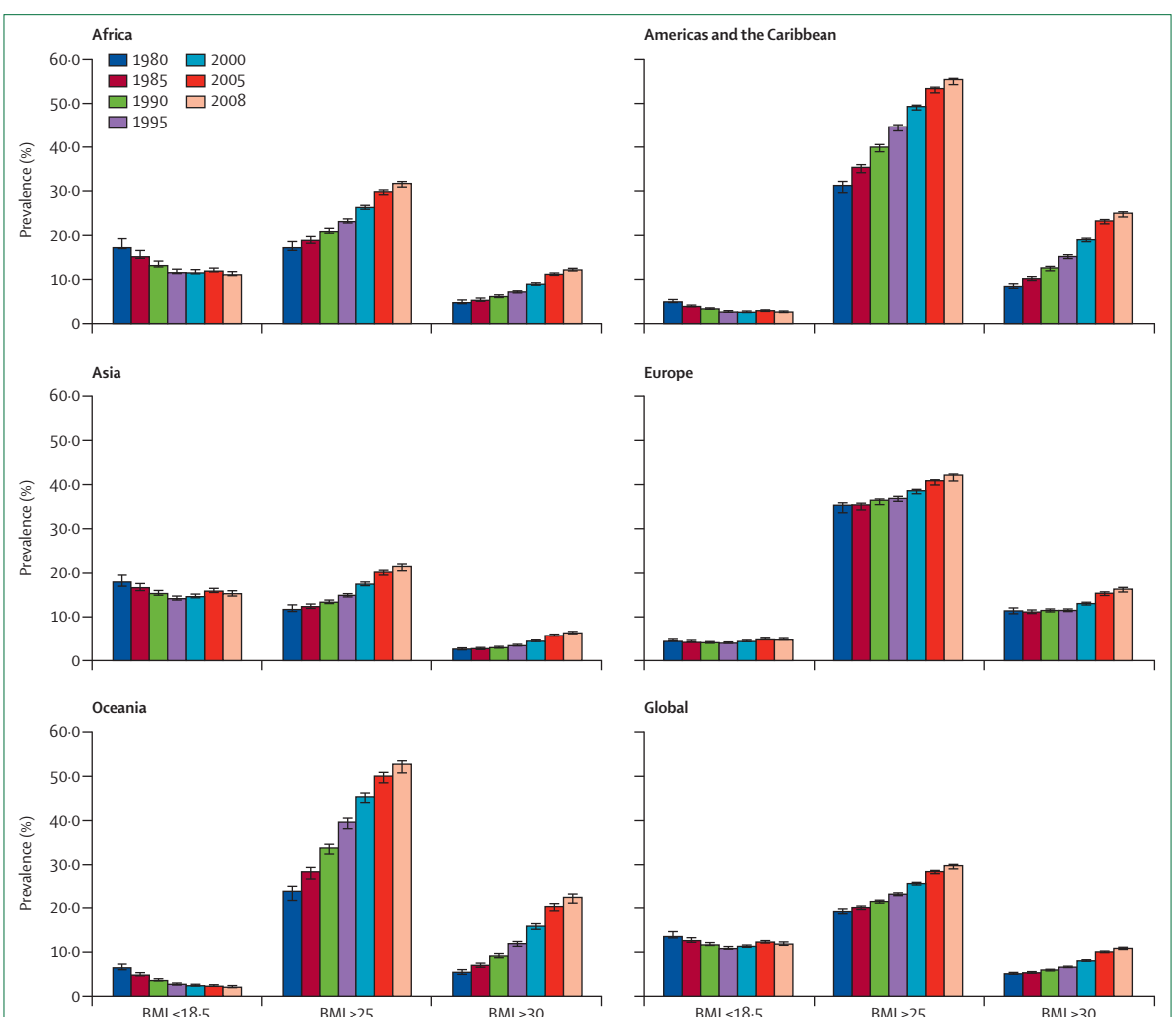

Figure 2: **Trends in thinness (BMI <18·5 kg/m²), overweight (BMI ≥25 kg/m²), and obesity (BMI ≥30 kg/m²), using population weighted average prevalences for women aged 20–49 years UN regions and globally, 1980–2008**
Error bars are 95% CIs. BMI=body-mass index.

pregnancy was inversely associated with all-cause maternal mortality up to 42 days post-partum after adjusting for numerous factors. An inverse association exists between maternal height and the risk of dystocia (difficult labour), as measured by cephalopelvic disproportion or assisted or caesarean deliveries.[19–23]

Figure 2 also shows trends for overweight and obesity in women aged 20–49 years in different UN regions. Oceania, Europe, and the Americas had the highest proportion of overweight and obese women; however northern and southern Africa, and central and west Asia also had high prevalences (appendix p 3).

Maternal obesity leads to several adverse maternal and fetal complications during pregnancy, delivery, and post-partum.[24] Obese pregnant women (pre-pregnant BMI ≥30 kg/m²) are four times more likely to develop gestational diabetes mellitus and two times more likely to develop pre-eclampsia compared with women with a BMI 18·5–24·9 kg/m²).[25–28] During labour and delivery, maternal obesity is associated with maternal death, haemorrhage, caesarean delivery, or infection;[29–31] and a higher risk of neonatal and infant death,[32] birth trauma, and macrosomic infants.[33–37] In the post-partum period, obese women are more likely to delay or fail to lactate and to have more weight retention than women of normal weight.[38] Obese women with a history of gestational diabetes have an increased risk of subsequent type two diabetes, metabolic syndrome, and cardiovascular disease.[39] The early intrauterine environment has a role in programming phenotype, affecting health in later life. Maternal overweight and obesity at the time of pregnancy increases the risk for childhood obesity that continues into adolescence and early adulthood, potentiating the transgenerational transmission of obesity.[40,41]

Maternal vitamin deficiencies

Anaemia and iron

Anaemia (haemoglobin <110 g/L), which might be attributable to low consumption or absorption in the diet or to blood loss, such as from intestinal worms, is highly prevalent during pregnancy. This Series focuses on anaemia amenable to correction with iron supplementation.[42] To establish the importance of iron deficiency as a cause of maternal anaemia we used the results of trials of iron supplementation to work out the shift in the population haemoglobin distribution. A meta-analysis of the effects of iron supplementation trials showed that, among pregnant women with anaemia at baseline, iron supplementation led to a 10·2 g/L increase in haemoglobin.[43] The corresponding figure for children was 8·0 g/L.[44] We applied these shifts to the present distributions of haemoglobin estimated by Stevens and colleagues[42] and calculated the proportion of pregnant women with anaemia whose blood haemoglobin would increase to at least 110 g/L. We likewise calculated the proportion of severe anaemia that would increase to at least 70 g/L. These results constitute the prevalence of iron amenable or iron deficiency anaemia (IDA) or severe IDA, defined as the proportion of anaemia or severe anaemia that would be reduced if only iron was provided, holding other determinants of anaemia unchanged. With this approach in 2011, Africa had the highest proportion of IDA for pregnant women followed closely by Asia (table 1,[45–47] appendix p 4). Likewise, Africa had the highest prevalence of severe IDA, but in all regions prevalence was less than 1%.

Our previous analyses[48] showed that anaemia in pregnancy increased the risk of maternal mortality. An updated analysis[49] with ten studies (four more than the

	Vitamin A deficiency[45]				Iodine deficiency[46] (UIC <100 µg/L)	Zinc deficiency[47] (weighted average of country means)	Iron deficiency anaemia (haemoglobin <110 g/L)	
	Children <5 years		Pregnant women				Children <5 years	Pregnant women
	Night blindness	Serum retinol <0·70 µmol/L	Night blindness	Serum retinol <0·70 µmol/L				
Global	0·9% (0·1–1·8)	33·3% (29·4–37·1)	7·8% (6·5–9·1)	15·3% (6·0–24·6)	28·5% (28·2–28·9)	17·3% (15·9–18·8)	18·1% (15·6–20·8)	19·2% (17·1–21·5)
Africa	2·1% (1·0–3·1)	41·6% (34·4–44·9)	9·4% (8·1–10·7)	14·3% (9·7–19·0)	40·0% (39·4–40·6)	23·9% (21·1–26·8)	20·2% (18·6–21·7)	20·3% (18·3–22·4)
Americas and the Carribean	0·6% (0·0–1·3)	15·6% (6·6–24·5)	4·4% (2·7–6·2)	2·0% (0·4–3·6)	13·7% (12·5–14·8)	9·6% (6·8–12·4)	12·7% (9·8–16·0)	15·2% (11·7–18·6)
Asia	0·5% (0·0–1·3)	33·5% (30·7–36·3)	7·8% (6·6–9·0)	18·4% (5·4–31·4)	31·6% (30·7–32·5)	19·4% (16·9–22·0)	19·0% (14·5–23·4)	19·8% (15·8–23·5)
Europe	0·7% (0·0–1·5)	14·9% (0·1–29·7)	2·9% (1·1–4·6)	2·2% (0·0–4·3)	44·2% (43·5–45·0)	7·6% (6·2–9·1)	12·1% (7·8–16·2)	16·2% (12·6–19·7)
Oceania	0·5% (0·1–1·0)	12·6% (6·0–19·2)	9·2% (0·3–18·2)	1·4% (0·0–4·0)	17·3% (16·6–18·1)	5·7% (1·0–10·3)	15·4% (7·0–25·2)	17·2% (9·7–25·6)

Data are % (95% CI). UIC=urine iodine concentration.

Table 1: **Prevalence of vitamin A deficiency (1995–2005), iodine deficiency (2013), inadequate zinc intake (2005), and iron deficiency anaemia (2011)**

previous analysis) showed that the odds ratio (OR) for maternal deaths was 0·71 (95% CI 0·60–0·85) for a 10 g/L greater mean haemoglobin in late pregnancy. Only two of the ten studies adjusted for socioeconomic confounding variables; one showed no attenuation and the other a 20% attenuation of the effect.

There is strong biological plausibility for a causal link between maternal IDA and adverse birth outcomes including low birthweight and increased perinatal mortality.[50–52] A meta-analysis[53] that included 11 trials indentified a significant 20% reduction in the risk of low birthweight associated with antenatal supplementation with iron alone or combined with folic acid (relative risk [RR] 0·80, 95% CI 0·71–0·90). A previous Cochrane review[54] had much the same findings. Dibley and colleagues[55] pooled data from demographic and health surveys from Indonesia for 1994, 1997, 2002–03, and 2007 and showed that risk of death of children younger than 5 years was reduced by 34% when the mother consumed any iron-folic acid supplements (hazard ratio [HR] 0·66; 95% CI 0·53–0·81). Dibley and colleagues further showed that the protective effect was greatest for deaths on the first day of life (0·40; 0·21–0·77), but the protective effect was also shown for neonatal deaths (0·69; 95% CI 0·49–0·97) and post-neonatal deaths (0·74; 0·56–0·99). A randomised controlled trial[56] from China showed a significant 54% (RR 0·46, 95% CI 0·21–0·98) reduction in neonatal mortality with antenatal iron and folic acid supplementation compared with folic acid alone as control. In Nepal, mortality from birth to 7 years was reduced by 31% (HR 0·69, 95% CI 0·49–0·99) in the offspring of mothers who had received iron and folic acid during pregnancy compared with controls who received vitamin A only.[57]

Randomised controlled trials from high-income countries have shown benefits of iron supplementation for improved maternal mental health and reduced fatigue.[58] Evidence from LMICs for the effect of maternal IDA on mothers' mental health and mother-child interactions is scarce. In a small South African trial,[59] iron supplementation of women with IDA from 10 weeks post-partum to 9 months led to lower maternal depression and perceived stress at 9 months compared with placebo. At 9 months, iron supplemented mothers had better maternal-child interactions.[60] By contrast, in Bangladesh higher levels of maternal iron supplementation decreased the quality of maternal-child interaction at age 3–4 months and had no effect on maternal distress (anxiety and depression).[61]

There is some evidence for whether maternal IDA affects child development. Infants of mothers identified as having IDA at 6–8 weeks post-partum had lower developmental levels at 10 weeks and 9 months compared with infants of control mothers without IDA.[60] In Nepal, children whose mothers received iron and folate supplementation during pregnancy had better general intelligence and cognitive functioning at age 7–9 years compared with children of mothers receiving placebo, suggesting that benefits can be detected in later childhood when more complex tasks can be measured.[62]

Vitamin A

Maternal vitamin A deficiency can cause visual impairment and possibly other health consequences. Deficiency is assessed in pregnant women as either a history of night blindness or serum or plasma retinol concentrations of less than 0·70 µmol/L (subclinical vitamin A deficiency). WHO provides prevalence estimates for 1995–2005 from 64 countries, which we used for estimates for the UN world regions (table 1).[45] Globally, the prevalence of night blindness in pregnant women is estimated to be 7·8% (95% CI 7·0–8·7), affecting 9·7 million women. An estimated 15·3% (7·4–23·2) of pregnant women globally (19·1 million women) have deficient serum retinol concentrations. The degree to which night blindness and low serum retinol overlap is not accounted for in this estimation, but night blindness is known to be associated with a four-times higher odds of low serum retinol (OR 4·02, 95% CI 2·2–7·4).[63] Night blindness is reduced by vitamin A supplementation in pregnancy.[63,64] Maternal night blindness has been associated with increased low birthweight[64] and infant mortality,[65] yet trials of vitamin A in pregnancy have not showed significant effects on these outcomes.[66–69]

Zinc

Zinc is a key micronutrient with a ubiquitous role in biological functions, including protein synthesis, cellular division, and nucleic acid metabolism. Estimates revised in 2012 suggest that 17% of the world's population is at risk of zinc deficiency, on the basis of an analysis of national diets.[47] Excess losses of zinc during diarrhoea also contribute to zinc deficiency. The effect of subclinical zinc deficiency (defined as low plasma zinc concentration without obvious signs of zinc deficiency) in women of reproductive age and during pregnancy on health and development outcomes is poorly understood, although zinc deficiency has been suggested as a risk factor with adverse long-term effects on growth, immunity, and metabolic status of surviving offspring.[70] Zinc deficiency due to a rare genetic abnormality—acrodermatitis enteropathica—in pregnancy results in a high risk of preterm and prolonged labour, post-partum haemorrhage, and fetal growth restriction.[70,71] A review of supplementation trials with zinc in pregnancy showed a significant 14% reduction in preterm births in women in low-income settings, but no significant effect on low birthweight.[72]

Iodine

Maternal iodine deficiency is of concern in regard to adverse effects on fetal development, yet few countries have nationally representative data from large-scale surveys of urinary iodine concentration in pregnant women. Because of the correlation between urinary iodine concentration in pregnant women and children

aged 6–12 years (r^2 0·69),[73] status assessment in school-age children is used to estimate country, regional, and global prevalence of iodine deficiency. Global estimates of iodine deficiency suggest that 28·5% of the world's population or 1·9 billion individuals are iodine-deficient (table 1).[46,74] This figure represents largely mild deficiency (defined as urinary iodine concentration of 50–99 ug/L).

Severe iodine deficiency in pregnancy causes cretinism, which can be eliminated with iodine supplementation before conception or in the first trimester of pregnancy.[75] Furthermore, two meta-analyses showed average deficits of 12·5–13·5 intelligence quotient (IQ) points in children associated with iodine deficiency of their mothers in pregnancy; however, they controlled for only a limited number of socioeconomic confounders.[76,77] A review of the effects of iodine supplementation in deficient populations showed a small increase in birthweight.[78] Effects of mild or moderate iodine deficiency on brain development are not well established.[78,79] The index of iodine deficiency (urinary iodine concentration) is a population measure and not an individual one,[80] therefore some individuals in regions of mild to moderate deficiency might have more severe deficiency.

Folate

The global prevalence of folate deficiency has not been estimated because of the scarcity of suitable population-based data.[81] A substantial proportion of neural tube defects (congenital malformations of the spinal cord and brain) are related to inadequate consumption of folic acid around the time of conception, in some populations associated with genetic factors that increase the need for dietary folic acid. A Cochrane review[82] in 2010 included five trials of folic acid (a synthetic form of folate) supplementation and identified a 72% (RR 0·28; 95% CI 0·15–0·52) reduction in the risk of neural tube defects. A more recent systematic review had much the same findings and estimated that in 2005 56 000 deaths were attributable to insufficient dietary folic acid.[83] These deaths were not added to the total deaths associated with undernutrition in the present analysis, because of the uncertainty about this estimate.

Calcium and vitamin D

Calcium is an essential nutrient for several body functions, including enzymatic and hormonal homoeostasis. Evidence for the association between maternal dietary calcium intake and maternal bone density and fetal mineralisation is inconsistent.[84] Epidemiological evidence does show an inverse association between calcium intake and development of hypertension in pregnancy.[85,86] Gestational hypertensive disorders are the second leading cause of maternal morbidity and mortality and are associated with increased risk of preterm birth and fetal growth restriction.[87,88]

Substantial evidence suggests that calcium supplementation in pregnancy is associated with a reduction in gestational hypertensive disorders and preterm birth.[89,90] However, the effect varies according to the baseline calcium intake of the population and pre-existing risk factors. A review of 15[91] randomised controlled trials suggested that calcium supplementation during pregnancy was associated with a reduction in the risk of gestational hypertension and a 52% reduction in the incidence of pre-eclampsia, along with a 24% reduction in preterm birth and an increase in birthweight of 85 g. There was no effect on low birthweight or perinatal or neonatal mortality. The effect was mainly noted in populations with low calcium intake.[92] The effects of calcium supplementation interventions are described in the accompanying report by Zulfiqar A Bhutta and colleagues.[93]

The US Institute of Medicine has defined adequate vitamin D status as having serum 25-hydroxyvitamin D ([OH]D) concentrations greater than 50 nmol/L in both the general population and pregnant women;[94] serum concentrations of less than 25 nmol/L denote vitamin D deficiency whereas concentrations of less than 50 nmol/L denote vitamin D insufficiency.[95] Although few nationally representative surveys exist for vitamin D status, an estimated 1 billion people globally residing in diverse geographies, many in LMICs, might be vitamin D insufficient or deficient.[96–103]

Vitamin D has an essential role in fetal development, ensuring fetal supply of calcium for bone development, enabling immunological adaptation required to maintain normal pregnancy, preventing miscarriage, and promoting normal brain development.[99,104–108] Poor maternal vitamin D status has been associated with severe pre-eclampsia (new-onset gestational hypertension and proteinuria after 20 weeks of gestation) in turn leading to an increased risk of perinatal morbidity and mortality.[99,109,110] Maternal vitamin D deficiency, especially in early pregnancy, has been associated with risk of pre-eclampsia (OR 2·09, 95% CI 1·50–2·90), preterm birth (1·58, 1·08–2·31), and small-for-gestational age (SGA; 1·52, 1·08–2·25).[109,111] A systematic review of three trials of vitamin D in pregnancy showed an overall reduction of low birthweight of borderline significance (relative risk [RR] 0·48; 95% CI 0·23–1·01).[111] These associations need to be better quantified before they can be included in the global disease burden related to undernutrition.

Effect of maternal stature or BMI on fetal growth restriction or postnatal growth

Maternal characteristics

The 2008 Maternal and Child Undernutrition Series examined the association of maternal nutritional status (BMI and short stature) and fetal growth restriction, defined as low birthweight at term. Here, we use data from nine (height) and seven (BMI) population-based

cohort studies and WHO perinatal facility-based data for 24 countries to examine associations separately for term and preterm SGA in LMICs.[112–121] Maternal stunting (height <145 cm) put infants at risk of term and preterm SGA (appendix p 5). Low maternal BMI in early pregnancy also put infants at higher risk of SGA (appendix p 5). BMI of 25 or greater was somewhat protective against term and preterm SGA (appendix p 5). Notably, most women in the BMI category of greater than 25 kg/m² were very mildly overweight with very few obese women, which might explain the protective effect.

Maternal stature is a composite indicator representing genetic and environmental effects on the growing period of childhood. In a study[122] involving 109 Demographic Health Surveys, analyses adjusted for wealth, education, and urban or rural residence showed that the absolute risk of dying among children younger than 5 years born to the tallest mothers (≥160 cm) was 0·073 (95% CI 0·072–0·074) and to those born to the shortest mothers (<145 cm) was 0·128 (0·126–0·130). The corresponding absolute risk for a child being stunted was 0·194 (0·192–0·196) for the tallest mothers and 0·682 (0·673–0·690) for the shortest. The association with wasting was significant but much weaker.[122]

Fetal growth restriction

Previous global and regional estimates of fetal growth restriction used the term low birthweight as a proxy for being SGA in the absence of population-based birthweight and gestational age data at that time.[1] Through recent analyses, we now have estimates of SGA prevalence from 22 population-based cohort studies and 23 countries with facility-based data,[114] which were used to model SGA as a function of low birthweight and other covariates (neonatal mortality rate, representativeness of facility delivery) to obtain country-specific SGA prevalence for 2010.[123] The numbers on which the model is based include all livebirths, but exclude babies who died so soon after birth that they were not weighed. Imputing birthweight for these infants did not change the estimation of SGA prevalence, although it did increase the mortality risk associated with being born SGA. Figure 3 shows prevalence of SGA separated into term and preterm SGA. By our estimate, in 2010 32·4 million babies were born SGA, 27% of all births in LMICs regions. When comparing the estimated numbers of children with SGA with those affected by stunting or wasting, it is important to note that the cutoff for SGA is the 10th centile of a reference population, whereas the cutoffs for wasting or stunting are two Z scores below the median, or the 2·3rd centile. Appendix p 8 shows prevalence with 95% CIs of term and preterm SGA by UN subregions. Notably, only 20% of preterm births in LMICs were also SGA. Appendix p 8 show the ten countries with the highest number of SGA births in 2010.

Associations between fetal growth restriction and infant survival have been previously reported,[124–129] although it is difficult to compare associations across studies that use different reference populations for SGA. Previous studies have also not separated SGA into term and preterm. In a pooled-analysis[130] of 22 population-based cohort studies in LMICs in Asia, sub-Saharan Africa, and Latin America, the RR for neonatal (1–28 day) mortality associated with SGA (<10th centile) was 1·83 (95% CI 1·34–2·50) and for post-neonatal (29–365 day) mortality was 1·90 (1·32–2·73), compared with appropriate-for-gestational-age (AGA) infants. The RR for term SGA was 3·06 (95% CI 2·21–4·23) for neonatal mortality and 1·98 (1·39–2·81) for post-neonatal

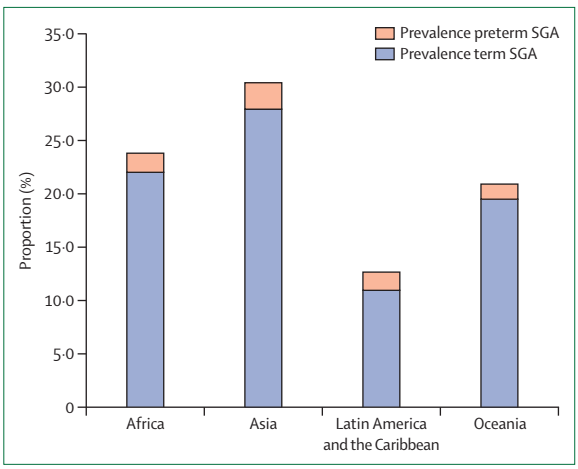

Figure 3: **Prevalence of small-for-gestational-age births, by UN regions**

	Attributable deaths with UN prevalences*	Proportion of total deaths of children younger than 5 years	Attributable deaths with NIMS prevalences†	Proportion of total deaths of children younger than 5 years
Fetal growth restriction (<1 month)	817 000	11·8%	817 000	11·8%
Stunting (1–59 months)	1 017 000*	14·7%	1 179 000†	17·0%
Underweight (1–59 months)	999 000*	14·4%	1 180 000†	17·0%
Wasting (1–59 months)	875 000*	12·6%	800 000†	11·5%
Severe wasting (1–59 months)	516 000*	7·4%	540 000†	7·8%
Zinc deficiency (12–59 months)	116 000	1·7%	116 000	1·7%
Vitamin A deficiency (6–59 months)	157 000	2·3%	157 000	2·3%
Suboptimum breastfeeding (0–23 months)	804 000	11·6%	804 000	11·6%
Joint effects of fetal growth restriction and suboptimum breastfeeding in neonates	1 348 000	19·4%	1 348 000	19·4%
Joint effects of fetal growth restriction, suboptimum breastfeeding, stunting, wasting, and vitamin A and zinc deficiencies (<5 years)	3 097 000	44·7%	3 149 000	45·4%

Data are to the nearest thousand. *Prevalence estimates from the UN. †Prevalence estimates from Nutrition Impact Model Study (NIMS).

Table 2: **Global deaths in children younger than 5 years attributed to nutritional disorders**

mortality, relative to term AGA infants. Infants born preterm and SGA were at highest risk with RR of 15·42 (9·11–26·12) for neonatal mortality and 5·22 (2·83–9·64) for post-neonatal mortality, relative to term AGA.

By applying the attributable fractions of deaths to the total neonatal and post-neonatal deaths for 2011 obtained from the UN Interagency Group on Mortality Estimation,[131] we estimated that the number of deaths attributed to SGA in 2011 was 817 000 in neonates and 418 000 in infants aged 1–11 months using standard methods.[1] The largest number of attributed deaths were in Asia (appendix p 22). For the calculation in the group who were both SGA and preterm, the counterfactual was AGA and preterm so that the SGA effect was separated from that of being preterm. In the estimation of the deaths attributed to several nutritional conditions, we attributed only the neonatal deaths to SGA; for children aged 1–59 months, we attributed deaths to wasting and stunting, to which SGA contributed (table 2).

Causes of childhood growth faltering are multifactorial, but fetal growth restriction might be an important contributor to stunting and wasting in children. To quantify the association between fetal growth restriction and child undernutrition, we did a systematic scientific literature search to identify longitudinal studies that had taken measurements of birthweight, gestational age, and child anthropometry. Data could be obtained from 19 birth cohort studies which were submitted to a meta-analysis to examine the odds of stunting, wasting, and underweight in children 12–60 months of age associated with SGA and preterm birth.[132] Four mutually exclusive exposure categories were created: AGA and preterm; SGA and term; SGA and preterm; and term AGA (as the reference group). The meta-analysis showed that SGA alone and preterm alone were associated with increased overall ORs of 2·43 (95% CI 2·22–2·66) and 1·93 (1·71–2·18), respectively, whereas both SGA and preterm increased the OR to 4·51 (3·42–5·93) for stunting (appendix p 23). These raised

Panel 1: Determinants of childhood stunting and overweight

The determinants of optimum growth and development (figure 1) consist of factors operating at different levels of causation, ranging from the most distal socioeconomic and political determinants to the proximate level where food, disease, and care have a crucial role. A mirror image of figure 1 would show the determinants of linear growth failure—the process leading to child stunting—and overweight. The large socioeconomic inequalities in stunting prevalence in almost all low-income and middle-income countries (LMICs) show the great importance of distal determinants. In particular, maternal education is associated with improved child-care practices related to health and nutrition and reduced odds of stunting, and better ability to access and benefit from interventions.

Almost all stunting takes place in the first 1000 days after conception. The few randomised controlled trials of breastfeeding promotion[145] that included nutritional status outcomes did not show any effects on the weight or length of infants. By contrast, there is strong evidence that the promotion of appropriate complementary feeding practices reduces the incidence of stunting.[93] A meta-analysis of zinc supplementation trials[146] has shown a significant protective effect against stunting.

Severe infectious diseases in early childhood—such as measles, diarrhoea, pneumonia, meningitis, and malaria—can cause acute wasting and have long-term effects on linear growth. However, studies have consistently shown that diarrhoea is the most important infectious disease determinant of stunting of linear growth. In a pooled analysis[147] of nine community-based studies in low-income countries with daily diarrhoea household morbidity and longitudinal anthropometry, the odds of stunting at 24 months of age increased multiplicatively with each diarrhoea episode or day of diarrhoea before that age. The proportion of stunting attributed to five previous episodes of diarrhoea was 25% (95% CI 8–38).

Environmental (or tropical) enteropathy is an acquired disorder, characterised by reduced intestinal absorptive capacity, altered barrier integrity, and mucosal inflammation, occurring in young children living in unsanitary settings.[148] These children also have high rates of symptomatic and asymptomatic infections with enteric pathogens, but the exact association of these infections or of other possible toxic enteric exposures with enteropathy is unclear. Some researchers have suggested that these functional changes and the associated inflammation have significant adverse effects on the growth of children. Alternatively, these changes might be a consequence of nutritional deficits very early in life, including in utero, that lead to intestinal microbial colonisation.

Optimum growth in the first 1000 days of life is also essential for prevention of overweight. Whereas attained weight at any age in early life is positively associated with adult body-mass index in LMIC cohorts,[2,149,150] rapid weight gains in the first 1000 days are strongly associated with adult lean mass, whereas weight gains later in childhood lead mainly to adult fat mass. In particular, evidence suggests that infants whose growth faltered in early life, and who gained weight rapidly later in childhood, might be at particular risk of adult obesity and non-communicable diseases.[2]

Child overweight is also related to growing up in an obesogenic environment, in which population changes in physical activity and diet are the main drivers. Modifiable risk factors for childhood obesity are maternal gestational diabetes; high levels of television viewing; low levels of physical activity; parents' inactivity; and high consumption of dietary fat, carbohydrate, and sweetened drinks, yet few interventions have been rigorously tested.[151–153]

ORs were also noted in the Asian, African, and Latin American UN regions (data not shown).

We estimated population attributable risk for childhood stunting for the risk categories of SGA and preterm birth. Because risk estimates were derived as ORs using logistic regression analysis, we used a method to approximate the risk ratio proposed by Zhang and Yu[133] for estimation of the population attributable risk. Using the approximated RR estimates across all 19 cohorts, population attributable risk for SGA-term for stunting was 0·16 (0·12–0·19), that for SGA-preterm was 0·04 (0·02–0·05), and that for AGA-preterm was 0·04 (0·02–0·06). The combined population attributable risk related to SGA for stunting was 0·20 and that for preterm birth was 0·08. Thus, overall we estimate that about a fifth of childhood stunting could have its origins in the fetal period, as shown by being born SGA.

Most studies of fetal growth restriction and childhood cognitive and motor development in LMICs involve term infants of low birthweight or examine birthweight adjusted for gestational age. Consistent evidence exists for associations of fetal growth restriction with lower psychomotor development levels in early childhood (up to age 36 months) with small to moderate effect sizes compared with infants of normal birthweight.[134,135] A study[136] from Bangladesh showed much the same associations for both mental and motor development. Evidence suggests that there is an effect on development that is attributable to birth size, independent of that attributable to poor postnatal growth.[137]

Evidence for effects of fetal growth restriction on cognition and behaviour after early childhood is less consistent. Birthweight was associated with attained schooling in the COHORTS analyses;[138] however, this was unadjusted for gestational age. Size at birth was not related to women's educational achievement in Guatemala[139] and term low birthweight was not associated with IQ and behaviour in school-aged children in Brazil[140] and Jamaica,[141] or behaviour in South Africa.[142] In Taiwan, term infants of low birthweight had lower academic achievement at age 15 years than did infants of normal birthweight,[143] and in Thailand birthlength was associated with IQ at age 9 years independent of postnatal growth to age 1 year;[144] however, in both cases effect sizes were small.

Childhood nutrition

Stunting, underweight, and wasting

Panel 1[2,145–153] describes the determinants of stunting and overweight in children. Estimates of the prevalence of stunting, underweight, and wasting worldwide and for UN subregions are based on analyses jointly done by UNICEF, WHO, and the World Bank[154] of 639 national surveys from 142 countries in the WHO database, using standard methods.[1,155,156] In 2011, globally, 165 million children younger than 5 years had a height-for-age *Z* score (HAZ) of –2 or lower (stunted) on the basis of

	Stunting (HAZ <–2)				Wasting (WHZ <–2)				Severe wasting (WHZ <–3)				Underweight (WAZ <–2)			
	UN[155]		NIMS[158]		UN		NIMS		UN		NIMS		UN		NIMS	
	Proportion	Number (millions)	Proportion	Number (millions)	Proportion	Number (millions)	Proportion	Number (millions)	Proportion	Number (millions)	Proportion	Number (millions)	Proportion	Number (millions)	Proportion	Number (millions)
Africa	35·6% (33·3–38·0)	56·3 (52·5–60·0)	35·5% (34·4–36·6)	56·6 (54·3–57·8)	8·5% (7·4–9·6)	13·4 (11·6–15·2)	7·9% (7·3–8·6)	12·5 (11·5–13·6)	3·5% (2·9–4·1)	5·5 (4·5–6·4)	2·8% (2·5–3·3)	4·4 (4·0–5·2)	17·7% (15·7–19·7)	27·9 (24·7–31·1)	18·4% (17·4–19·1)	29·0 (27·5–30·1)
Asia	26·8% (23·2–30·5)	95·8 (82·8–108·8)	29·5% (26·4–31·3)	103·5 (92·5–109·8)	10·1% (7·9–12·3)	36·1 (28·2–44·0)	10·0% (8·2–11·4)	5·2 (4·3–5·9)	3·6% (2·4–4·8)	12·9 (8·4–17·3)	3·6% (2·7–4·7)	12·7 (9·4–16·4)	19·3% (14·6–24·1)	69·1 (52·1–86·1)	21·9% (18·8–24·0)	76·6 (65·9–84·1)
Latin America and the Caribbean	13·4% (9·4–17·7)	7·1 (4·8–9·4)	14·6% (13·6–15·5)	7·8 (7·3–8·2)	1·4% (0·9–1·9)	0·7 (0·5–1·0)	1·5% (1·3–1·8)	0·8 (0·7–1·0)	0·3% (0·2–0·4)	0·2 (0·1–0·2)	0·4% (0·4–0·6)	0·2 (0·2–0·3)	3·4% (2·3–4·5)	1·8 (1·2–2·4)	3·7% (3·5–4·1)	2·0 (1·8–2·2)
Oceania	35·5% (16·0–61·4)	0·5 (0·2–0·8)	34·7% (27·8–39·5)	0·4 (0·3–0·5)	4·3% (3·0–6·2)	0·1 (0·0–0·1)	5·1% (3·3–6·8)	0·1 (0·0–0·1)	0·7% (0·5–1·1)	0·0 (0·0–0·0)	1·5% (0·9–2·4)	0·0 (0·0–0·0)	14·0% (8·0–23·2)	0·2 (0·1–0·3)	13·9% (10·7–16·8)	0·2 (0·1–0·2)
LMICs	28% (25·6–30·4)	159·7 (145·9–173·4)	29·9% (27·9–31·0)	168·3 (157·3–174·6)	8·8% (7·4–10·3)	50·3 (42·1–58·4)	9·3% (8·4–10·4)	52·6 (47·4–58·5)	3·3% (2·5–4·0)	18·5 (14·0–23·1)	3·1% (2·6–3·8)	17·3 (14·4–21·5)	17·4% (14·3–20·4)	99·0 (81·7–116·3)	19·4% (17·3–20·5)	109·1 (97·2–115·4)
High-income countries	7·2% (4·1–12·6)	5·1 (2·9–8·9)	..	..	1·7% (0·8–3·5)	1·2 (0·6–2·5)	..	..	0·3% (0·0–1·3)	0·2 (0·0–0·9)	..	..	2·4% (1·7–3·4)	1·7 (1·2–2·4)	..	..
Global	25·7% (23·5–27·9)	164·8 (150·8–178·8)	..	..	8·0% (6·8–9·3)	51·5 (43·3–59·6)	..	..	2·9% (2·2–3·6)	18·7 (14·2–23·2)	..	..	15·7% (13·0–18·4)	100·7 (83·3–118·0)	..	..

Data are % (95% CI). HAZ=height-for-age *Z* score. WHZ=weight-for-height *Z* score. WAZ=weight-for-age *Z* score. LMICs=low-income and middle-income countries.

Table 3: **Prevalence and numbers of children younger than 5 years with stunting, wasting, severe wasting, and underweight using estimates from UN and NIMS, by UN regions for 2011**

the WHO Child Growth Standards (table 3)—a 35% decline from an estimated 253 million in 1990. The prevalence decreased from an estimated 40% in 1990, to an estimated 26% in 2011—an average annual rate of reduction of 2·1% per year (figure 4[154]). East and west Africa, and south-central Asia have the highest prevalence estimates in UN subregions with 42% (east Africa) and 36% (west Africa and south-central Asia); the largest number of children affected by stunting, 69 million, live in south-central Asia (appendix p 9).

The surveys in the WHO database and other population-representative data were also analysed with a Bayesian hierarchical mixture model to estimate *Z*-score distributions of anthropometric indices by the Nutrition Impact Model Study (NIMS).[157] These distributions were used to assess trends in stunting and underweight in children, the present prevalence of these measures, and the present prevalence of wasting. These methods have the advantage of estimating the full distribution of anthropometric variables and therefore measure the full extent of mild-to-severe undernutrition without restrictive assumptions. They also allow for non-linear time trends. NIMS analyses resulted in much the same estimates of the prevalence of stunting, underweight, and wasting as those of the UN in 2011 (table 3, appendix p 10). The complete trend analysis showed that the largest reductions in stunting since 1985 have been in Asia, whereas Africa had an increase until the mid-1990s and subsequently a modest reduction in the prevalence.[157] However, with the increase in population in Africa, this is the only major world region with an increase in the number of stunted children in the past decade.

The complex interplay of social, economic, and political determinants of undernutrition (figure 1) results in substantial inequalities between population subgroups. In our analysis, using previously described methods,[158] of 79 countries with population-based surveys since the year 2000 (figure 5), stunting prevalence among children younger than 5 years was 2·47 times (range 1·00–7·64) higher in the poorest quintile of households than in the richest quintile. Sex inequalities in child nutrition tend to be substantially smaller than economic inequalities (appendix p 24). In 81 countries with data, stunting prevalence is slightly higher (1·14 times, range 0·83–1·53) in boys than in girls. This finding is consistent with the higher mortality in children younger than 5 years in boys than in girls in most countries in the world. Place of residence is also an important correlate of the risk of stunting (appendix p 24). In 81 countries with data, stunting was 1·45 times higher (range 0·94 to 2·94) in rural than in urban areas.

According to UN estimates, globally in 2011, more than 100 million children younger than 5 years, or 16%, were underweight (weight-for-age *Z* score [WAZ] <–2 on the basis of the WHO Child Growth Standards), a 36% decrease from an estimated 159 million in 1990.[154] Estimated prevalences in NIMS were slightly higher at

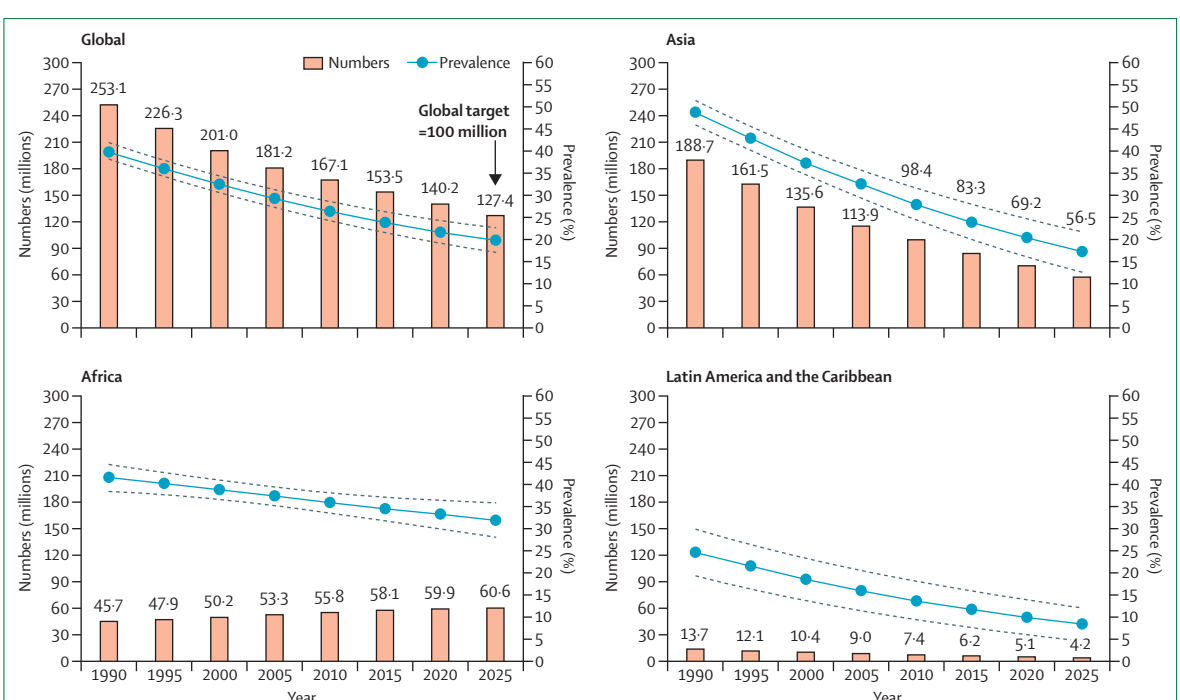

Figure 4: **Trends in prevalence and numbers of children with stunted growth (HAZ <–2), by selected UN regions and globally, 1990–2010, and projected to 2025 on the basis of UN prevalence estimates**

HAZ=height-for-age *Z* score. Data from UNICEF, WHO, World Bank.[154]

110 million (19·4%).[155] Prevalences were highest in south-central Asia and western Africa where 30% and 22%, respectively, were underweight (appendix p 9).

The UN estimate for wasting (weight-for-height *Z* score [WHZ] <–2 on the basis of WHO Child Growth Standards) was 8% (52 million) globally in 2011, an 11% decrease from an estimated 58 million in 1990.[154] 70% of the world's children with wasting live in Asia, most in south-central Asia, where an estimated 15% (28 million) are affected. Much the same regional pattern occurs for

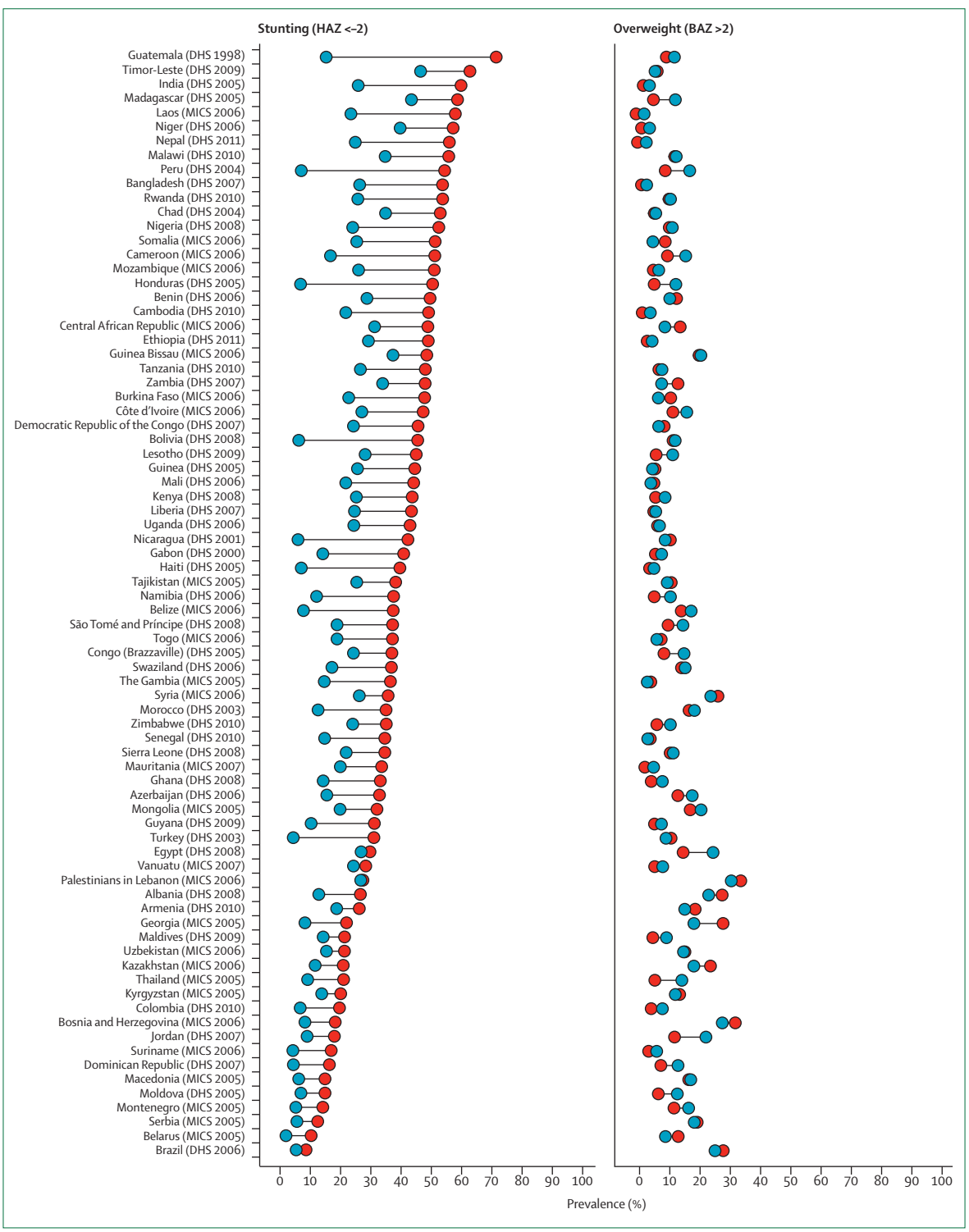

Figure 5: **Prevalence of stunting (HAZ <–2 *Z* scores below median) and overweight (BAZ >2 *Z* scores above median) for highest and lowest wealth quintiles in selected countries**
Blue circles are lowest wealth quintiles, red circles are highest wealth quintiles. HAZ=height-for-age *Z* score. DHS=Demographic and Health Survey. MICS=Multiple Indicator Cluster Survey. BAZ=body-mass index for age *Z* score.

severe wasting (WHZ <–3), with a global prevalence in 2011 of 3% or 19 million children. The highest percentages of children with severe wasting are in south-central Asia (5·1%) and central Africa (5·6%).

Suboptimum growth, according to anthropometric measures indicative of stunting, wasting, and underweight, has been shown to increase the risk of death from infectious diseases in childhood.[159,160] This association has been recently re-examined with the pooled analysis of individual-level data from ten longitudinal studies involving more than 55 000 child-years of follow-up and 1315 deaths in children younger than 5 years.[161] As with previous analyses, all degrees of stunting, wasting, and underweight had higher mortality and the risk increased as *Z* scores decreased (appendix p 11). Undernutrition can be deemed the cause of death in a synergistic association with infectious diseases; if the undernutrition did not exist, the deaths would not have occurred.[1] All anthropometric measures of undernutrition were associated with increased hazards of death from diarrhoea, pneumonia, and measles; the association was also noted for other infectious diseases, but not malaria. We calculated the population attributable fractions for stunting, underweight, wasting, and its subset of severe wasting using the UN and NIMS prevalence data with standard methods.[1] These fractions were multiplied by the corresponding age-specific and cause-specific deaths[162] to estimate the number of deaths attributable to each anthropometric measure (table 2).[162] For the percentage of total deaths the denominator was 6·934 million.[131] Details of these estimates for UN subregions and causes of death are in appendix pp 12–13. Stunting and underweight have the highest proportions of attributed child deaths, about 14% for both; wasting accounts for 12·6% (severe wasting 7·4%) of child deaths. Table 2 and appendix pp 14–15 show estimations using the NIMS prevalence data. In these estimates stunting and underweight each account for 17% of child deaths and wasting for 11·5% (severe wasting 7·8%).

Stunting is a well established risk factor for poor child development with numerous cross-sectional studies showing associations between stunting and motor and cognitive development. Several longitudinal studies show stunting before age 2–3 years predicts poorer cognitive and educational outcomes in later childhood and adolescence.[135,163] Effect sizes for the longitudinal studies comparing children with HAZ of –2 or lower with non-stunted children (HAZ ≥1) are moderate to large.[163] Length-for-age *Z* score (LAZ) at age 2 years was consistently associated with higher cognitive *Z* scores in children aged 4–9 years (0·17–0·19 per unit change LAZ) across four cohorts with moderate (24–32%) or high (67–86%) stunting prevalence.[164] Associations with underweight have also been reported.[163]

Stunted children show behavioural differences in early childhood including apathy, more negative affect, and reduced activity, play, and exploration.[165,166] The first 2 years of life are a crucial period linking growth and development; growth from birth to 24 months but not from 24 to 36 months was associated with child development in Guatemala,[167] and weight gain in the first 2 years predicted school outcomes in five cohorts.[138] Analyses from the COHORTS group that are presented here suggest that growth in the first 2 years of life, but not at later ages, is associated with achieved school grades in adults.[168] However, some evidence suggests that growth after 24 months of age might also be associated with lower cognitive ability, but with a smaller effect size than for early growth.[169] In a Malawi cohort, height gain from 18 to 60 months predicted mathematics ability at 12 years. Height gain at 1 month and change from 1 to 6 months and 6 to 18 months were not significant predictors.[170]

We analysed changes in stunting prevalence between 1996 and 2008 in Bangladesh, Brazil, and Nigeria, according to wealth and urban or rural status (panel 2, figure 6).

Overweight and obesity

The prevalence of overweight worldwide and for UN regions is based on the joint analyses done by UNICEF, WHO, and the World Bank.[154] In 2011, globally, an estimated 43 million children younger than 5 years, or 7%, were overweight (ie, WHZ greater than two *Z* scores above the median WHO standard), on the basis of the WHO Child Growth Standards (appendix p 9)—a 54% increase from an estimated 28 million in 1990. This trend is expected to continue and reach a prevalence of 9·9% in 2025 or 64 million children (figure 7). Increasing trends in child overweight are taking place in most world regions, not only in high-income countries, where prevalence is the highest (15% in 2011). However, most overweight children younger than 5 years (32 million in 2011) live in LMICs. In Africa, the estimated prevalence increased from 4% in 1990 to 7% in 2011, and is expected to reach 11% in 2025 (figure 7). Prevalence of overweight is lower in Asia (5% in 2011), but the number of affected children is higher compared with Africa (17 and 12 million, respectively).

Differences in childhood overweight prevalence between the richest and poorest quintiles are small in most countries (figure 5), and in general prevalence tends to be higher in the richest quintile than in the poorest. In 78 countries with data, prevalence in the richest quintile was on average 1·31 (range 0·55–3·60) times higher than in the poorest quintile. Overweight is much the same between the sexes (appendix p 24) and slightly more prevalent in urban than in rural areas (appendix p 25). In 81 countries with data, urban prevalence was 1·08 times higher on average (range 0·44–1·46) than rural prevalence.

Childhood overweight results in both immediate and longer-term risks to health. Among the immediate risks are metabolic abnormalities including raised cholesterol,

triglycerides, and glucose, type 2 diabetes, and high blood pressure.[171] Childhood overweight is also a strong risk factor for adult obesity and its consequences.[2,172]

Childhood vitamin deficiencies

Anaemia and iron

The percentages of children with anaemia (haemoglobin <110 g/L) and severe anaemia (haemoglobin <70 g/L) due to inadequate iron, (ie, anaemia that is correctable by oral iron supplements, calculated as described earlier) are 18·1% and 1·5%, respectively. The prevalence is highest in Africa and Asia for all IDA and in Africa for severe IDA (table 1). However, the proportion of all childhood anaemia corrected by iron supplementation ranges from 63% in Europe to 34% in Africa where there are other major causes of anaemia; the proportion of severe anaemia corrected by iron supplementation in Africa is 57% (appendix p 4).

Iron supplementation in children aged 5 years and older with IDA generally benefits their cognition, but studies of children younger than 3 years have had mostly negative findings.[135,173–175] Most cohort and cross-sectional studies of children younger than 3 years with IDA find developmental deficits and studies from the past 15 years provide evidence of neurophysiological changes suggestive of delayed brain maturation.[135] However, IDA is associated with many social disadvantages that also affect child development and, thus, randomised controlled trials are necessary to establish a causal association. A previous systematic review showed that iron supplementation resulted in a small improvement in mental development scores in children with IDA aged older than 7 years, but had no effect in children younger than 27 months.[173] To further assess this scientific literature, we identified seven double-blind randomised controlled trials[176–182] of iron lasting at least 8 weeks in children younger than 4 years. Five trials[177–180,181,182] showed benefits in motor development and two did not.[176,180] Only one showed benefits in language,[178] and a small study showed benefits in mental development.[177] In an eighth randomised controlled trial,[183] children given iron in infancy showed no cognitive benefit when followed up at age 9 years. Four additional randomised controlled trials[184–187] examined the combined effects of iron and folate supplementation in children younger than 36 months of age. One showed benefits to motor milestones,[184] others showed no benefits to motor[185,186] or language[186] milestones, and one showed no benefit to cognitive function.[187] Thus, there is some evidence that iron deficiency affects motor development in children younger than 4 years, but no consistent evidence for an effect on mental development. However, many of the supplementation trials produced only small differences in iron status between the treated and control groups, possibly limiting their ability to affect development. It is also possible that mental development takes longer to

***Panel 2:* How do inequalities in stunting evolve with time?**

Increased availability of survey data, including several surveys from different years, allowed the analyses of time trends in nutritional indicators according to population subgroups. Figure 6A compares trends in stunting by wealth quintile in three countries. In Nigeria, there was almost no change in stunting prevalence from 2003 to 2008, and the degree of inequality remained almost unchanged. In Bangladesh, stunting prevalence decreased in all subgroups, but inequality also remained at the same magnitude. In Brazil, where prevalence of stunting is much lower, equity improved because of a substantial decrease in stunting the poorest populations.

Figure 6B shows the corresponding results for urban and rural differences over time. In Nigeria, rural prevalence was higher than urban prevalence in 2003, and both remained at similar levels by 2008. In Bangladesh, both urban and rural rates decreased, but the gap was reduced over time. In Brazil, where there was a two-times rural-urban gap in 1996, full equality had been reached by 2006.

Increased data availability has led to the ability to study trends over time for subnational groups. Such data should be used for advocacy purposes, showing which population groups require closer attention, and also as a means to assess the effect of nutrition-specific and nutrition-sensitive interventions, as well as of broader developmental programmes and initiatives.

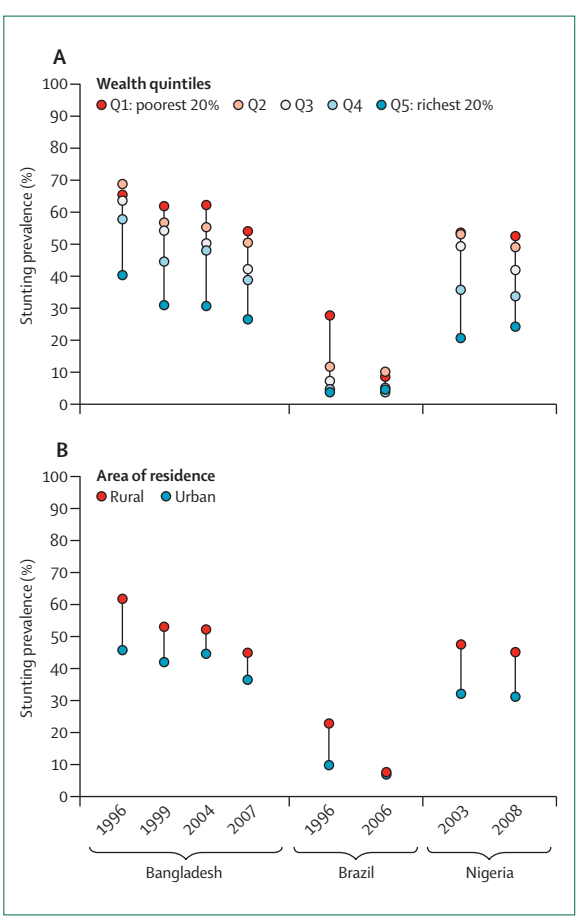

***Figure 6:* Changes in stunting over time, in Bangladesh, Brazil, and Nigeria**
(A) Stunting prevalence by wealth quintile. The longer the line between two groups, the greater the inequality. (B) Stunting prevalence by urban or rural location.

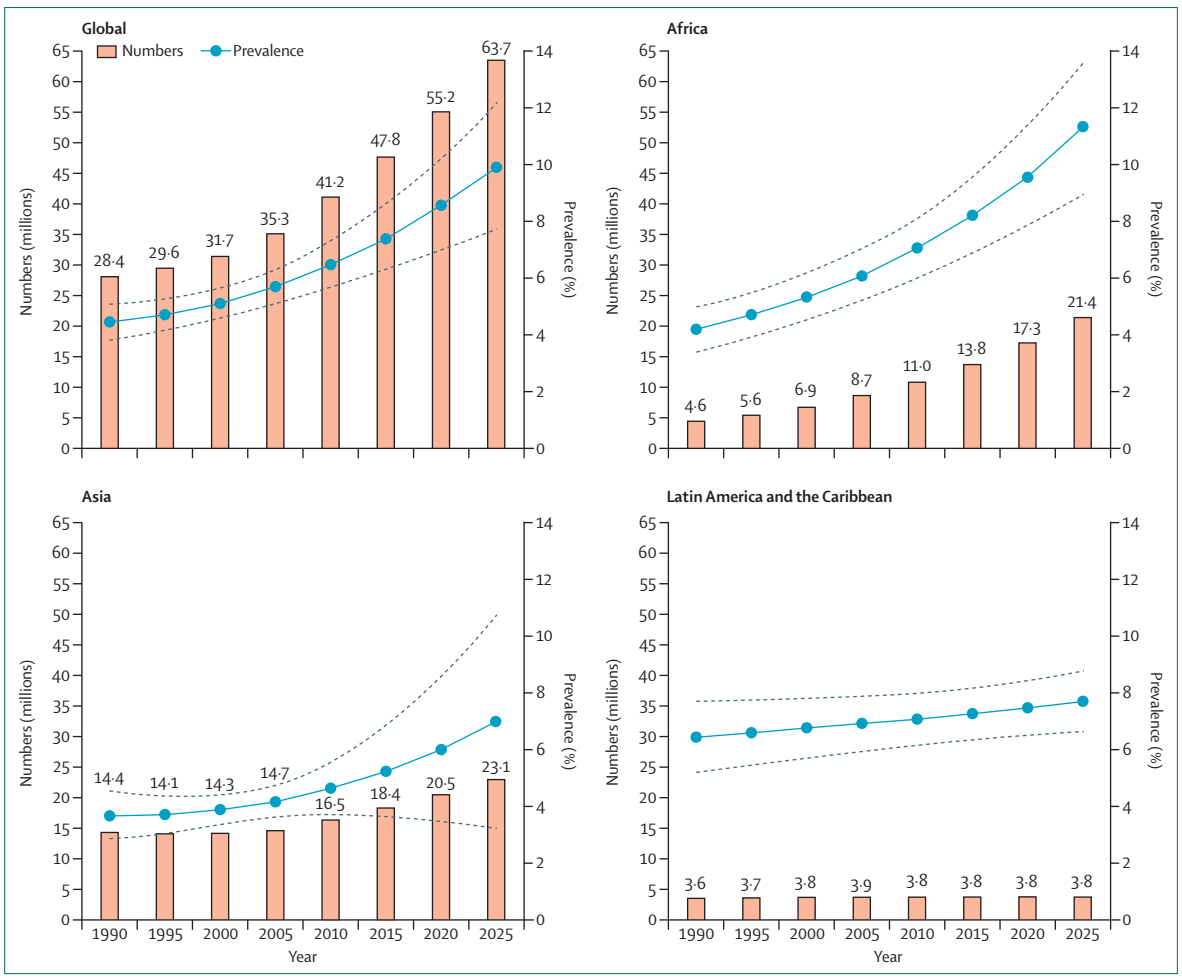

Figure 7: **Trends in prevalence and numbers of overweight (WHZ >2) children, by selected UN regions and globally, 1990–2010, and projected to 2025, on the basis of UN prevalence estimates**
WHZ=weight-for-height Z score.

improve than the duration of the trials or that the effects of iron deficiency early in life are irreversible.

Vitamin A

Clinical assessment of ocular symptoms and signs of xerophthalmia and biochemical assessment of serum concentration of retinol are the two common methods in population surveys for estimation of prevalence of vitamin A deficiency. WHO provides prevalence estimates of vitamin A deficiency in preschool children (<5 years) for 1995–2005 from 99 countries.[45] Globally, 0·9% (95% CI 0·3–1·5) or 5·17 million preschool age children are estimated to have night blindness and 33·3% (31·1–35·4) or 90 million to have subclinical vitamin A deficiency, defined as serum retinol concentration of less than 0·70 μmol/L. Vitamin A deficiency using night blindness prevalence can be defined as a global problem of mild public health importance,[45] although the prevalence in Africa (2%) is higher than elsewhere. Although prevalence of clinical symptoms has declined, probably because of large-scale vitamin A supplementation programmes in many countries, subclinical vitamin A deficiency affects high proportions of children in Africa and southeast Asia (table 2).

Many randomised controlled trials have been done to examine the effect of supplementation every 4–6 months and fortification on survival of children aged 6 months and older; these studies provide the best evidence for deaths attributable to vitamin A deficiency.[188–191] Meta-analyses of these trials show a mortality reduction of 23%,[188] 30%,[189] and 24%[190] in children aged 6–59 months. With publication of a large programme effectiveness study from India, a revised meta-analysis shows a mortality effect of 11%, still a statistically significant benefit.[192] In our calculations we use only the effects in the trials on particular causes of death, not the effects on overall deaths because the causes of death at the time of the trials and nowadays are probably different (eg, diarrhoea and measles account for a much smaller proportion of child deaths now than

10–20 years ago).[162] To derive the risk of vitamin A deficiency the inverse (1/risk reduction) of the cause-specific mortality reduction identified in the trials was deemed to be the risk of deficiency and adjusted with the assumption that all the effect was in the subset of the trial population with low serum retinol (appendix p 16). Much the same adjustment was done for the effect of vitamin A deficiency on diarrhoea incidence (appendix p 17). This allows the adjusted RR to be applied to the present prevalence of low serum retinol to estimate the attributable deaths or disease episodes. Although results of trials[193–195] in south Asia show a newborn supplementation effect on mortality in the first 6 months of life, the evidence from Africa is less clear, and further studies are underway. Therefore, we do not estimate deaths attributable to vitamin A deficiency in the first 6 months of life. Child deaths attributable to vitamin A deficiency for 2011 are estimated to be 157 000 (table 2).

Zinc

Zinc deficiency in populations could be assessed by a shift of the population distribution of serum zinc concentrations to lower values as recommended by the International Zinc Nutrition Consultative Group;[196] however, insufficient data exist to classify countries or subnational populations. Instead the proportion of the national population estimated to have an inadequate zinc intake on the basis of national food availability and dietary requirements is used.[70] According to this method, an estimated 17% of the world's population has an inadequate zinc intake; substantial regional variation exists, with Asia and Africa having the highest prevalences (table 1). A systematic review[197] showed that zinc supplementation resulted in a 9% reduction (RR 0·91, 95% CI 0·82–1·01) of borderline significance in all-cause child mortality. A separate analysis of available trials showed a significant 18% reduction (RR 0·82, 0·70–0·96) in all-cause mortality in children aged 1–4 years.[198] There were suggestive benefits on diarrhoea-specific (RR 0·82, 95% CI 0·64–1·05) and pneumonia-specific (0·85, 0·65–1·11) mortality.[197] This and previous analyses have included cause-specific mortality effects even when they were not statistically significant when the effect on all-cause mortality was statistically significant.[199,200] These trials were not powered for cause-specific mortality effects. Supporting evidence for the cause-specific mortality effects comes from randomised controlled trials that showed significant reductions in diarrhoea incidence (RR 0·87, 95% CI 0·81–0·94) and pneumonia incidence (0·81, 0·73–0·90).[197] To derive the risk of zinc deficiency, we adjusted the inverse of the cause-specific mortality (appendix p 18) and incidence (appendix p 19) reductions noted in the trials with the assumption that all the effect was in the subset of the trial population at risk of zinc deficiency, as estimated from the availability of food in national diets.[70] This method allows the adjusted RRs to be applied to the present prevalence of inadequate zinc intake in countries to estimate the attributable deaths. The population attributable fractions for diarrhoea and pneumonia were multiplied by the number of these deaths in 2011.[162] The number of child deaths attributed to zinc deficiency in 2011 is 116 000 (table 2).

Zinc deficiency also has a small negative effect on growth. A meta-analysis of randomised controlled trials of zinc supplementation showed a significant benefit for linear growth in children aged 0–5 years.[201] The effect was a gain of 0·37 cm in zinc-supplemented children. Trials that used a dose of zinc of 10 mg per day for 24 weeks, rather than lower doses, showed a larger benefit of 0·46 cm.

Breastfeeding practices

Present recommendations are that babies should be put on the breast within 1 h after birth, be exclusively breastfed for the first 6 months, and for an additional 18 months or longer, be breastfed along with complementary foods. There are no recently published systematic compilations of data for breastfeeding patterns so we analysed data from 78 countries with surveys done in LMICs during 2000–10 (appendix p 20). Early initiation of breastfeeding (within 1 h) is highest in Latin America (mean 58%, 95% CI 50–67), intermediate in Africa (50%, 45–55) and Asia (50%, 42–58), and lowest in eastern Europe (36%, 23–50). Except for eastern Europe, where the lowest rates of breastfeeding are recorded, globally about half of children younger than 1 month, and three in every ten children aged 1–5 months are exclusively breastfed. Breastfeeding in 6–23 month olds is most frequent in Africa (mean 77%, 95% CI 73–81) followed by Asia (62%, 54–71) and Latin America (60%, 50–69), with lower occurrence in eastern Europe (33%, 24–42).

The risks of increased mortality and morbidity due to deviation from present breastfeeding recommendations are well documented.[1] Updated systematic reviews of these risks have results that are much the same as our previous estimates (appendix p 21).[1,202,203] The number of child deaths attributed to suboptimum breastfeeding in 2011 is 804 000 or 11·6% of all deaths (table 2).

Three prospective case-cohort studies provide data for the association of early breastfeeding initiation (within 24 h) with neonatal mortality.[204] Although early initiation was associated with lower neonatal mortality (RR 0·56, 95% CI 0·46–0·79), in babies who were exclusively breastfed the mortality risk was not significantly reduced (0·69, 0·27–1·75). The possible benefit of early initiation of breastfeeding was therefore not deemed to be additive to the effects of exclusive breastfeeding in our analyses.

A systematic review shows that breastfeeding is consistently associated with an increase in IQ of about three points,[205] even after adjustment for several confounding factors including maternal IQ. Evidence for the protection afforded by breastfeeding against risk factors for non-communicable diseases is less consistent. A series

of meta-analyses,[205] based mainly on studies in adults from high-income settings, showed no evidence of protection against total cholesterol levels or diastolic blood pressure. When the meta-analysis was restricted to high-quality studies, breastfeeding was associated on average with a 1 mm reduction in systolic blood pressure, and with a 12% reduction in the risk of overweight or obesity. Studies of diabetes or glucose levels were too few to allow a firm conclusion.

Joint effects of nutritional conditions on child mortality

To estimate the population attributable fraction and the number of deaths attributable to several risk factors, we used Comparative Risk Assessment methods.[206] We calculated attributable deaths from four specific causes of mortality (diarrhoea; measles; pneumonia; and other infections, excluding malaria) associated with different nutritional status measures. In the neonatal period all deaths were deemed to be associated only with sub-optimum breastfeeding and fetal growth restriction. The Comparative Risk Assessment methods allow the estimation of the reduction in death that would take place if the risk factors were reduced to a minimum theoretical level or counterfactual level of exposure.[206] For the assessment the following formula was used:

$$PAF = \frac{\sum_{i=1}^{n} P_i\left(RR_i - 1\right)}{\sum_{i=1}^{n} P_i\left(RR_i - 1\right) + 1}$$

For the purpose of this analysis, RR_i equals the RR of mortality for the ith exposure category, associated with specific UN regions. P_i equals the proportion of children in the ith exposure in theoretical or counterfactual category. P equals the population weighted mean of countries' prevalence estimates for different levels of fetal growth restriction, stunting, wasting, deficiencies of vitamin A and zinc, and suboptimum breastfeeding practices in their relevant age groups.

Because specific causes of deaths could potentially be caused by more than one factor, the population attributable fractions for multiple risk factors that affect the same disease outcome overlap and cannot be combined by simple addition. For this reason, the joint population attributable fraction was estimated with the formula: Joint PAF_i=1–product (1–PAF_i), where PAF_i equals the population attributable fraction of the different risk factors.[207] All analyses were done for relevant age groups of that risk factor and then the results from the age groups were aggregated. For stunting and wasting we did calculations separately with UN and NIMS prevalence estimates.

The resulting 3·1 million deaths constitute 45% of global deaths in children younger than 5 years in 2011, attributed jointly to fetal growth restriction, suboptimum breastfeeding, stunting, wasting, and deficiencies of vitamin A and zinc. The overall results were the same using UN or NIMS prevalence estimates. As part of this total, the joint distribution of suboptimum breastfeeding and fetal growth restriction in the neonatal period contributes 1·3 million deaths or 19% of all deaths of children younger than 5 years.

Effects of fetal and early childhood undernutrition on adult health

In *The Lancet*'s 2008 Series on maternal and child undernutrition,[2] consequences of early childhood nutrition on adult health and body composition were assessed by reviewing the scientific literature and doing meta-analyses of five birth cohorts from LMICs (India, the Philippines, South Africa, Guatemala, Brazil), an effort that gave rise to the COHORTS collaboration.[208] On the one hand, the conclusions were that small size at birth and at 2 years of age (particularly height) were associated with reduced human capital: shorter adult height, less schooling, reduced economic productivity, and for women, lower offspring birthweight. On the other hand, larger child size at 24 months of age was a risk factor for high glucose concentrations, blood pressure, and harmful lipid levels once adjustment for adult BMI was made, suggesting that rapid weight gain, especially after infancy, is linked to these conditions.

The COHORTS group later did pooled analyses that use conditional growth variables that remove the correlation between growth measures across ages, allowing inferences to be made about the relative association between growth during specific age intervals and outcomes.[149] Also, because gains in height and weight are correlated, these analyses use conditionals that separate linear growth from weight gain. The conclusions were that heavier birthweight and faster linear growth from 0 to 2 years lead to large gains in human capital, but have little association with adult cardiovascular risk factors. Also, faster weight gain independent of linear growth has little benefit for human capital. After the age of 2 years, and particularly after the age of 4 years, rapid weight gains show adverse effects on adult cardiovascular risk. The COHORTS analyses control for confounding and the findings are broadly much the same across the five cohorts.

Additional longitudinal studies report effects on later mental health with higher levels of depression and anxiety and lower self-esteem in adolescents who were stunted by age 2 years compared with non-stunted;[209] increased depression in adolescents who had severe acute malnutrition in infancy;[210] increased risk of suicidal ideation associated with lower HAZ at 24 months,[211] and higher levels of hyperactivity in late adolescence and attention deficit in adults.[209,212] Although observational, the findings are persuasive and consistent with the little quasi-experimental evidence available. Follow-up studies of a community randomised nutrition trial in Guatemala

have shown long-term effects of exposure to improved nutrition during the first 2–3 years, but not after 3 years, on education,[213] and wages.[214] Effects of improved nutrition in the first several years of life on risk factors for chronic diseases were minor but in some cases beneficial.[215] Exposure to improved nutrition during childhood affected the growth of the next generation in girls and their future children.[2]

Famines are another source of information about long-term effects of poor nutrition in early life. The Dutch famine of 1944–45 (brief, intense, but affecting a previously well-nourished population) suggests effects of prenatal exposure on schizophrenia, no effects on human capital (height, cognitive function), and weak and inconsistent effects on cardiovascular risk factors.[216] The 1959–61 Chinese famine (prolonged, severe, and affecting an already malnourished population) suggests effects of exposure during pregnancy and the first 2 years of life on height, wealth, income, mental health, and intergenerational effects on birthweight.[217–220] Surprisingly, some findings suggest protective effects of famine exposure, which might be explained by high mortality and intense selection of the hardiest.[219–221]

Discussion

Nutrition has profound effects on health throughout the human life course and is inextricably linked with cognitive and social development, especially in early childhood. In settings with insufficient material and social resources, children are not able to achieve their full growth and developmental potential. Consequences range broadly from raised rates of death from infectious diseases and decreased learning capacity in childhood to increased non-communicable diseases in adulthood.

Nutrition and growth in adolescence is important for a girl's health and adult stature. Women with short stature are at risk of complications in delivery, such as obstructed labour. Nutritional status at the time of conception and during pregnancy is crucial for fetal growth. Babies with fetal growth restriction, as shown by being SGA, are at increased risk of death throughout infancy. We estimate that 32 million babies are born SGA, 27% of births in LMICs, and about 800 000 neonatal deaths and 400 000 post-neonatal infant deaths can be attributed to the increased risk associated with having fetal growth restriction. The use of more appropriate methods than those in our previous review[1] to understand the prevalence and risk of SGA presented here resulted in estimates that are more than double our previous estimate of attributable neonatal deaths related to term low birthweight. This new finding contradicts the widespread assumption that SGA infants, by contrast with preterm babies, are not at a substantially increased risk of mortality. Additionally, babies who are SGA have an increased risk of growth faltering in the first 2 years of life; our estimates suggest that 20% of stunting might be attributable to fetal growth restriction. The links between fetal growth restriction and maternal nutritional conditions, short stature, and low BMI, should lead to more emphasis on nutritional interventions before and during pregnancy. These interventions would have benefits for health of adolescents and women, could reduce complications of pregnancy and delivery for the mother, and enhance fetal growth and development.

Stunted linear growth has become the main indicator of childhood undernutrition, because it is highly prevalent in all developing regions of the world, and has important consequences for health and development. It should replace underweight as the main anthropometric indicator for children. Underweight indices include children who are short, but who can have an increased WHZ, being therefore at increased risk of long-term adverse health outcomes. Linear growth assessment in primary care is an essential component of country efforts to reduce childhood stunting. More experience is needed in the operational aspects of the assessment and interpretation of linear growth by health workers and in the effective intervention responses.

Prevalence of stunting in children younger than 5 years in developing countries in 2011 was about 28%, a decrease from 40% or more in 1990 and the 32% estimate in our 2008 nutrition Series for 2004.[1] The number of stunted children globally has decreased from 253 million in 1990 to 165 million in 2011. Another reported estimate was 167 million in developing countries for 2010.[157] The 13-year Comprehensive Implementation Plan (2012–25) on Maternal, Infant and Young Child Nutrition, endorsed at the 2012 World Health Assembly, includes six global nutrition targets, the first of which calls for a 40% reduction of the global number of children younger than 5 years who are stunted by 2025 (compared with the baseline of 2010).[222] This goal would translate into a 3·9% relative reduction per year and imply reducing the number of stunted children from the 171 million in 2010 to about 100 million. However, at the present rate of decline, prevalence of stunting is expected to reach 20%, or 127 million, in 2025. In Africa, only small reductions in prevalence are anticipated on the basis of present trends. However, in view of the rising number of births, the actual number of stunted children will increase from 56 to 61 million. By contrast, Asia is projected to show a substantial decrease in stunting prevalence and in the absolute number of children affected.

Stunted, underweight, and wasted children have an increased risk of death from diarrhoea, pneumonia, measles, and other infectious diseases. Recalculated risks of cause-specific mortality[161] confirmed previous estimates[1,159,160] and were used in estimation of the deaths attributable to these conditions. The attributable fraction of deaths for these nutritional status measures has remained nearly the same as in previous calculations, but the number of attributed deaths has declined because of the decrease in the prevalence of these measures and a decline in the affected causes of death. By our estimates

more than 1 million deaths can be attributed to stunting and about 800 000 to wasting, about 60% of which are attributable to severe wasting. These attributable deaths cannot be added because of the overlap of these and other nutritional conditions, but are instead included in the calculation of the deaths attributed to the joint effects of all nutritional conditions. Our estimate of about 1 million child deaths due to underweight is higher than the recently published 860 000 deaths in the Global Burden of Disease (GBD).[200] The GBD Study did not estimate deaths attributed to stunting or wasting.

Deficiencies of vitamins and minerals have important health consequences, both through their direct effects, such as iron deficiency anaemia, xerophthalmia due to vitamin A deficiency, and iodine deficiency disorders, and because they increase the risk of serious infectious diseases. In the latter category, vitamin A and zinc deficiencies have been shown to have the greatest effects among the micronutrients. Our estimate of the nearly 157 000 child deaths attributed to vitamin A deficiency is smaller than our previous estimate (668 000).[1] Notably, we did not include the risk of mortality in the first 6 months of life, as we did last time for Asia, because of more uncertainty about this risk; several trials of neonatal vitamin A supplementation are underway in Asia and Africa to assess the benefits. Likewise, our estimate of 116 000 child deaths attributed to zinc deficiency is much smaller than the 450 000 in our previous estimates, partly because we now estimate the risk of pneumonia and diarrheal mortality beginning at 12 rather than 6 months of age. In both cases there have also been changes in our methods of estimating the prevalence of the conditions and the risk associations, and combining these factors to get attributed fractions of deaths. These methods are much the same as those reported by the GBD Study.[200] Our estimates are 20% higher for zinc and 30% higher for vitamin A, than the GBD estimates. The reduction from our estimates for the year 2004 is partly explained by decreases in the prevalences of these deficiencies—for vitamin A mostly because of large-scale implementation of high-dose supplementation programmes, and a reduction in deaths from diarrhoea and measles affected by vitamin A deficiency and in deaths from diarrhoea and pneumonia affected by zinc deficiency. Some of this mortality reduction (eg, for diarrhoea) could be attributable to the vitamin A supplementation, but might be also related to improvement in nutritional status measures (eg, stunting), water and sanitation, and illness treatment, and for measles is largely attributable to improved coverage with measles vaccine. Although the number of deaths attributed to the present prevalence of vitamin A deficiency is relatively small, importantly, a reduction in present coverage of vitamin A interventions would probably result in an increase in mortality, because in most LMICs dietary intake is still inadequate.

Breastfeeding exclusively for the first 6 months and then along with complementary food to 24 months of age is highly beneficial. Data from developing regions show that present practices are far from optimum, despite improvements in some countries. Our previous estimates suggested that 1·4 million deaths were attributed to suboptimum breastfeeding, especially related to non-exclusive breastfeeding in the first 6 months of life. Our new estimates are 804 000 deaths, a substantial reduction since our estimate for the year 2004. Although present estimates of the risks associated with suboptimum breastfeeding practices are almost unchanged from what was used previously, the reduction in infectious disease deaths in the past 10 years results in a lower number of preventable deaths.[173] Our number is higher than the estimated 545 000 deaths attributed to suboptimum breastfeeding in the GBD Study.[200] Insufficient methods are provided by GBD to understand the reasons for differences, but one reason is probably the lower estimates of affected diarrhoea and pneumonia deaths than the UN estimates we used.[223]

To work out the total deaths attributed to nutritional conditions, we calculated the joint distribution of stunting, wasting, fetal growth restriction, deficiencies of vitamin A and zinc, and suboptimum breastfeeding. The resulting 3·1 million deaths constitute 45% of the 6·9 million global child deaths in 2011. The total number of attributed deaths is reduced from the 3·5 million we estimated for 2004, despite the population attributable fraction increasing from 35% to 45%. In this period the mortality in children younger than 5 years decreased from 10 million to 6·9 million deaths and there were even larger decreases in the causes of death—such as measles, diarrhoea, and pneumonia[162]—that are most affected by nutritional conditions. The increase in the percentage of attributed deaths compared with the previous series is largely because of the more appropriate inclusion of the effects of SGA (about 800 000 deaths) instead of term low birthweight (337 000 deaths) and the inclusion of all wasting (WHZ <–2) instead of severe wasting (WHZ <–3) in the joint calculations.

The number of children affected by excessive body-weight relative to length or height is increasing globally. Although the prevalence of overweight in high-income countries is more than double that in LMICs, three quarters of the global total live in LMICs. The recorded trends in the prevalence of early childhood overweight are probably a consequence of changes in dietary and physical activity patterns over time. These behavioural changes are affected by many social and environmental factors, including interpersonal (family, peers, and social networks), community (school, workplace, and institutions), and governmental (local, state, and national policies).[224] Studies show that the trend toward childhood obesity can start as early as age 6 months.[225,226] In LMICs, rapid weight gain after 2 years of age is particularly associated with adult fat mass.[2,168] Intrauterine, infant, and preschool periods are deemed to be possible crucial periods for programming long-term regulation of energy balance.[227–229]

If trends are not reversed, increasing rates of childhood overweight and obesity will have vast implications not only for future health-care expenditures but also for the overall development of nations. These findings confirm the need for effective interventions and programmes to reverse anticipated trends. The early recognition of excessive weight gain relative to linear growth is essential. Routine assessment of both weight and length in all children needs to become standard clinical practice from very early childhood.

We have reported previously and confirmed in a new analysis that anaemia that is reduced by supplemental iron in pregnancy is a risk factor for more than a quarter of maternal deaths. Anaemia is probably a particularly important risk factor for haemorrhage, the leading cause of maternal deaths (23% of total deaths).[223] Additionally, there is now sound evidence that calcium deficiency increases the risk of pre-eclampsia, now the second most important cause of maternal death (19% of total deaths).[223] Thus, addressing deficiencies of these two minerals could result in substantial reduction of maternal deaths.

Nutrition is crucial for optimum child development throughout the first 1000 days of life and beyond. Maternal nutrition affects fetal growth and brain development with clear evidence for the need to continue and strengthen programmes to prevent maternal iodine deficiency. Fetal growth restriction and postnatal growth affect motor and cognitive development, with the largest effects from stunting before age 2–3 years. Growth later in childhood might also affect development though with a smaller effect size. Iron deficiency anaemia affects motor development; effects on cognitive development have been more clearly shown in children older than 5 years than in younger children.

Promotion of good early nutrition is essential for children to attain their developmental potential; however, poor nutrition occurs with other risks for development, in particular inadequate stimulation during early childhood. Interventions to promote home stimulation and learning opportunities in addition to good nutrition will be needed to ensure good early development and longer-term gains in human capital, with integration and coordination of programmes and policies across sectors.

Panel 3 lists research priorities. Additionally, there is a general need for better data on micronutrient deficiencies and other nutritional conditions at national and subnational levels. This work should involve the development and use of improved biomarkers that could be used to describe nutritional conditions and increase knowledge about how they affect health and development. Such information is needed to guide intervention programmes in countries and priorities for support globally.

In the 5 years since our last series there have been some improvements in nutritional conditions, especially for child growth. Nonetheless, the extent of these conditions remains high with serious detrimental health consequences, with a high child mortality burden related to both stunting and wasting. New evidence in this paper supports the focus on pregnancy and the first 2 years of life, the crucial 1000 days, which we called for in the previous series, but adds more emphasis to the nutritional conditions in adolescence, at the time of conception, and during pregnancy, as important for maternal health and survival, fetal growth and subsequent early childhood survival, growth, and development. Fetal growth restriction and poor growth early in infancy are now recognised as important determinants of neonatal and infant mortality, stunting, and overweight and obesity in older children and adults. Preventive efforts should continue to focus on the 1000 days, while therapeutic efforts continue to target severe wasting.

***Panel 3:* Research priorities**

- How much of the effect of the underlying economic and social determinants of optimum growth and development is mediated through known, measurable proximate determinants?
- What are the consequences of calcium or vitamin D deficiencies for maternal health, fetal growth, birth outcomes, and infant health?
- What is the importance of zinc deficiency or other micronutrient deficiencies in the risk of preterm delivery?
- What is the role of nutrition in adolescence, at the time of conception, and in pregnancy in healthy fetal growth and development?
- What factors are associated with regional variation in fetal growth restriction and do its consequences on growth and mortality vary by setting?
- What is the interaction of fetal growth restriction and post-partum infections and diet in contributing to stunting?
- What is the role of vitamin A deficiency in newborn babies or the first 6 months of life in neonatal and infant mortality?
- Are there benefits from iron supplementation for mental development in children younger than 5 years with iron deficiency anaemia?
- Do deficiencies of any micronutrients other than vitamin A and zinc increase the risk of mortality from infectious diseases?
- Can the risk of stunting be explained by specific dietary factors, micronutrient deficiencies, and clinical or subclinical infections?
- How can the rapid decreases in stunting noted in selected countries be explained by changes in intervention coverage and in distal determinants?
- Are there benefits of early initiation of breastfeeding that are independent of the practice of exclusive breastfeeding?
- How can developmental differences associated with nutritional deficiencies at various ages of childhood be best quantified and related to functioning and productivity in adulthood?
- What are the optimum physical growth rates in the first year of life to avoid both undernutrition and obesity?
- What are the effects of physical growth rates and stunting on cognitive abilities and psychological functioning?
- Can health workers effectively and efficiently assess and interpret height-for-age measures of linear growth in health and nutrition programmes?
- How important is optimum growth and nutritional status in the fetal and early childhood period (first 1000 days of life) in the development of adult obesity and non-communicable diseases?

Contributors

REB conceptualised and coordinated the analyses, did the first draft of the paper, responded to reviewer comments and incorporated all revisions until publication. CGV contributed with analyses of inequalities, breastfeeding patterns, and long-term consequences of early nutrition, and served as a coordinator for this paper. SPW contributed sections on the effect on child development of maternal IDA, fetal growth restriction, and childhood undernutrition, maternal IDA, and mental health and served as a coordinator for this paper. ZAB assisted with conceptualising the paper and contributed sections on micronutrients and adolescent nutrition. PC contributed to writing the sections on maternal and childhood micronutrient deficiencies (vitamin A and iodine), mortality and morbidity effects of maternal low BMI and short stature, and micronutrient deficiencies and effects of fetal growth restriction on childhood stunting. MdO contributed global and regional analyses on childhood stunting, wasting, underweight, and overweight. ME contributed to exposures for various child and maternal nutritional indicators, to selected aetiological effect sizes for childhood exposures, and provided advice on methods for calculation of attributable burden. SG-MG reviewed the scientific literature on iron and iodine deficiency and contributed to these sections. JK contributed analyses and text on maternal risk factors for, prevalence of, and mortality consequences of fetal growth restriction and the mortality effect of vitamin A supplementation. RM contributed the sections on adolescent nutrition, the consequences of short maternal stature, and long-term consequences of early nutrition. RU contributed to sections on maternal obesity, considering causes and short-term and long-term consequences to mothers, neonates, and infants. All authors contributed to the final paper.

Maternal and Child Nutrition Study Group

Robert E Black (Johns Hopkins Bloomberg School of Public Health, USA), Harold Alderman (International Food Policy Research Institute, USA), Zulfiqar A Bhutta (Aga Khan University, Pakistan), Stuart Gillespie (International Food Policy Research Institute, USA), Lawrence Haddad (Institute of Development Studies, UK), Susan Horton (University of Waterloo, Canada), Anna Lartey (University of Ghana, Ghana), Venkatesh Mannar (The Micronutrient Initiative, Canada), Marie Ruel (International Food Policy Research Institute, USA), Cesar Victora (Universidade Federal de Pelotas, Brazil), Susan Walker (The University of the West Indies, Jamaica), Patrick Webb (Tufts University, USA)

Series Advisory Committee

Marc Van Ameringen (Gain Health Organization, Switzerland), Mandana Arabi (New York Academy of Sciences, USA), Shawn Baker (Helen Keller International, USA), Martin Bloem (United Nations World Food Programme, Italy), Francesco Branca (WHO, Switzerland), Leslie Elder (The World Bank, USA), Erin McLean (Canadian International Development Agency, Canada), Carlos Monteiro (University of São Paulo, Brazil), Robert Mwadime (Makerere School of Public Health, Uganda), Ellen Piwoz (Bill & Melinda Gates Foundation, USA), Werner Schultink (UNICEF, USA), Lucy Sullivan (1000 Days, USA), Anna Taylor (Department for International Development, UK), Derek Yach (The Vitality Group, USA). The Advisory Committee provided advice in a meeting with Series Coordinators for each paper at the beginning of the process to prepare the Series and in a meeting to review and critique the draft reports.

Other contributors

Tanya Malpica-Llanos, Li Liu, and Jamie Perin assisted with analyses of attributable deaths and Rachel White provided administrative support for this paper and the series. Aluisio Barros, Giovanny França, and Maria Clara Restrepo contributed to the analyses of inequalities and of breastfeeding patterns. Anne CC Lee and Naoko Kozuki contributed to analyses on fetal growth restriction. Monika Blössner and Elaine Borghi contributed to the analyses of global and regional estimates of stunting, wasting, underweight, and overweight. Gretchen Stevens and Yuan Lu conducted analysis of maternal BMI; Yuan Lu analysed the studies on the effects of vitamin A and zinc deficiencies.

Conflicts of interest

REB serves on the Boards of the Micronutrient Initiative, Vitamin Angels, the Child Health and Nutrition Research Initiative, and the Nestle Creating Shared Value Advisory Committee. VM serves on the Nestle Creating Shared Value Advisory Committee. MdO is a staff member of the World Health Organization. MdO alone is responsible for the views expressed in this publication; they do not necessarily represent the decisions or policies of the World Health Organization. The other authors declare that they have no conflicts of interest. As corresponding author Robert E Black states that he had full access to all data and final responsibility for the decision to submit for publication.

Acknowledgments

Funding for the preparation of the Series was provided to the Johns Hopkins Bloomberg School of Public Health through a grant from the Bill & Melinda Gates Foundation. The sponsor had no role in the analysis and interpretation of the evidence or in writing the paper and the decision to submit for publication.

References

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

2 Victora CG, Adair L, Fall C, et al, for the Maternal and Child Undernutrition Group. Maternal and child undernutrition: consequences for adult health and human capital. *Lancet* 2008; **371:** 340–57.

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

4 Bryce J, Coitinho D, Darnton-Hill I, et al, for the Maternal and Child Undernutrition Group. Maternal and child undernutrition: effective action at national level. *Lancet* 2008; **371:** 510–26.

5 Morris SS, Cogill B, Uauy R. Effective international action against undernutrition: why has it proven so difficult and what can be done to accelerate progress? *Lancet* 2008; **371:** 608–21.

6 Maternal and Child Nutrition Study Group. Maternal and child nutrition: building momentum for impact. *Lancet* 2013; published online June 6. http://dx.doi.org/10.1016/S0140-6736(13)60988-5.

7 Cappa C, Wardlaw T, Langevin-Falcon C, et al. Progress for children: a report card on adolescents. *Lancet* 2012; **379:** 2323–25.

8 Prentice AM, Ward KA, Goldberg GR, et al. Critical windows for nutritional interventions against stunting. *Am J Clin Nutr* 2013; **93:** 911–18.

9 UNICEF. Progress for children: a report card on maternal mortality. New York: United Nations Children's Fund, 2008.

10 Kozuki N, Lee AC, Vogel J, et al. The association of parity and maternal age with small-for-gestational age, preterm and neonatal and infant mortality: a meta-analysis. *BMC Public Health* (in press).

11 Gibbs CM, Wendt A, Peters S, et al. The impact of early age at first childbirth on maternal and infant health. *Paediatr Perinat Epidemiol* 2012; **26** (suppl 1)**:** 259–84.

12 Gigante DP, Rasmussen KM, Victora CG. Pregnancy increases BMI in adolescents of a population-based birth cohort. *J Nutr* 2005; **135:** 74–80.

13 Rah JH, Christian P, Shamim AA, et al. Pregnancy and lactation hinder growth and nutritional status of adolescent girls in rural Bangladesh. *J Nutr* 2008; **138:** 1505–11.

14 Ministy of Health and Family Welfare Government of India. International Institute for Population Sciences, Macro International. National family health survey (NFHS-3), 2005–06: India: Volume I. Mumbai: IIPS, 2007. http://www.measuredhs.com/pubs/pdf/FRIND3/FRIND3-Vol1AndVol2.pdf (accessed May 20, 2013).

15 Ministerio de Salud Pública y Asistencia Social, Instituto Nacional de Estadística, Centros de Control y Prevención de Enfermedades., Encuesta Nacional de Salud Materno-infantil 2008 (ENSMI-2008/2009). Guatemala, 2010.

16 Finucane MM, Stevens GA, Cowan MJ, et al, on behalf of the Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Blood Glucose). National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9·1 million participants. *Lancet* 2011; **377:** 557–67.

17 Stevens GA, Singh GM, Lu Y, et al. National, regional, and global trends in adult overweight and obesity prevalences. *Popul Health Metr* 2012; **10:** 22.

18 Christian P, Katz J, Wu L, et al. Risk factors for pregnancy-related mortality: a prospective study in rural Nepal. *Public Health* 2008; **122:** 161–72.

19 WHO. Maternal anthropometry and pregnancy outcomes. A WHO collaborative study. *Bull World Health Organ* 1995; **73** (suppl)**:** S1–98.

20 Dujardin B, van Cutsem R, Lambrechts T. The value of maternal height as a risk factor of dystocia: a meta-analysis. *Trop Med Int Health* 1996; **1:** 510–21.

21 Mazouni C, Porcu G, Cohen-Solal E, et al. Maternal and anthropomorphic risk factors for shoulder dystocia. *Acta Obstet Gynecol Scand* 2006; **85:** 567–70.

22 Sheiner E, Levy A, Katz M, et al. Short stature—an independent risk factor for cesarean delivery. *Eur J Obstet Gynecol Reprod Biol* 2005; **120:** 175–78.

23 Chan BCP, Lao TTH. The impact of maternal height on intrapartum operative delivery: a reappraisal. *J Obstet Gynaecol Res* 2009; **35:** 307–14.

24 Van Lieshout RJ, Taylor VH, Boyle MH. Pre-pregnancy and pregnancy obesity and neurodevelopmental outcomes in offspring: a systematic review. *Obes Rev* 2011; **12:** e548–59.

25 Torloni MR, Betran AP, Horta BL, et al. Prepregnancy BMI and the risk of gestational diabetes: a systematic review of the literature with meta-analysis. *Obes Rev* 2009; **10:** 194–203.

26 Tsoi E, Shaikh H, Robinson S, et al. Obesity in pregnancy: a major healthcare issue. *Postgrad Med J* 2010; **86:** 617–23.

27 Sohlberg S, Stephansson O, Cnattingius S, et al. Maternal body mass index, height, and risks of preeclampsia. *Am J Hypertens* 2012; **25:** 120–25.

28 O'Brien TE, Ray JG, Chan WS. Maternal body mass index and the risk of preeclampsia: a systematic overview. *Epidemiology* 2003; **14:** 368–74.

29 Aviram A, Hod M, Yogev Y. Maternal obesity: implications for pregnancy outcome and long-term risks-a link to maternal nutrition. *Int J Gynaecol Obstet* 2011; **115** (suppl 1)**:** S6–10.

30 Norman JE, Reynolds RM. The consequences of obesity and excess weight gain in pregnancy. *Proc Nutr Soc* 2011; **70:** 450–56.

31 Denison FC, Roberts KA, Barr SM, et al. Obesity, pregnancy, inflammation, and vascular function. *Reproduction* 2010; **140:** 373–85.

32 Chen A, Feresu SA, Fernandez C, et al. Maternal obesity and the risk of infant death in the United States. *Epidemiology* 2009; **20:** 74–81.

33 Stothard KJ, Tennant PW, Bell R, et al. Maternal overweight and obesity and the risk of congenital anomalies: a systematic review and meta-analysis. *JAMA* 2009; **301:** 636–50.

34 Koyanagi A, Zhang J, Dagvadorj A, et al. Macrosomia in 23 developing countries: an analysis of a multicountry, facility-based, cross-sectional survey. *Lancet* 2013; **381:** 476–83.

35 Gunatilake RP, Perlow JH. Obesity and pregnancy: clinical management of the obese gravida. *Am J Obstet Gynecol* 2011; **204:** 106–19.

36 Gilboa SM, Correa A, Botto LD, et al. Association between prepregnancy body mass index and congenital heart defects. *Am J Obstet Gynecol* 2010; **202:** 51, e1–10.

37 Cresswell JA, Campbell OM, De Silva MJ, et al. Effect of maternal obesity on neonatal death in sub-Saharan Africa: multivariable analysis of 27 national datasets. *Lancet* 2012; **380:** 1325–30.

38 Temple R, Murphy H. Type 2 diabetes in pregnancy—an increasing problem. *Best Pract Res Clin Endocrinol Metwab* 2010; **24:** 591–603.

39 O'Sullivan JB. Body weight and subsequent diabetes mellitus. *JAMA* 1982; **248:** 949–52.

40 McGuire W, Dyson L, Renfrew M. Maternal obesity: consequences for children, challenges for clinicians and carers. *Semin Fetal Neonatal Med* 2010; **15:** 108–12.

41 Catalano PM. Obesity and pregnancy—the propagation of a viscous cycle? *J Clin Endocrinol Metab* 2003; **88:** 3505–06.

42 Stevens GA, Finucane MM, De-Regil LM, et al, on behalf of Nutrition Impact Model Study Group (Anaemia). Global, regional, and national trends in haemaglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. *Lancet Glob Health* (in press).

43 Haider BA, Olofin I, Wang M, et al. Anaemia, prenatal iron use, and risk of adverse pregnancy outcomes: systematic review and meta-analysis. *BMJ* (in press).

44 De-Regil LM, Jefferds ME, Sylvetsky AC, et al. Intermittent iron supplementation for improving nutrition and development in children under 12 years of age. *Cochrane Database Syst Rev* 2011; **12:** CD009085.

45 WHO. Global prevalence of vitamin A deficiency in populations at risk 1995–2005: WHO global database on vitamin A deficiency. Geneva: World Health Organization, 2009.

46 Andersson M, Karumbunathan V, Zimmermann MB. Global iodine status in 2011 and trends over the past decade. *J Nutr* 2012; **142:** 744–50.

47 Wessells KR, Brown KH. Estimating the global prevalence of zinc deficiency: results based on zinc availability in national food supplies and the prevalence of stunting. *PloS One* 2012; **7:** e50568.

48 Stoltzfus RJ, Mullany L, Black RE. Iron deficiency anaemia. In: Ezzati M, Lopez AD, Rodgers A, Murray CJ, eds. Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Geneva: World Health Organization, 2004: 163–209.

49 Murray-Kolb LE, Chen L, Chen P, et al. CHERG iron report: maternal mortality, child mortality, perinatal mortality, child cognition, and estimates of prevalence of anemia due to iron deficiency. cherg.org/publications/iron-report.pdf (accessed March 11, 2013).

50 Rasmussen KM, Stoltzfus RJ. New evidence that iron supplementation during pregnancy improves birth weight: new scientific questions. *Am J Clin Nutr* 2003; **78:** 673–74.

51 Allen LH. Biological mechanisms that might underlie iron's effects on fetal growth and preterm birth. *J Nutr* 2001; **131:** S581–89.

52 Christian P. Micronutrients, birth weight, and survival. *Annu Rev Nutr* 2010; **30:** 83–104.

53 Imdad A, Bhutta ZA. Routine iron/folate supplementation during pregnancy: effect on maternal anaemia and birth outcomes. *Paediatr Perinat Epidemiol* 2012; **26** (S1)**:** 168–77.

54 Pena-Rosas JP, De-Regil LM, Dowswell T, et al. Intermittent oral iron supplementation during pregnancy. *Cochrane Database Syst Rev* 2012; **7:** CD009997.

55 Dibley MJ, Titaley CR, d'Este C, et al. Iron and folic acid supplements in pregnancy improve child survival in Indonesia. *Am J Clin Nutr* 2012; **95:** 220–30.

56 Zeng L, Dibley MJ, Cheng Y, et al. Impact of micronutrient supplementation during pregnancy on birth weight, duration of gestation, and perinatal mortality in rural western China: double blind cluster randomised controlled trial. *BMJ* 2008; **337:** a2001.

57 Christian P, Stewart CP, LeClerq SC, et al. Antenatal and postnatal iron supplementation and childhood mortality in rural Nepal: a prospective follow-up in a randomized, controlled community trial. *Am J Epidemiol* 2009; **170:** 1127–36.

58 Murray-Kolb LE. Iron status and neuropsychological consequences in women of reproductive age: what do we know and where are we headed? *J Nutr* 2011; **141:** S747–55.

59 Beard JL, Hendricks MK, Perez EM, et al. Maternal iron deficiency anemia affects postpartum emotions and cognition. *J Nutr* 2005; **135:** 267–72.

60 Perez EM, Hendricks MK, Beard JL, et al. Mother-infant interactions and infant development are altered by maternal iron deficiency anemia. *J Nutr* 2005; **135:** 850–55.

61 Frith AL, Naved RT, Ekstrom EC, et al. Micronutrient supplementation affects maternal-infant feeding interactions and maternal distress in Bangladesh. *Am J Clin Nutr* 2009; **90:** 141–48.

62 Christian P, Murray-Kolb LE, Khatry SK, et al. Prenatal micronutrient supplementation and intellectual and motor function in early school-aged children in Nepal. *JAMA* 2010; **304:** 2716–23.

63 Christian P, West KP Jr, Khatry SK, et al. Vitamin A or β-carotene supplementation reduces but does not eliminate maternal night blindness in Nepal. *J Nutr* 1998; **128:** 1458–63.

64 Tielsch JM, Rahmathullah L, Katz J, et al. Maternal night blindness during pregnancy is associated with low birthweight, morbidity, and poor growth in South India. *J Nutr* 2008; **138:** 787–92.

65 Christian P, West KP Jr, Khatry SK, et al. Maternal night blindness increases risk of mortality in the first 6 months of life among infants in Nepal. *J Nutr* 2001; **131:** 1510–12.

66 West KP, Christian P, Labrique AB, et al. Effects of vitamin A or beta carotene supplementation on pregnancy-related mortality and infant mortality in rural Bangladesh: a cluster randomized trial. *JAMA* 2011; **305:** 1986–95.

67 Edmond K, Hurt L, Fenty J, et al. Effect of vitamin A supplementation in women of reproductive age on cause-specific early and late infant mortality in rural Ghana: ObaapaVitA double-blind, cluster-randomised, placebo-controlled trial. *BMJ Open* 2012; **2:** e000658.

68 Christian P, Klemm R, Shamim AA, et al. Effects of vitamin A and beta-carotene supplementation on birth size and length of gestation in rural Bangladesh: a cluster-randomized trial. *Am J Clin Nutr* 2013; **97:** 188–94.

69 Katz J, West KP Jr, Khatry SK, et al. Maternal low-dose vitamin A or beta-carotene supplementation has no effect on fetal loss and early infant mortality: a randomized cluster trial in Nepal. *Am J Clin Nutr* 2000; **71:** 1570–76.

70 King JC. Determinants of maternal zinc status during pregnancy. *Am J Clin Nutr* 2000; **71:** S1334–43.

71 Simmer K, Thompson RP. Maternal zinc and intrauterine growth retardation. *Clin Sci* 1985; **68:** 395–99.

72 Mori R, Ota E, Middleton P, et al. Zinc supplementation for improving pregnancy and infant outcome. *Cochrane Database Syst Rev* 2012; **7:** CD000230.

73 Wong EM, Sullivan KM, Perrine CG, et al. Comparison of median urinary iodine concentration as an indicator of iodine status among pregnant women, school-age children, and nonpregnant women. *Food Nutr Bull* 2011; **32:** 206–12.

74 Zimmermann MB, Andersson M. Assessment of iodine nutrition in populations: past, present, and future. *Nutr Rev* 2012; **70:** 553–70.

75 Pharoah P, Buttfield I, Hetzel B. Neurological damage to the fetus resulting from severe iodine deficiency during pregnancy. *Lancet* 1971; **297:** 308–10.

76 Bleichrodt N, Born MP. A meta-analysis of research on iodine and its relationship to cognitive development. In: Stanbury JB, ed. The damaged brain of iodine deficiency. New York, NY: Cognizant Communication, 1994: 195–200.

77 Qian M, Wang D, Watkins WE, et al. The effects of iodine on intelligence in children: a meta-analysis of studies conducted in China. *Asia Pacific J Clin Nutr* 2005; **14:** 32–42.

78 Zimmermann MB. The effects of iodine deficiency in pregnancy and infancy. *Paediatr Perinat Epidemiol* 2012; **26** (S1)**:** 108–17.

79 Skeaff SA. Iodine deficiency in pregnancy: the effect on neurodevelopment in the child. *Nutrients* 2011; **3:** 265–73.

80 WHO, UNICEF, International Council for the Control of Iodine Deficiency Disorders. Assessment of iodine deficiency disorders and monitoring their elimination: a guide for programme managers, 3rd edn. Geneva: World Health Organization, 2007.

81 McLean E, de Benoist B, Allen LH. Review of the magnitude of folate and vitamin B12 deficiencies worldwide. *Food Nutr Bull* 2008; **29** (suppl 2)**:** S38–51.

82 De-Regil LM, Fernandez-Gaxiola AC, Dowswell T, et al. Effects and safety of periconceptional folate supplementation for preventing birth defects. *Cochrane Database Syst Rev* 2010; **10:** CD007950.

83 Blencowe H, Cousens S, Modell B, et al. Folic acid to reduce neonatal mortality from neural tube disorders. *Int J Epidemiol* 2010; **39** (suppl 1)**:** i110–21.

84 Prentice A. Maternal calcium requirements during pregnancy and lactation. *Am J Clin Nutr* 1994; **59** (suppl 2)**:** S477–82.

85 Villar J, Belizan JM, Fischer PJ. Epidemiologic observations on the relationship between calcium intake and eclampsia. *Int J Gynecol Obstet* 1983; **21:** 271–78.

86 Ortega RM, Martinez RM, Lopez-Sobaler AM, et al. Influence of calcium intake on gestational hypertension. *Ann Nutr Metabol* 1999; **43:** 37–46.

87 Srinivas SK, Edlow AG, Neff PM, et al. Rethinking IUGR in preeclampsia: dependent or independent of maternal hypertension? *J Perinatol* 2009; **29:** 680–84.

88 Duley L. The global impact of pre-eclampsia and eclampsia. *Semin Perinatol* 2009; **33:** 130–37.

89 Hofmeyr GJ, Lawrie TA, Atallah A, et al. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. *Cochrane Database Syst Rev* 2010; **8:** CD001059.

90 Bucher HC, Cook RJ, Guyatt GH, et al. Effects of dietary calcium supplementation on blood pressure. A meta-analysis of randomized controlled trials. *JAMA* 1996; **275:** 1016–22.

91 Imdad A, Bhutta ZA. Effects of calcium supplementation during pregnancy on maternal, fetal and birth outcomes. *Paediatr Perinat Epidemiol* 2012; **26** (suppl 1)**:** 138–52.

92 WHO. World Health Organization recommendations for prevention and treatment of pre-eclampsia and eclampsia. Geneva: World Health Organization, 2011.

93 Bhutta ZA, Das JK, Rizvi A, et al, *The Lancet* Nutrition Interventions Review Group and the Maternal and Child Nutrition Study Group. Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? *Lancet* 2013; published online June 6. http://dx.doi.org/10.1016/S0140-6736(13)60996-4.

94 Ross AC, Taylor CL, Yaktine AL, et al. Dietary reference intakes for calcium and vitamin D. Washington, DC; National Academies Press, 2010.

95 Ross AC, Manson JE, Abrams SA, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. *J Clin Endocrinol Metab* 2011; **96:** 53–58.

96 Alfaham M, Woodhead S, Pask G, et al. Vitamin D deficiency: a concern in pregnant Asian women. *Br J Nutr* 1995; **73:** 881–87.

97 Bodnar LM, Catov JM, Simhan HN, et al. Maternal vitamin D deficiency increases the risk of preeclampsia. *J Clin Endocrinol Metabol* 2007; **92:** 3517–22.

98 Davis L, Chang SC, Mancini J, et al. Vitamin D insufficiency is prevalent among pregnant African American adolescents. *J Pediatr Adoles Gynecol* 2010; **23:** 45–52.

99 Hypponen E, Boucher BJ. Avoidance of vitamin D deficiency in pregnancy in the United Kingdom: the case for a unified approach in national policy. *Br J Nutr* 2010; **104:** 309–14.

100 Kazemi A, Sharifi F, Jafari N, et al. High prevalence of vitamin D deficiency among pregnant women and their newborns in an Iranian population. *J Women Health* 2009; **18:** 835–39.

101 Madar AA, Stene LC, Meyer HE. Vitamin D status among immigrant mothers from Pakistan, Turkey and Somalia and their infants attending child health clinics in Norway. *Br J Nutr* 2009; **101:** 1052–58.

102 Sachan A, Gupta R, Das V, et al. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. *Am J Clin Nutr* 2005; **81:** 1060–64.

103 van der Meer IM, Karamali NS, Boeke AJP, et al. High prevalence of vitamin D deficiency in pregnant non-Western women in The Hague, Netherlands. *Am J Clin Nutr* 2006; **84:** 350–53.

104 Brooke OG, Brown IR, Bone CD, et al. Vitamin D supplements in pregnant Asian women: effects on calcium status and fetal growth. *BMJ* 1980; **280:** 751–54.

105 Dawodu A, Wagner CL. Mother-child vitamin D deficiency: an international perspective. *Arch Dis Child* 2007; **92:** 737–40.

106 Javaid MK, Crozier SR, Harvey NC, et al, and the Princess Anne Hospital Study Group. Maternal vitamin D status during pregnancy and childhood bone mass at age 9 years: a longitudinal study. *Lancet* 2006; **367:** 36–43.

107 Mackay-Sim A, Feron F, Eyles D, et al. Schizophrenia, vitamin D, and brain development. *Int Rev Neurobiol* 2004; **59:** 351–80.

108 Shenoy S, Swift P, Cody D, et al. Maternal vitamin D deficiency, refractory neonatal hypocalcaemia, and nutritional rickets. *Arch Dis Child* 2005; **90:** 437–38.

109 Dror DK. Vitamin D status during pregnancy: maternal, fetal, and postnatal outcomes. *Curr Opin Obstet Gynecol* 2011; **23:** 422–26.

110 MacKay AP, Berg CJ, Atrash HK. Pregnancy-related mortality from preeclampsia and eclampsia. *Obstet Gynecol* 2001; **97:** 533–38.

111 De-Regil LM, Palacios C, Ansary A, et al. Vitamin D supplementation for women during pregnancy. *Cochrane Database Syst Rev* 2012; **2:** CD008873.

112 Victora CG, Hallal PC, Araujo CL, et al. Cohort profile: the 1993 Pelotas (Brazil) birth cohort study. *Int J Epidemiol* 2008; **37:** 704–09.

113 Victora CG, Barros FC. Cohort profile: the 1982 Pelotas (Brazil) birth cohort study. *Int J Epidemiol* 2006; **35:** 237–42.

114 Shah A, Faundes A, Machoki M, et al. Methodological considerations in implementing the WHO Global Survey for Monitoring Maternal and Perinatal Health. *Bull World Health Organ* 2008; **86:** 126–31.

115 Santos IS, Barros AJ, Matijasevich A, et al. Cohort profile: the 2004 Pelotas (Brazil) birth cohort study. *Int J Epidemiol* 2011; **40:** 1461–68.

116 Roberfroid D, Huybregts L, Lanou H, et al. Effects of maternal multiple micronutrient supplementation on fetal growth: a double-blind randomized controlled trial in rural Burkina Faso. *Am J Clin Nutr* 2008; **88:** 1330–40.

117 Osrin D, Vaidya A, Shrestha Y, et al. Effects of antenatal multiple micronutrient supplementation on birthweight and gestational duration in Nepal: double-blind, randomised controlled trial. *Lancet* 2005; **365:** 955–62.

118 Isaranurug S, Mo-suwan L, Choprapawon C. A population-based cohort study of effect of maternal risk factors on low birthweight in Thailand. *J Med Assoc Thai* 2007; **90:** 2559–64.

119 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.

120 Christian P, West KP, Khatry SK, et al. Effects of maternal micronutrient supplementation on fetal loss and infant mortality: a cluster-randomized trial in Nepal. *Am J Clin Nutr* 2003; **78:** 1194–202.

121 Caulfield LE, Zavaleta N, Figueroa A, et al. Maternal zinc supplementation does not affect size at birth or pregnancy duration in Peru. *J Nutr* 1999; **129:** 1563–68.

122 Özaltin E, Hill K. Subramanian S. V. Association of maternal stature with offspring mortality, underweight, and stunting in low- to middle-income countries. *JAMA* 2010; **303:** 1507–16.

123 Lee AC, Katz J, Blencowe H, et al, for the CHERG SGA-Preterm Birth Working Group. National and regional estimates of term and preterm babies born small-for-gestational age in 138 low-income and middle-income countries in 2010. *Lancet Glob Health* (in press).

124 Regev RH, Reichman B. Prematurity and intrauterine growth retardation—double jeopardy? *Clin Perinatol* 2004; **31:** 453–73.

125 Pulver LS, Guest-Warnick G, Stoddard GJ, et al. Weight for gestational age affects the mortality of late preterm infants. *Pediatrics* 2009; **123:** e1072–77.

126 Narchi H, Skinner A, Williams B. Small for gestational age neonates—are we missing some by only using standard population growth standards and does it matter? *J Matern Fetal Neonatal Med* 2010; **23:** 48–54.

127 Kristensen S, Salihu HM, Keith LG, et al. SGA subtypes and mortality risk among singleton births. *Early Hum Dev* 2007; **83:** 99–105.

128 Grisaru-Granovsky S, Reichman B, Lerner-Geva L, et al. Mortality and morbidity in preterm small-for-gestational-age infants: a population-based study. *Am J Obstet Gynecol* 2012; **206:** 150 e1–7.

129 Clausson B, Cnattingius S, Axelsson O. Preterm and term births of small for gestational age infants: a population-based study of risk factors among nulliparous women. *Br J Obstet Gynaecol* 1998; **105:** 1011–17.

130 Katz J, Lee AC, Kozuki N, et al, and the CHERG Small-for-Gestational-Age-Preterm Birth Working Group. Mortality risk in preterm and small-for-gestational-age infants in low-income and middle-income countries: a pooled country analysis. *Lancet* 2013; published online June 6. http://dx.doi.org/10.1016/S0140-6736(13)60993-9.

131 UNICEF, WHO, World Bank, UNPD. Levels and trends in child mortality, report 2011. New York, NY: United Nations International Children's Fund, 2011.

132 Christian P, Lee S, Donahue M and the CHERG Working Group. Risk of childhood undernutrition related to small-for-gestational age and preterm birth in developing countries. *Int J Epidemiol* (in press).

133 Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. *JAMA* 1998; **280:** 1690–91.

134 Walker SP, Wachs TD, Gardner JM, et al. Child development: risk factors for adverse outcomes in developing countries. *Lancet* 2007; **369:** 145–57.

135 Walker SP, Wachs TD, Grantham-McGregor S, et al. Inequality in early childhood: risk and protective factors for early child development. *Lancet* 2011; **378:** 1325–38.

136 Tofail F, Hamadani J, Ahmed A, et al. The mental development and behavior of low-birth-weight Bangladeshi infants from an urban low-income community. *Eur J Clin Nutr* 2011; **66:** 237–43.

137 Kuklina EV, Ramakrishnan U, Stein AD, et al. Early childhood growth and development in rural Guatemala. *Early Hum Dev* 2006; **82:** 425–33.

138 Martorell R, Horta BL, Adair LS, et al. Weight gain in the first two years of life is an important predictor of schooling outcomes in pooled analyses from five birth cohorts from low- and middle-income countries. *J Nutr* 2010; **140:** 348–54.

139 Li H, DiGirolamo AM, Barnhart HX, et al. Relative importance of birth size and postnatal growth for women's educational achievement. *Early Hum Dev* 2004; **76:** 1–16.

140 Emond AM, Lira PIC, Lima MC, et al. Development and behaviour of low-birthweight term infants at 8 years in northeast Brazil: a longitudinal study. *Acta Paediatr* 2007; **95:** 1249–57.

141 Walker SP, Chang SM, Younger N, et al. The effect of psychosocial stimulation on cognition and behaviour at 6 years in a cohort of term, low-birthweight Jamaican children. *Dev Med Child Neurol* 2010; **52:** e148–54.

142 Sabet F, Richter LM, Ramchandani PG, et al. Low birthweight and subsequent emotional and behavioural outcomes in 12-year-old children in Soweto, South Africa: findings from birth to twenty. *Int J Epidemiol* 2009; **38:** 944–54.

143 Wang WL, Sung YT, Sung FC, et al. Low birth weight, prematurity, and paternal social status: impact on the basic competence test in Taiwanese adolescents. *J Pediatr* 2008; **153:** 333–38.

144 Pongcharoen T, Ramakrishnan U, DiGirolamo AM, et al. Influence of prenatal and postnatal growth on intellectual functioning in school-aged children. *Arch Pediatr Adol Med* 2012; **166:** 411–16.

145 Haroon S, Das JK, Salam RA, et al. Breastfeeding promotion interventions and breastfeeding practices: a systematic review. *BMC Public Health* (in press).

146 Imdad A, Bhutta ZA. Effect of preventive zinc supplementation on linear growth in children under 5 years of age in developing countries: a meta-analysis of studies for input to the lives saved tool. *BMC Public Health* 2011; **11** (suppl 3)**:** S22.

147 Checkley W, Buckley G, Gilman RH, et al. Multi-country analysis of the effects of diarrhoea on childhood stunting. *Int J Epidemiol* 2008; **37:** 816–30.

148 Humphrey JH. Child undernutrition, tropical enteropathy, toilets, and handwashing. *Lancet* 2009; **374:** 1032–35.

149 Adair LS, Fall C, Osmond C, et al. Associations of linear growth and relative weight gain during early life with adult health and human capital in countries of low and middle income: findings from five birth cohort studies. *Lancet* 2013; published online March 28. http://dx.doi.org/10.1016/S1040-6736(13)60103-8.

150 Kuzawa CW, Hallal PC, Adair L, et al. Birth weight, postnatal weight gain, and adult body composition in five low and middle income countries. *Am J Hum Biol* 2012; **24:** 5–13.

151 Kipping RR, Jago R, Lawlor DA. Obesity in children. Part 1: Epidemiology, measurement, risk factors, and screening. *BMJ* 2008; **337:** a1824.

152 Kipping RR, Jago R, Lawlor DA. Obesity in children. Part 2: Prevention and management. *BMJ* 2008; **337:** a1848.

153 Han JC, Lawlor DA, Kimm SY. Childhood obesity. *Lancet* 2010; 375: 1737–48.

154 UNICEF, WHO, World Bank. Levels and trends in child malnutrition. Joint child malnutrition estimates. New York, NY: United Nations International Children's Fund; Geneva: World Health Organization; Washington, DC: World Bank, 2012.

155 de Onis M, Blössner M, Borghi E, et al. Methodology for estimating regional and global trends of child malnutrition. *Int J Epidemiol* 2004; **33:** 1260–70.

156 de Onis M, Blössner M, Borghi E. Prevalence and trends of stunting among pre-school children, 1990–2020. *Pub Health Nutr* 2011; **15:** 142–48.

157 Stevens GA, Finucane MM, Paciorek CJ, et al. Trends in mild, moderate, and severe stunting and underweight, and progress towards MDG 1 in 141 developing countries: a systematic analysis of population representative data. *Lancet* 2012; **380:** 824–34.

158 Barros AJ, Victora C. Measuring coverage in MNCH: determining and interpreting inequalities in coverage of maternal, newborn, and child health interventions. *PLoS Med* 2013; **10:** e1001390.

159 Pelletier DL, Frongillo EA Jr, Schroeder DG, et al. The effects of malnutrition on child mortality in developing countries. *Bull World Health Organ* 1995; **73:** 443–48.

160 Caulfield LE, de Onis M, Blossner M, et al. Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria, and measles. *Am J Clin Nutr* 2004; **80:** 193–98.

161 Olofin I, McDonald CM, Ezzati M, et al, for the Nutrition Impact Model Study (anthropometry cohort pooling). Associations of suboptimal growth with all-cause and cause-specific mortality in children under five years: pooled analysis of ten prospective studies. *PLoS One* (in press).

162 Liu L, Johnson HL, Cousens S, et al. Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet* 2012; **379:** 2151–61.

163 Grantham-McGregor S, Cheung YB, Cueto S, et al. Developmental potential in the first 5 years for children in developing countries. *Lancet* 2007; **369:** 60–70.

164 Walker CLF, Lamberti L, Adair L, et al. Does childhood diarrhea influence cognition beyond the diarrhea-stunting pathway? *PloS One* 2012; **7:** e47908.

165 Aburto NJ, Ramirez-Zea M, Neufeld LM, et al. Some indicators of nutritional status are associated with activity and exploration in infants at risk for vitamin and mineral deficiencies. *J Nutr* 2009; **139:** 1751–57.

166 Gardner JM, Grantham-McGregor SM, Himes J, et al. Behaviour and development of stunted and nonstunted Jamaican children. *J Child Psychol Psychiatry* 1999; **40:** 819–27.

167 Kuklina EV, Ramakrishnan U, Stein AD, et al. Early childhood growth and development in rural Guatemala. *Early Hum Dev* 2006; **82:** 425–33.

168 Adair LS, Fall CH, Osmond C, et al, for the COHORTS group. Associations of linear growth and relative weight gain during early life with adult health and human capital in countries of low and middle income: findings from five birth cohort studies. *Lancet* 2013; published online March 28. http://dx.doi.org.10.1016/S0140-6736(13)60103-8.

169 Cheung YB, Ashorn P. Continuation of linear growth failure and its association with cognitive ability are not dependent on initial length-for-age: a longitudinal study from 6 months to 11 years of age. *Acta Paediatr* 2010; **99:** 1719–23.

170 Gandhi M, Ashorn P, Maleta K, et al. Height gain during early childhood is an important predictor of schooling and mathematics ability outcomes. *Acta Paediatr* 2011; **100:** 1113–18.

171 Koplan JP, Liverman CT, Kraak VI, Committee on Prevention of Obesity in Children and Youth. Preventing childhood obesity: health in the balance: executive summary. *J Am Diet Assoc* 2005; **105:** 131–38.

172 Lloyd LJ, Langley-Evans SC, McMullen S. Childhood obesity and risk of the adult metabolic syndrome: a systematic review. *Int J Obes (Lond)* 2012; **36:** 1–11.

173 Sachdev H, Gera T, Nestel P. Effect of iron supplementation on mental and motor development in children: systematic review of randomised controlled trials. *Public Health Nutr* 2005; **8:** 117–32.

174 Szajewska H, Ruszczynski M, Chmielewska A. Effects of iron supplementation in nonanemic pregnant women, infants, and young children on the mental performance and psychomotor development of children: a systematic review of randomized controlled trials. *Am J Clin Nutr* 2010; **91:** 1684–90.

175 Grantham-McGregor S, Baker-Henningham H. Iron deficiency in childhood: causes and consequences for child development. *Ann Nestlé* 2010; **68:** 105–19.

176 Aukett M, Parks Y, Scott P, et al. Treatment with iron increases weight gain and psychomotor development. *Arch Dis Child* 1986; **61:** 849–57.

177 Idjradinata P, Pollitt E. Reversal of developmental delays in iron-deficient anaemic infants treated with iron. *Lancet* 1993; **341:** 1–4.

178 Stoltzfus RJ, Kvalsvig JD, Chwaya HM, et al. Effects of iron supplementation and anthelmintic treatment on motor and language development of preschool children in Zanzibar: double blind, placebo controlled study. *BMJ* 2001; **323:** 1389–93.

179 Lind T, Lönnerdal B, Stenlund H, et al. A community-based randomized controlled trial of iron and zinc supplementation in Indonesian infants: interactions between iron and zinc. *Am J Clin Nutr* 2003; **77:** 883–90.

180 Black MM, Baqui AH, Zaman K, et al. Iron and zinc supplementation promote motor development and exploratory behavior among Bangladeshi infants. *Am J Clin Nutr* 2004; **80:** 903–10.

181 Friel JK, Aziz K, Andrews WL, et al. A double-masked, randomized control trial of iron supplementation in early infancy in healthy term breast-fed infants. *J Pediatr* 2003; **143:** 582–86.

182 Moffatt M, Longstaffe S, Besant J, et al. Prevention of iron deficiency and psychomotor decline in high-risk infants through use of iron-fortified infant formula: a randomized clinical trial. *J Pediatr* 1994; **125:** 527–34.

183 Pongcharoen T, DiGirolamo AM, Ramakrishnan U, et al. Long-term effects of iron and zinc supplementation during infancy on cognitive function at 9 y of age in northeast Thai children: a follow-up study. *Am J Clin Nutr* 2011; **93:** 636–43.

184 Olney DK, Pollitt E, Kariger PK, et al. Combined iron and folic acid supplementation with or without zinc reduces time to walking unassisted among Zanzibari infants 5- to 11-mo old. *J Nutr* 2006; **136:** 2427–34.

185 Katz J, Khatry SK, Leclerq SC, et al. Daily supplementation with iron plus folic acid, zinc, and their combination is not associated with younger age at first walking unassisted in malnourished preschool children from a deficient population in rural Nepal. *J Nutr* 2010; **140:** 1317–21.

186 Surkan PJ, Siegel EH, Patel SA, et al. Effects of zinc and iron supplementation fail to improve motor and language milestone scores of infants and toddlers. *Nutrition* 2013; **29:** 542–48.

187 Siegel EH, Kordas K, Stoltzfus RJ, et al. Inconsistent effects of iron-folic acid and/or zinc supplementation on the cognitive development of infants. *J Health Popul Nutr* 2011; **29:** 593–604.

188 Beaton GH, Martorell R, Aronson K, et al. Effectiveness of vitamin A supplementation in the control of young child morbidity and mortality in developing countries—nutrition policy discussion paper no 13. Toronto, ON: International Nutrition Program, 1993.

189 Fawzi WW, Chalmers TC, Herrera MG, et al. Vitamin A supplementation and child mortality. *JAMA* 1993; **269:** 898–903.

190 Mayo-Wilson E, Imdad A, Herzer K, et al. Vitamin A supplements for preventing mortality, illness, and blindness in children aged under 5: systematic review and meta-analysis. *BMJ* 2011; **343:** d5094.

191 Imdad A, Yakoob MY, Sudfeld C, et al. Impact of vitamin A supplementation on infant and childhood mortality. *BMC Public Health* 2011; **11** (suppl 3)**:** S20

192 Awasthi S, Peto R, Read S, et al. Population deworming every 6 months with albendazole in 1 million pre-school children in north India: DEVTA, a cluster-randomised trial. *Lancet* 2013; **381:** 1478–86.

193 Rahmathullah L, Tielsch JM, Thulasiraj RD, et al. Impact of supplementing newborn infants with vitamin A on early infant mortality: community based randomised trial in southern India. *BMJ* 2003; **327:** 254.

194 Klemm RD, Labrique AB, Christian P, et al. Newborn vitamin A supplementation reduced infant mortality in rural Bangladesh. *Pediatrics* 2008; **122:** e242–50.

195 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.

196 International Zinc Nutrition Consultative Group, Brown KH, Rivera JA, et al. International Zinc Nutrition Consultative Group (IZiNCG) technical document #1. Assessment of the risk of zinc deficiency in populations and options for its control. *Food Nutr Bull* 2004; **25** (1 suppl 2)**:** S99–203.

197 Yakoob MY, Theodoratou E, Jabeen A, et al. Preventive zinc supplementation in developing countries: impact on mortality and morbidity due to diarrhea, pneumonia and malaria. *BMC Public Health* 2011; **11** (suppl 3)**:** S23.

198 Brown KH, Peerson JM, Baker SK, et al. Preventive zinc supplementation among infants, preschoolers, and older prepubertal children. *Food Nutr Bull* 2009; **30** (suppl 1)**:** S12–40.

199 Rice AL, West KP Jr, Black RE. Vitamin A deficiency. In: WHO. Comparative quantification of health risks: global and regional burden of disease attributes to selected major risk factors. Geneva: World Health Organization, **2004:** 211–56.

200 Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2013; **380:** 2224–60.

201 Imdad A, Bhutta ZA. Effect of preventive zinc supplementation on linear growth in children under 5 years of age in developing countries: a meta-analysis of studies for input to the lives saved tool. *BMC Public Health* 2011; **11** (suppl 3)**:** S22.

202 Lamberti LM, Fischer Walker CL, Noiman A, et al. Breastfeeding and the risk for diarrhea morbidity and mortality. *BMC Public Health* 2011; **11** (suppl 3)**:** S15.

203 Lamberti LM, Zakarija-Grkovic I, Fischer Walker CL, et al. Breastfeeding for reducing the risk of pneumonia morbidity and mortality in children under two: a systematic literature review and meta-analysis. *BMC Public Health* (in press).

204 Debes AK, Kohli A, Walker N, et al. Time to initation of breastfeeding and neonatal mortality and morbidity: a systematic review. *BMC Public Health* (in press).

205 Horta BL, Victora C. Long-term effects of breastfeeding: a series of systematic reviews. Geneva: World Health Organization, 2013.

206 Ezzati M, Lopez AD, Rodgers A, et al, and the Comparative Risk Assessment Collaborating Group. Selected major risk factors and global and regional burden of disease. *Lancet* 2002; **360:** 1347–60.

207 Ezzati M, Hoorn SV, Rodgers A, et al, and the Comparative Risk Assessment Collaborating Group. Estimates of global and regional potential health gains from reducing multiple major risk factors. *Lancet* 2003; **362:** 271–80.

208 Richter LM, Victora CG, Hallal PC, et al. Cohort profile: the consortium of health-orientated research in transitioning societies. *Int J Epidemiol* 2012; **41:** 621–26.

209 Walker SP, Chang SM, Powell CA, et al. Early childhood stunting is associated with poor psychological functioning in late adolescence and effects are reduced by psychosocial stimulation. *J Nutr* 2007; **137:** 2464–69.

210 Galler JR, Bryce CP, Waber D, et al. Early childhood malnutrition predicts depressive symptoms at ages 11–17. *J Child Psychol Psychiatry* 2010; **51:** 789–98.

211 Cheung YB, Ashorn P. Linear growth in early life is associated with suicidal ideation in 18-year-old Filipinos. *Paediatr Perinat Epidemiol* 2009; **23:** 463–71.

212 Galler JR, Bryce CP, Zichlin ML, et al. Infant malnutrition is associated with persisting attention deficits in middle adulthood. *J Nutr* 2012; **142:** 788–94.

213 Maluccio JA, Hoddinott J, Behrman JR, et al. The impact of improving nutrition during early childhood on education among Guatemalan adults. *Econ J* 2009; **119:** 734–63.

214 Hoddinott J, Maluccio JA, Behrman JR, et al. Effect of a nutrition intervention during early childhood on economic productivity in Guatemalan adults. *Lancet* 2008; **371:** 411–16.

215 Stein AD, Wang M, Ramirez-Zea M, et al. Exposure to a nutrition supplementation intervention in early childhood and risk factors for cardiovascular disease in adulthood: evidence from Guatemala. *Am J Epidemiol* 2006; **164:** 1160–70.

216 Lumey LH, Stein AD, Susser E. Prenatal famine and adult health. *Ann Rev Public Health* 2011; **32:** 237–62.

217 Chen Y, Zhou L-A. The long-term health and economic consequences of the 1959–1961 famine in China. *J Health Econ* 2007; **26:** 659–81. 218 Huang C, Li Z, Wang M, et al. Early life exposure to the 1959–1961 Chinese famine has long-term health consequences. *J Nutr* 2010; **140:** 1874–78.

219 Song S, Wang W, Hu P. Famine, death, and madness: schizophrenia in early adulthood after prenatal exposure to the Chinese great leap forward famine. *Soc Sci Med* 2009; **68:** 1315–21.

220 Huang C, Phillips MR, Zhang Y, et al. Malnutrition in early life and adult mental health: evidence from a natural experiment. *Soc Sci Med* 2012; published online Dec 20. DOI:10.1016/j.socscimed.2012.09.051.

221 Huang C, Li Z, Venkat Narayan KM, et al. Bigger babies born to women survivors of the 1959–1961 Chinese famine: a puzzle due to survival selection? *J Dev Orig Health Dis* 2010; **1:** 412–18.

222 WHO. Discussion paper. Proposed global targets for maternal, infant and young child nutrition. Geneva: World Health Organization, 2012.

223 Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2013; **380:** 2095–128.

224 de Onis M, Blössner M, Borghi E. Global prevalence and trends of overweight and obesity among preschool children. *Am J Clin Nutr* 2010; **92:** 1257–64.

225 McCormick DP, Sarpong K, Jordan L, et al. Infant obesity: are we ready to make this diagnosis? *J Pediatr* 2010; **157:** 15–19.

226 Evellen vanDijk C, Innis SM. Growth-curve standards and the assessment of early excess weight gain in infancy. *Pediatrics* 2009; **123:** 102–08.

227 Bruce KD, Hanson MA. The developmental origins, mechanisms, and implications of metabolic syndrome. *J Nutr* 2010; **140:** 648–52.

228 Gewa CA. Childhood overweight and obesity among Kenyan pre-school children: association with maternal and early child nutritional factors—erratum. *Pub Health Nutr* 2009; **13:** 496–503.

229 Griffiths L, Hawkins S, Cole T, et al. Risk factors for rapid weight gain in preschool children: findings from a UK-wide prospective study. *Int J Obes (Lond)* 2010; **34:** 624–32.