Maternal and Child Undernutrition 1

Maternal and child undernutrition: global and regional exposures and health consequences

*Robert E Black, Lindsay H Allen, Zulfiqar A Bhutta, Laura E Caulfield, Mercedes de Onis, Majid Ezzati, Colin Mathers, Juan Rivera, for the Maternal and Child Undernutrition Study Group**

Maternal and child undernutrition is highly prevalent in low-income and middle-income countries, resulting in substantial increases in mortality and overall disease burden. In this paper, we present new analyses to estimate the effects of the risks related to measures of undernutrition, as well as to suboptimum breastfeeding practices on mortality and disease. We estimated that stunting, severe wasting, and intrauterine growth restriction together were responsible for 2·2 million deaths and 21% of disability-adjusted life-years (DALYs) for children younger than 5 years. Deficiencies of vitamin A and zinc were estimated to be responsible for 0·6 million and 0·4 million deaths, respectively, and a combined 9% of global childhood DALYs. Iron and iodine deficiencies resulted in few child deaths, and combined were responsible for about 0·2% of global childhood DALYs. Iron deficiency as a risk factor for maternal mortality added 115 000 deaths and 0·4% of global total DALYs. Suboptimum breastfeeding was estimated to be responsible for 1·4 million child deaths and 44 million DALYs (10% of DALYs in children younger than 5 years). In an analysis that accounted for co-exposure of these nutrition-related factors, they were together responsible for about 35% of child deaths and 11% of the total global disease burden. The high mortality and disease burden resulting from these nutrition-related factors make a compelling case for the urgent implementation of interventions to reduce their occurrence or ameliorate their consequences.

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

*Members listed at end of paper

Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA (Prof R E Black MD, Prof L E Caulfield PhD)**; USDA, ARS Western Human Nutrition Research Center, Davis, CA, USA** (Prof L H Allen PhD)**; Aga Khan University, Karachi, Pakistan** (Prof Z A Bhutta, MD)**; World Health Organization, Geneva, Switzerland** (M de Onis MD, C Mathers PhD)**; Harvard School of Public Health, Boston, MA, USA** (M Ezzati PhD)**; and Mexico National Institute of Public Health, Cuernavaca, Mexico** (Prof J Rivera PhD)

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

Introduction

Maternal and child undernutrition remain pervasive and damaging conditions in low-income and middle-income countries. A framework developed by UNICEF recognises the basic and underlying causes of undernutrition, including the environmental, economic, and sociopolitical contextual factors, with poverty having a central role (figure 1). Although addressing general deprivation and inequity would result in substantial reductions in undernutrition[1] and should be a global priority, major reductions in undernutrition can also be made through programmatic health and nutrition interventions. This paper is the first in a Series of five papers that focus on the disease burden attributable to undernutrition and the interventions affecting household food availability and use, maternal and child care, and control of infectious diseases. The first two papers quantify the prevalence of maternal and child undernutrition and consider the short-term consequences in terms of deaths and disease burden, as measured by disability-adjusted life-years (DALYs). They also discuss the long-term educational and economic effects and associations with adult chronic diseases, particularly as countries go through the demographic, epidemiological, and nutritional transitions.[2–6] The third paper estimates the potential benefits of implementing health and nutrition interventions that current evidence indicates are effective and applicable in low-income and middle-income countries. The final two papers consider the current state of such interventions and how they could be implemented fully through actions at national and global levels.

Undernutrition encompasses stunting, wasting, and deficiencies of essential vitamins and minerals (collectively referred to as micronutrients) as one form of the condition known as malnutrition, with obesity or over-consumption of specific nutrients as another form. The term hunger, which literally describes a feeling of discomfort from not eating, has also been used to describe

Key messages

- Maternal and child undernutrition is the underlying cause of 3·5 million deaths, 35% of the disease burden in children younger than 5 years and 11% of total global DALYs
- The number of global deaths and DALYs in children less than 5 years old attributed to stunting, severe wasting, and intrauterine growth restriction constitutes the largest percentage of any risk factor in this age group
- Vitamin A and zinc deficiencies have by far the largest remaining disease burden among the micronutrients considered
- Iodine and iron deficiencies have small disease burdens, partly because of intervention programmes, but sustained effort is needed to further reduce their burden
- Suboptimum breastfeeding, especially non-exclusive breastfeeding in the first 6 months of life, results in 1·4 million deaths and 10% of disease burden in children younger than 5 years
- Maternal short stature and iron deficiency anaemia increase the risk of death of the mother at delivery, accounting for at least 20% of maternal mortality

undernutrition, especially in reference to food insecurity, wherein people do not have "physical and economic access to sufficient, safe, nutritious, and culturally acceptable food to meet their dietary needs".[7,8] Undernutrition is an important determinant of maternal and child health.[9–12]

The Millennium Development Goals (MDGs) state as the first goal "to halve between 1990 and 2015 the proportion of people who suffer from hunger."[7] One indicator to monitor progress for this target is the proportion of children who are underweight—ie, low weight compared with that expected for a well-nourished child of that age and sex. This anthropometric indicator can indicate wasting (ie, low weight-for-height, indicating acute weight loss), or much more commonly, stunting (ie, low height-for-age, indicating chronic restriction of a child's potential growth). Those two conditions can have different determinants and respond to different interventions.[13] Therefore, consideration of wasting and stunting is more useful than consideration of underweight. This series primarily uses these two indicators, but also presents information on underweight because weight-for-age has been used in previous analyses.[9–11] Reduction of fetal growth restriction and micronutrient deficiencies is also essential to achieving the MDGs and deserves high priority, even though there are no MDG indicators for these conditions. This Series also examines the consequences of low body-mass index and short stature in women.

See Online for webtable 1

See Online for webtable 2

This paper consists mainly of new analyses of the prevalence of nutritional conditions, risk factors, and consequent disease burden; if this was not possible or necessary, previously published results are presented. The burden of disease attributable to maternal and child undernutrition is presented for three world regions—Africa, Asia, and Latin America—that include primarily low-income and middle-income countries; only 1% of deaths in children younger than 5 years occur outside these regions. UN regions and subregions (webtable 1) were used.

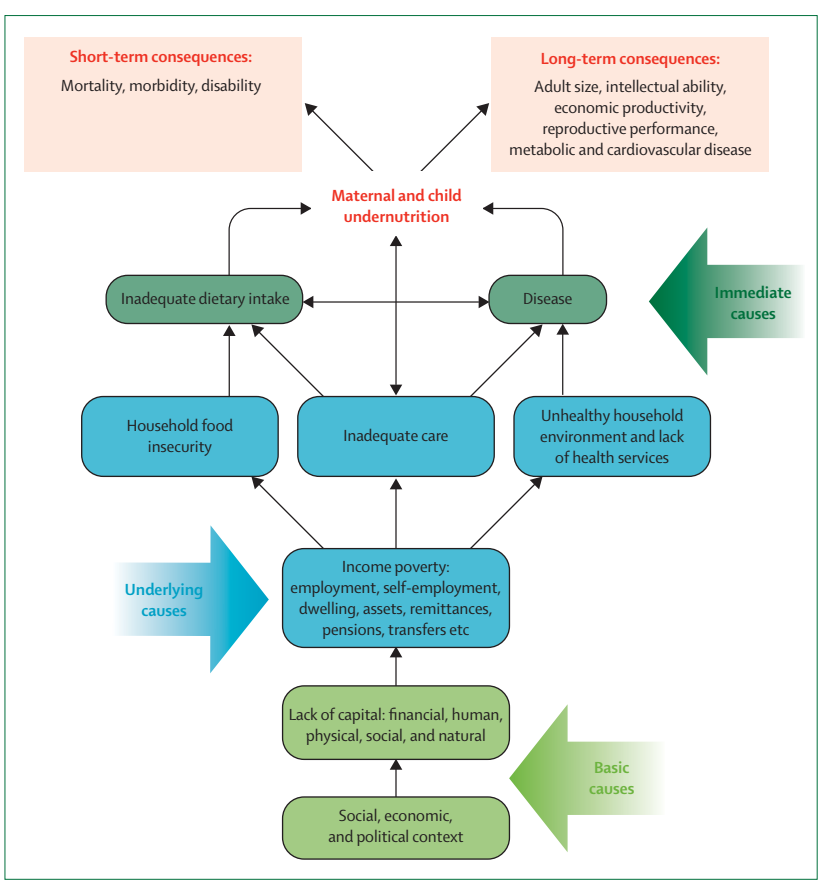

Figure 1: **Framework of the relations between poverty, food insecurity, and other underlying and immediate causes to maternal and child undernutrition and its short-term and long-term consequences**

Prevalence and consequences

Maternal short stature and low body-mass index in pregnancy and lactation

Maternal undernutrition, including chronic energy and micronutrient deficiencies, is prevalent in many regions, especially in south-central Asia, where in some countries more than 10% of women aged 15–49 years are shorter than 145 cm (webtable 2). Maternal undernutrition—ie, body-mass index of less than 18·5 kg/m²—ranges from 10% to 19% in most countries. A serious problem of maternal undernutrition is evident in most countries in sub-Saharan Africa, south-central and southeastern Asia, and in Yemen, where more than 20% of women have a body-mass index of less than 18·5 kg/m². With a prevalence of low body-mass index around 40% in women, the situation can be considered critical in India, Bangladesh, and Eritrea. Maternal short stature and low body-mass index have independent adverse effects on pregnancy outcomes.

The nutritional status of a woman before and during pregnancy is important for a healthy pregnancy outcome.[14,15] Maternal short stature is a risk factor for caesarean delivery, largely related to cephalopelvic disproportion. A meta-analysis of epidemiological studies found a 60% (95% CI 50–70) increased need for assisted delivery among women in the lowest quartile of stature (146 cm to 157 cm, depending on the region) compared with women in the highest quartile.[16] If operative delivery to ensure a healthy birth is not available to women who need it, both mother and baby are at risk.[17] Even if operative delivery is accessible, affordable, and safe, anaesthesia and laparotomy increase the risk of maternal morbidity.[18] Low maternal body-mass index does not seem to increase the risk of pregnancy complications and assisted delivery.[16] Rather, there seems to be a synergistic positive effect of short stature and higher maternal body-mass index on increasing these complications.[19,20]

Low maternal body-mass index is associated with intrauterine growth restriction.[11] Previous analyses estimated the disease burden of low maternal body-mass index as a risk factor for perinatal conditions,[11] whereas the estimates presented in this paper consider intrauterine

	Children <5 years in millions[27]	Percentage stunted (95% CI)	Number stunted in millions (95% CI)	Percentage severely wasted (95% CI)	Number severely wasted in millions (95% CI)	Percentage underweight (95% CI)	Number underweight in millions (95% CI)
Africa	141·914	40·1 (36·8–43·4)	56·9 (52·2–61·6)	3·9 (2·2–5·7)	5·6 (3·0–8·0)	21·9 (19·8–24·0)	31·1 (28·1–34·0)
Eastern	48·807	50·0 (42·3–57·9)	24·4 (20·7–28·3)	3·6 (1·5–8·4)	1·8 (0·7–4·1)	28·0 (23·6–32·9)	13·7 (11·5–16·1)
Middle	20·197	41·5 (38·3–44·8)	8·4 (7·7–9·1)	5·0 (2·0–12·0)	1·0 (0,4–2·4)	22·5 (19·2–26·1)	4·5 (3·9–5·3)
Northern	22·171	24·5 (17·3–33·9)	5·4 (3·8–7·5)	3·3 (1·2–8·9)	0·7 (0·3–2·0)	6·8 (2·8–15·3)	1·5 (0·6–3·4)
Southern	6·075	30·2 (25·4–35·6)	1·8 (1·5–2·2)	2·7 (1·0–6·8)	0·2 (·06–0·4)	11·4 (8·0–15·7)	0·7 (0·5–1·0)
Western	44·663	37·7 (33·5–42·1)	16·8 (15·0–18·8)	4·3 (1·8–9·6)	1·9 (0·8–4·3)	23·9 (21·0–26·9)	10·7 (9·4–12·0)
Asia	356·879	31·3 (27·5–35·1)	111·6 (98·1–125·1)	3·7 (1·2–6·2)	13·3 (4·4–22·3)	22·0 (18·5–25·6)	78·6 (65·9–91·3)
Eastern	95·070	14·5 (13·5–15·5)	13·7 (12·8–14·7)	0·7 (0·3–1·6)	0·7 (0·3–1·6)	5·1 (4·8–5·4)	4·8 (4·5–5·1)
South-central	181·481	40·7 (34·2–47·7)	73·8 (62·0–86·5)	5·7 (2·4–12·8)	10·3 (4·4–23·3)	33·1 (26·6–40·3)	60·1 (48·3–73·0)
Southeastern	54·970	34·3 (26·5–43·5)	18·9 (14·5–23·9)	3·6 (1·4–8·8)	2·0 (0·8–4·9)	20·7 (17·2–24·6)	11·4 (9·5–13·5)
Western	25·358	20·6 (10·0–38·8)	5·2 (2·5–9·8)	1·6 (0·4–5·8)	0·4 (0·1–1·5)	8·9 (2·8–24·2)	2·2 (0·7–6·1)
Latin America	56·936	16·1 (9·4–22·8)	9·2 (5·3–13·0)	0·6 (0·2–1·0)	0·3 (0·1–0·6)	4·8 (3·1–6·4)	2·7 (1·8–3·7)
Caribbean	3·657	8·2 (3·9–16·7)	0·3 (0·1–0·6)	1·0 (0·4–2·5)	0·03 (0·01–0·9)	5·1 (2·7–9·6)	0·2 (0·1–0·4)
Central America	16·161	23·1 (13·9–36·4)	3·7 (2·2–5·9)	0·6 (0·2–1·7)	0·1 (0·04–0·3)	6·2 (3·4–11·0)	1·0 (0·5–1·8)
South America	37·118	13·8 (6·9–26·3)	5·1 (2·6–9·8)	0·6 (0·2–1·6)	0·2 (0·07–0·6)	4·1 (2·5–6·7)	1·5 (0·9–2·5)
All developing countries	555·729	32·0 (29·3–34·6)	177·7 (162·9–192·5)	3·5 (1·8–5·1)	19·3 (10·0–28·6)	20·2 (17·9–22·6)	112·4 (99·3–125·5)

Stunting=height-for-age less than –2 SD. Severe wasting=weight-for-length or weight-for-height less than –3 SD. Underweight=weight-for-age less than –2 SD.

Table 1: **Childhood stunting, severe wasting, and underweight estimates and numbers affected in 2005 based on the WHO Child Growth Standards by UN regions and subregions**

growth restriction to be the risk factor for neonatal conditions. Additional work is needed to quantify the relative effects of low maternal body-mass index, extent of weight gain in pregnancy, and maternal micronutrient deficiencies on the occurrence and severity of intrauterine growth restriction.

Maternal undernutrition has little effect on the volume or composition of breast milk unless malnutrition is severe. The concentration of some micronutrients (vitamin A, iodine, thiamin, riboflavin, pyridoxine, and cobalamin) in breast milk is dependent on maternal status and intake, so the risk of infant depletion is increased by maternal deficiency.[21] This factor is most evident in the case of vitamin A, where the content in breast milk is the main determinant of infant status because stores are low at birth. Maternal supplementation with these micronutrients increases the amount secreted in breast milk, which can improve infant status.

Childhood underweight, stunting, and wasting

The prevalences of underweight, stunting, and wasting worldwide and for UN regions are based on analysis of 388 national surveys from 139 countries, applying comparable methods, including use of the new WHO Child Growth Standards.[22–26] In 2005, 20% of children younger than 5 years in low-income and middle-income countries had a weight-for-age *Z* score of less than –2 (table 1). The prevalences were highest in south-central Asia and eastern Africa where 33% and 28%, respectively, were underweight.

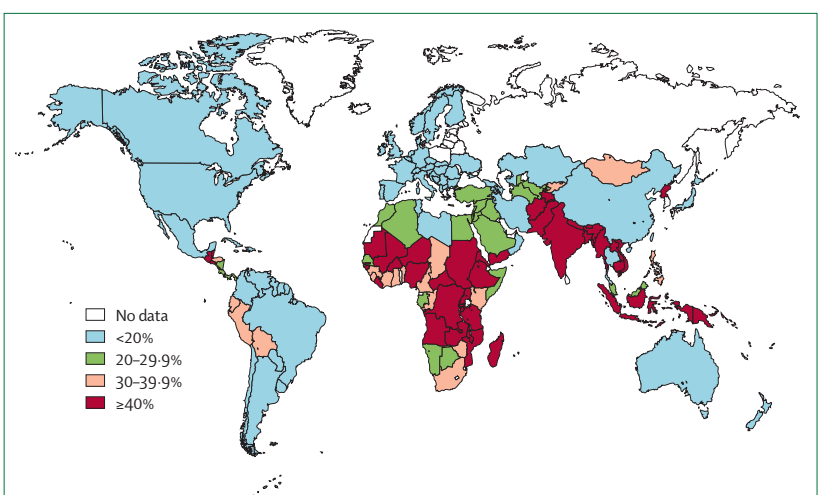

Figure 2: **Prevalence of stunting in children under 5 years**

For all developing countries, an estimated 32% (178 million) of children younger than 5 years had a height-for-age *Z* score of less than –2 in 2005 (table 1).[22,23] Eastern and middle Africa have the highest prevalence estimates in UN subregions with 50% and 42%, respectively; the largest number of children affected by stunting, 74 million, live in south-central Asia.

Of the 40 countries with a child stunting prevalence of 40% or more, 23 are in Africa, 16 in Asia, and one in Latin America; and of the 52 countries with prevalence of less than 20%, 17 are in Latin America and the Caribbean, 16 in Asia, 11 in Europe, and four each in Africa and

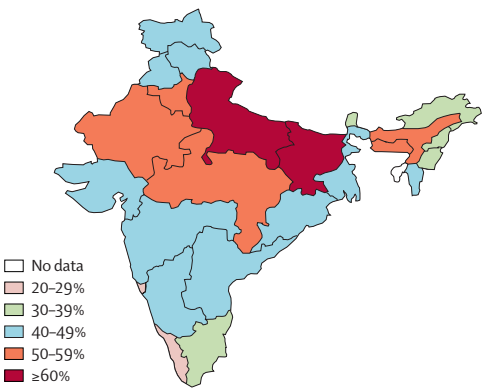

Figure 3: **Prevalence of stunting among children under 5 years old in India by state**

Oceania (figure 2). Including only countries with a stunting prevalence of 20% or more, 36 countries account for 90% of all stunted children worldwide (webtable 3). These countries will be the focus of estimations of the effects of interventions on disease burden.[28] 21 of these countries are in Africa and, although fewer countries are in Asia (13), they account for 61% of the total stunted children because of their large populations. India, with an estimated prevalence of 51%, has more than 61 million stunted children, 34% of the global total; however, the prevalence varies substantially by state within India (figure 3). Within countries the prevalence of stunting is generally highest for the poorest segments of the population (panel 1, figure 4).[29]

See Online for webtable 3

The global estimate of wasting (weight-for-height *Z* score of less than –2) is 10% (55 million children). South-central Asia is estimated to have the highest prevalence (16%) and numbers affected (29 million). The same regional pattern is seen for severe wasting (weight-for-height *Z* score of less than –3), often used as a criterion for therapeutic feeding interventions, with a prevalence of 3·5% or 19 million children (table 1). The highest percentages of children with severe wasting are seen in south-central Asia and middle Africa. Of the 36 countries with 90% of stunted children, the prevalence of severe wasting varies from 0·1% to 12% (webtable 4).

See Online for webtable 4

For the disease burden estimations, it is important to know the extent of overlap of the populations of children younger than 5 years who are stunted (height-for-age *Z* score <–2) and those who have severe wasting. To examine this question, data from 19 Demographic and Health Surveys were analysed.[30] The surveys were done between 1998 and 2005, and included two from south Asia, ten from Africa, and seven from Latin America and the Caribbean. The prevalence of severe wasting was higher at younger ages and declined by 24 months. Conversely, stunting prevalence increased progressively until reaching a plateau around 24 months. In these countries, severe wasting was not accompanied by stunting in 80–100% of younger children and 40–50% of older children. Thus,

Panel 1: Disparities in stunting and dietary diversity

This Series of papers on maternal and child nutrition builds on a framework that recognises the underlying causes of undernutrition, including the environmental, economic, and political contextual factors, in particular poverty. Figure 4A shows the disparities in stunting prevalence between the top and bottom wealth quintiles of the population, based on data from Demographic and Health Surveys for 11 of the 36 focus countries. In most countries the poor children have about twice as much stunting as the wealthier children.

The three proximate determinants of child nutritional status include food security, adequate care, and health. Each of these is strongly affected by poverty. For example, animal-source foods are an important component of child diets, as a major source of protein and micronutrients; low intake of these foods is a risk factor for stunting. Figure 4B shows the gap between the proportions of children in the top and bottom wealth quintiles who received these foods in the 24 h before the survey, in selected countries with available data. Wide gaps are evident in most countries.

Like stunting, micronutrient deficiencies are also linked to poverty. In India, for example, anaemia affects 79% of children in the lowest wealth quintile, compared with the still high prevalence of 64% in the top quintile.[29]

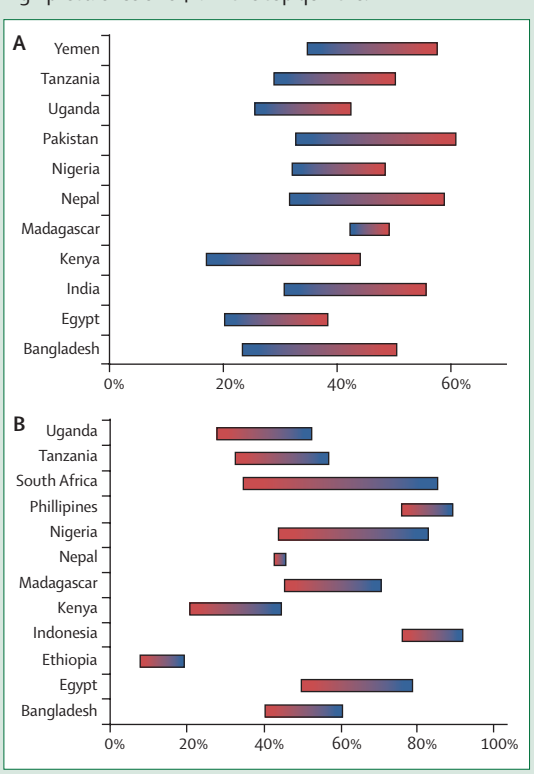

Figure 4: **Stunting and dietary diversity**
(A) Children aged 0–59 months who were stunted. Bars show the gap between prevalence in the poorest (red) and least poor (blue) wealth quintiles. (B) Children aged 12–23 months who ate meat, fish, poultry, or eggs in the 24 h before the survey. Bars show the gap between intake in the poorest (red) and least poor (blue) wealth quintiles.

	<–3 (95% CI)	–3 to <–2 (95% CI)	–2 to <–1 (95% CI)	More than –1
Weight-for-age (*Z* score)				
Overall*	9·7 (5·2–17·9)	2·5 (1·8–3·6)	1·8 (1·2–2·7)	1·0
Diarrhoea*	9·5 (5·5–16·5)	3·4 (2·7–4·4)	2·1 (1·6–2·7)	1·0
Pneumonia*	6·4 (3·9–10·4)	1·3 (0·9–2·0)	1·2 (0·7–1·9)	1·0
Malaria†	1·6 (1·0–2·7)	1·2 (0·5–3·5)	0·8 (0·2–3·2)	1·0
Measles‡	6·4 (4·6–9·1)	2·3 (1·7–3·2)	1·3 (1·1–1·5)	1·0
Height-for-age (*Z* score)				
Overall*	4·1 (2·6–6·4)	1·6 (1·3–2·2)	1·2 (0·9–1·5)	1·0
Diarrhoea*	4·6 (2·7–8·1)	1·6 (1·1–2·5)	1·2 (0·9–1·7)	1·0
Pneumonia*	3·2 (1·5–6·7)	1·3 (0·9–2·1)	1 (0·6–1·6)	1·0
Malaria†	2·1 (0·9–4·9)	1·0 (0·4–2·4)	0·7 (0·5–0·9)	1·0
Measles‡	2·8 (1·4–5·8)	1·7 (0·8–3·6)	0·7 (0·5–0·9)	1·0
Weight-for-height (*Z* score)				
Overall*	9·4 (5·3–16·8)	3·0 (2·0–4·5)	1·5 (1·2–1·9)	1·0
Diarrhoea*	6·3 (2·7–14·7)	2·9 (1·8–4·5)	1·2 (0·7–1·9)	1·0
Pneumonia*	8·7 (4·8–15·6)	4·2 (3·2–5·5)	1·6 (1·1–2·4)	1·0
Malaria†	2·3 (1·6–3·2)	3·0 (1·0–8·9)	0·9 (0·3–2·6)	1·0
Measles‡	6·0 (4·3–8·2)	3·7 (2·5–5·5)	1·8 (0·9–3·6)	1·0

*Ghana, Senegal, Guinea Bissau, the Philippines, India, Nepal, Bangladesh, Pakistan. †Ghana, Senegal, and Guinea Bissau. ‡Nepal, Ghana, Senegal, Guinea Bissau, and the Philippines.

Table 2: **Odds ratio for mortality by weight-for-age, height-for-age and weight-for-height by cause of death**

identifying children who are stunted will not capture most of those with severe wasting. Furthermore, stunting and severe wasting are not necessarily associated on a geographical or ecological basis—ie, countries with a similar stunting prevalence can have a several-fold difference in the prevalence of severe wasting.[31]

Eight data sets from low-income countries (Ghana, Guinea Bissau, Senegal, the Philippines, Nepal, Pakistan, India, and Bangladesh)[32–38] were used for analysis of disease risks associated with childhood undernutrition. These data were from specific study populations, but were broadly representative of these countries and low-income countries in general. Children were grouped by *Z* score as less than –3, –3 to less than –2, –2 to less than –1, and –1 or more for each of these indices. Generalised linear mixed models were used to estimate the risk of all-cause mortality, as well as of death due to diarrhoea, pneumonia, malaria, and measles for each of the groups with *Z* scores less than –1. The estimated odds ratios were then adjusted for confounding due to socioeconomic factors that affect mortality through other pathways, such as non-nutritional determinants of infection or access to better clinical care. The adjustment used data sets with robust measurement of socioeconomic status from Nepal[36,37] and Honduras[39] and showed that odds ratios were attenuated by 10% and 20%, respectively. On the basis of these results, 15% attenuation was applied to the odds ratios calculated with the generalised linear mixed models for underweight, stunting, and wasting. The odds ratios derived for cause-specific mortality were also used for diarrhoea, pneumonia, and malaria morbidity.

The risk of death increases with descending *Z* scores for underweight, stunting, or wasting (table 2). The increased risks are all significant for the below –3 category, as are many in the other two categories.

	Low birthweight (% <2500 g)[45]	IUGR–LBW (estimated %)[40]	IUGR–LBW (% 2000–2499 g)	IUGR–LBW (% 1500–1999 g)	Livebirths (thousands)[45]	Number 2000–2499 g (thousands)	Number 1500–1999 g (thousands)
Africa	14·3	8·89	7·85	1·04	30 305	2666·9	28·0
Eastern	13·5	8·27	7·30	0·97	10 649	871·9	8·5
Middle	12·3	7·24	6·40	0·84	4413	317·0	2·7
Northern	15·3	9·8	8·66	1·14	4587	444·5	5·1
Southern	14·6	9·21	8·14	1·07	1243	113·2	1·2
Western	15·4	9·89	8·74	1·15	9412	920·0	10·7
Asia	18·3	12·39	10·94	1·45	77 490	9463·8	138·8
Eastern	5·9	1·79	1·58	0·21	20 537	366·1	0·8
South-central	27·1	19·87	17·55	2·32	39 937	7749·8	184·0
Southeastern	11·6	6·65	5·87	0·78	11 743	774·5	6·1
Western	15·4	9·89	8·74	1·15	5273	515·4	6·0
Latin America	10	5·29	4·67	0·62	11 671	613·9	3·8
Caribbean	13·7	8·44	7·46	0·98	754	63·0	0·6
Central America	10·1	5·37	4·74	0·63	3423	182·5	1·2
South America	9·6	4·94	4·36	0·58	7494	368·2	2·1
All developing countries	16	10·81	9·55	1·26	119 466	12 752·3	162·9

IUGR-LBW=Intrauterine growth restriction-low birthweight.

Table 3: **Prevalence of intrauterine growth restriction-low birthweight and its components by UN region in 2004**

Term low-birthweight

Babies born at term (ie, who have completed 37 weeks of gestation), but of low birthweight (<2500 g) are likely to have had intrauterine growth restriction; we will refer to this group as intrauterine growth restriction-low birthweight. Various steps are used to estimate the prevalence of this condition,[40] which in developing countries is present in 10·8% of livebirths each year. The proportions of infants born at term weighing 1500–1999 g and those weighing 2000–2499 g were estimated with data sets from five countries (Bhutta Z, unpublished).[41–44] These proportions were applied to regional (table 3) and national (webtable 5) data to estimate that, of babies born at term globally, 9·55% weigh 2000–2499 g, and 1·26% weigh 1500–1999 g.[45]

See Online for webtable 5

Poor fetal growth is rarely a direct cause of death, but rather can contribute indirectly to neonatal deaths, particularly those due to birth asphyxia and infections (sepsis, pneumonia, and diarrhoea), which together account for about 60% of neonatal deaths. To quantify the risk of neonatal death associated with intrauterine growth restriction-low birthweight, data from five community-sampled prospective birth cohorts were analysed: two from Nepal,[42,44] and one each from India,[43] Pakistan (Bhutta Z, unpublished), and Brazil.[41] Each cohort provided data for gestational age, birthweight, survivorship, and cause of death during the first 28 days of life.

The risks of all-cause mortality and death due to birth asphyxia and infections for newborn babies weighing 1500–1999 g, 2000–2499 g, and 2500 g or more (reference group) were examined. Babies weighing less than 1500 g were excluded from the analysis because they were likely to have been born preterm. Birth asphyxia and infections as causes of death were selected for analysis because of strong biological associations with impaired fetal growth.[46–52] With weighted linear regression techniques to estimate the relation between birthweight category and the log mortality rate, the relative risks for all-cause mortality (five studies) and for deaths due to birth asphyxia (two studies) and infection (four studies) were calculated. Infants born at term weighing 1500–1999 g were 8·1 (95% CI 3·3–19·3) times more likely to die, and those weighing 2000–2499 g were 2·8 (95% CI 1·8–4·4) times more likely to die from all causes during the neonatal period than were those weighing more than 2499 g at birth. Based on two studies from South Asia, for deaths due to birth asphyxia, the relative risks were 5·4 (95% CI 1·8–16·8) for those weighing 1500–1999 g and 2·3 (1·3–4·1) for those weighing 2000–2499 g at birth. For infectious causes, the relative risks were 4·2 (1·5–11·7) for those weighing 1500–1999 g and 2·0 (1·2–3·4) for those weighing 2000–2499 g.

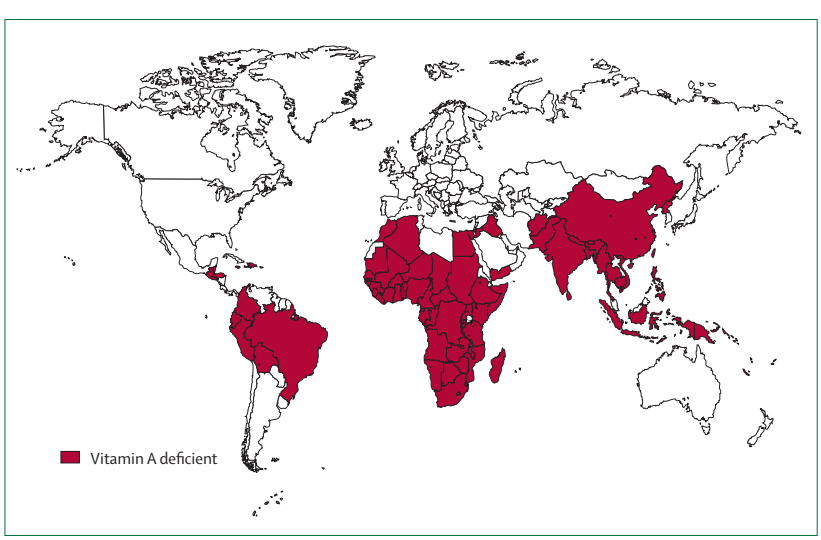

Figure 5: **Prevalence of vitamin A deficiency in children under 5 years**

Vitamin A deficiency

Countries were classified (figure 5) as having vitamin A deficiency on the basis of the most recent data for several indicators (serum retinol, conjunctival impression cytology, and xerophthalmia) with criteria previously described.[53] Brazil and China have subnational areas of deficiency so only populations from these areas were considered at risk. For these calculations all children in a country (or portions of the country for Brazil and China) classified as having vitamin A deficiency were considered at risk—ie, analogous to the baseline status of populations in which vitamin A intervention trials have been done. This prevalence was then reduced on the basis of the latest figures for coverage available (2005) from UNICEF of children receiving two doses of vitamin A supplements in the past year (considered to be fully protected from deficiency) or one dose (considered to be protected for half the year).

Blindness from corneal scarring that is directly due to xerophthalmia has an estimated disease burden from direct sequelae.[54] The relative risks of cause-specific mortality as a result of vitamin A deficiency were derived from a meta-analysis[55] of the nine randomised placebo-controlled trials in children 6–59 months showing risk reduction with supplementation—ie, by inverting the reduced risk shown by intervention.[55,56] This calculation yields a relative risk of 1·47 (95% CI 1·25–1·75) for diarrhoea mortality and 1·35 (0·96–1·89) for measles mortality related to vitamin A deficiency in the non-supplemented population as a whole. Additionally, the findings from three trials[43,57,58] of vitamin A supplementation of newborn infants in Asia show reductions in mortality in the first 6 months of life. The results from these trials are applied in the first 6 months of life to indicate a relative risk of 1·25 for all deaths due to infection and two-thirds of deaths due to prematurity—ie, excluding a third of early neonatal deaths from extreme prematurity. There has been an elevated risk of morbidity from diarrhoea in observational studies;[59] however, placebo-controlled trials have shown an effect only on diarrhoea severity, not incidence.[55,60] One trial reported an

effect of vitamin A on malaria morbidity,[61] but another did not;[62] thus, this effect is not included in our estimates. An increased risk of maternal mortality due to vitamin A deficiency was not included because results from trials in Nepal[63] and Bangladesh[64] are inconsistent, leading to a non-significant pooled estimate.

Zinc deficiency

The International Zinc Nutrition Consultative Group has proposed a method for assessment of the population's risk of zinc deficiency based on indirect indicators—ie, the prevalence of stunting, one of the clinical manifestations of zinc deficiency, and the adequacy of absorbable zinc in the food supply at the country level.[65,66]

The population's risk of zinc deficiency was estimated for the 178 countries for which information is available from the UN Food and Agriculture Organization. The latest prevalence of stunting for 131 countries was obtained from the WHO Global Database on Child Growth and Malnutrition.[24] Data from other sources were used to classify 35 additional countries by stunting prevalence. Each country was classified into three categories of risk of zinc deficiency on the basis of the combination of stunting prevalence and adequacy of zinc in the food supply.[65,66] Countries at high risk of zinc deficiency are those with a stunting prevalence of more than 20% and estimated prevalence of inadequate zinc intake of more than 25%; countries at low risk of zinc deficiency are those with stunting prevalence of less than 10% and inadequate zinc intake of less than 15%; countries at medium risk of zinc deficiency are those with all other combinations of the categories of stunting prevalence and adequacy of zinc in the food supply. All the trials of zinc supplementation included in the disease burden risk estimates were done in countries classified as having medium-high zinc deficiency. The national prevalence of zinc deficiency is high in south Asia, most of sub-Saharan Africa, and parts of Central and South America (figure 6). In countries classified as having zinc deficiency, all children were considered to be at risk.

Zinc deficiency in children results in increased risk of diarrhoea, pneumonia, and malaria, as evidenced by many randomised placebo-controlled trials done in various populations in all regions of the world.[67–71] The relative risk of deficiency for outcomes in the at-risk populations can be calculated by inverting the reduction in morbidity and mortality seen in the trials of zinc supplementation. The pooled relative risk for morbidity associated with zinc deficiency is 1·09 (95% CI 1·01–1·18) for diarrhoea, 1·25 (1·09–1·43) for pneumonia, and 1·56 (1·29–1·89) for malaria.[72,73] For mortality in infants aged 1–59 months the relative risk is estimated to be 1·27 (0·96–1·63) for diarrhoea, 1·18 (0·90–1·54) for pneumonia, and 1·11 (0·94–1·30) for malaria, based on a meta-analysis (S Sazawal, unpublished) of randomised controlled trials in Bangladesh,[74] Nepal,[71] and Zanzibar.[69] These values were used in the estimates of disease burden for the age group 6–59 months because this age group has a more consistent benefit in supplementation trials than infants younger than 6 months.

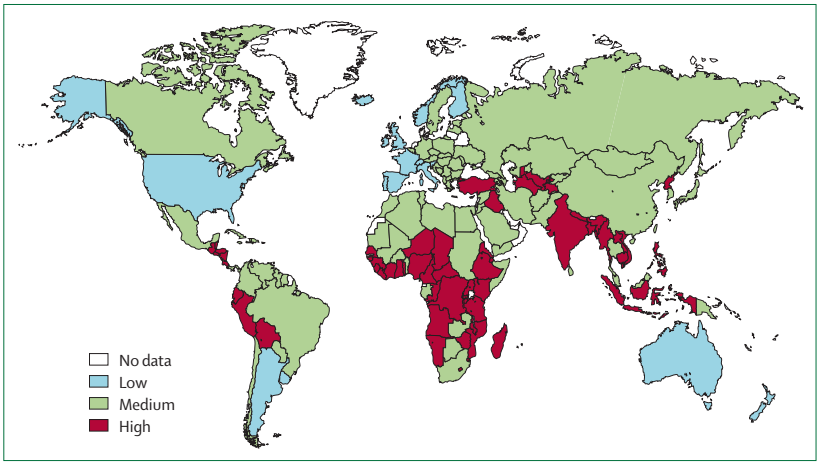

Figure 6: **National risk of zinc deficiency in children under 5 years**

Iron deficiency anaemia

According to a WHO review of nationally representative surveys from 1993 to 2005, 42% of pregnant women and 47% of preschool children worldwide have anaemia.[75] For these analyses, 60% of this anaemia was assumed to be due to iron deficiency in non-malaria areas and 50% in malaria areas.[76]

The major cause of iron deficiency anaemia is low consumption of meat, fish, or poultry, especially in poor people (panel 1).[77] In young children the peak prevalence of iron deficiency anaemia occurs around 18 months of age and then falls as iron requirements decline and iron intake is increased through complementary foods. Women of childbearing age are at high risk for negative iron balance because of blood loss during menstruation and the substantial iron demands of pregnancy.

Previous analyses examined the relation between anaemia in pregnancy and risk of maternal mortality.[12] An odds ratio of 0·8 (95% CI 0·70–0·91) for maternal mortality was found for a 10 g/L increase in mean haemoglobin in late pregnancy. These analyses also assessed the effects of anaemia on child cognition: the combined analysis of the five available trials found 1·73 (95% CI 1·04–2·41) lower IQ points per 10 g/L decrease in haemoglobin.[12] A separate meta-analysis of iron supplementation trials an overall benefit of 1–2 IQ points, in children receiving iron, but there was no effect in children younger than 27 months.[78]

Iodine deficiency

The prevalence of sequelae of iodine deficiency, such as goitre, congenital hypothyroidism, and developmental disability, have been estimated and assigned disability weights to calculate disease burden.[79] More recently the prevalence of iodine deficiency has been measured by an

Outcome	0–5 months			6–23 months
	Predominant breastfeeding	Partial breastfeeding	Not breastfeeding	Not breastfeeding
All cause mortality	1·48 (1·13–1·92)[34,88,89]	2·85 (1·59–5·10)[34,88,89]	14·40 (6·09–34·05)[34,88]	3·68 (1·46–9·29)[34,90]
Diarrhoea mortality	2·28 (0·85–6·11)[34,88]	4·62 (1·81–11·77)[34,88]	10·53 (2·80–39·64)[34,88]	2·83 (0·15–54·82)[34]
Pneumonia mortality	1·75 (0·48–6·43)[34,88]	2·49 (1·03–6·04)[34,88]	15·13 (0·61–373·84)[34,88]	1·52 (0·09–27·06)[34]
Diarrhoea incidence	1·26 (0·81–1·95)[91]	3·04 (1·32–7·00)[91,92]	3·65 (1·69–7·88)[91,92]	1·20 (1·05–1·38)[91–93]
Pneumonia incidence	1·79 (1·29–2·48)[92]	2·48 (0·23–27·15)[92]	2·07 (0·19–22·64)[92]	1·17 (0·37–3·65)[92]

Data are point estimate (95% CI), references.

Table 4: **Relative risk of suboptimum breastfeeding (compared with exclusive breastfeeding from 0 to 5 months and any breastfeeding from 6 to 23 months)**

indicator of low urinary iodine concentration; however, the rates of resulting sequelae have not been linked to this new exposure measure. Thus, previously used methods have been retained for the analysis in this paper. Iodine deficiency has adverse effects on both pregnancy outcome and child development. Even mild, subclinical maternal iodine deficiency during pregnancy impairs motor and mental development of the fetus and increases risk of miscarriage and fetal growth restriction. Maternal supplementation with iodine in more severe deficiency improves pregnancy outcomes especially if done by the second trimester, and improves neurological and cognitive development of the infant.[80] There are insufficient data on benefits to pregnancy outcomes from interventions when deficiency is mild.[81] Breast milk iodine content is very low in areas of endemic iodine deficiency, exacerbating depletion in infants and increasing their risk of impaired development. A meta-analysis showed that populations with chronic deficiency have a 13·5 point reduction in IQ.[82]

See Online for webtable 6

Folic acid, vitamin B12, and other micronutrient deficiencies

Other micronutrient deficiencies of concern in maternal and child health include calcium, iodine, the B vitamins (especially folic acid and vitamin B12), and vitamin D. Calcium deficiency is recognised as the main cause of rickets in Africa and some parts of tropical Asia, and increasingly in other parts of the world.[83] An estimated 35–80% of children in countries such as Turkey, India, Egypt, China, Libya, and Lebanon are vitamin D deficient (serum 25[OH]D <15 ng/mL) owing to the practice of shrouding, avoidance of skin exposure to sunlight, and the fact that few foods are fortified with vitamin D.[84] Vitamin D deficiency in utero can cause poor fetal growth and skeletal mineralisation and is followed by lower concentrations of the vitamin in breast milk. Rickets and poor bone mineralisation subsequently appear during the first years of life. The fetus is relatively protected from maternal calcium deficiency, but calcium deficiency rickets can result from low intakes in young children.

Poor folate status at conception, especially in the subgroup of women who are genetically susceptible, increases risk of neural tube and other birth defects, and possibly pre-eclampsia and other adverse outcomes.[85] In some but not all studies maternal vitamin B12 deficiency is a risk factor for neural tube defects and early fetal loss.[86] In women with deficiency the content of B12 in breast milk can be so low that symptoms of deficiency appear in their breastfed infants, including failure-to-thrive, stunting, poor neurocognitive function, and global developmental delays, all of which can be irreversible. Adverse pregnancy outcomes have been seen in association with thiamin, riboflavin, and vitamin B6 deficiencies in the few published studies, and a recently reported trial of a supplement containing B vitamins along with vitamins C and E found a reduction in births with intrauterine growth restriction.[87]

Risks associated with child feeding practices

Suboptimum breastfeeding

The recommended feeding of children is exclusive breastfeeding for the first 6 months of life and continued breastfeeding through the second year of life. In Africa, Asia, and Latin America and the Caribbean only 47–57% of infants younger than 2 months are exclusively breastfed, an estimate that is based on an analysis of recent national survey data (figure 7 and webtable 6 for 36 countries). For children 2–5 months of age this percentage falls to 25–31%. For children aged 6–11 months, 6% in Africa and 10% in Asia have stopped breastfeeding, as have 32% in Latin America and the Caribbean.

The risk of morbidity and mortality from suboptimum breastfeeding in young children has been documented in observational studies.[34,88] A random effects meta-analysis, which included all identified papers with appropriate data, was used to estimate the increased risk of cause-specific morbidity and mortality in relation to four patterns of breastfeeding in children younger than 6 months (exclusive—ie, nothing but breastmilk; predominant—only water or teas in addition to breast-milk; partial—other liquids or solids in addition to breast-milk; and not breastfeeding), and two patterns (breastfeeding or not) in children aged 6–23 months.[34,88–93] Previous estimates did not separate predominant and partial breastfeeding.[94] In the first 6 months of life, the relative risks were increased for each of the three patterns that were compared with the reference pattern—ie, exclusive breastfeeding, for diarrhoea and pneumonia morbidity and mortality (table 4). The relative risks were significant for predominant breastfeeding for all-cause mortality and pneumonia incidence, and there were similar, but not significant, point estimates for diarrhoea and pneumonia mortality and diarrhoea incidence. Compared with exclusive breastfeeding, partial breastfeeding had moderately higher relative risks than

predominant breastfeeding, and not breastfeeding had very high relative risks. In infants aged 6–23 months there was a statistically raised risk of not breastfeeding for all-cause mortality and diarrhoea incidence, but there was no significant raised risk for other outcomes.

Complementary feeding

Even with optimum breastfeeding children will become stunted if they do not receive an adequate quantity and quality of complementary foods after 6 months of age. Most incident stunting (and wasting outside of famine situations) happens in the first 2 years of life when children have a high demand for nutrients and there are limitations in the quality and quantity of their diets, especially after the period of exclusive breastfeeding.[95] This age group (younger than 2 years) also has a high rate of infectious diseases such as diarrhoea that adversely affect growth and nutritional status. A study that quantified the relative effects of poor complementary diet and infectious diseases on reduced growth found that they were of roughly equal importance in one setting in rural Bangladesh,[96] but this result might vary in other settings. Suboptimum complementary feeding is clearly a determinant of stunting, and improvements in most settings need to focus on both feeding frequency and energy density, and ensure an adequate quality diet, including sufficient micronutrients.[97] There is a clear disparity in dietary quality, as indicated by the lower consumption of animal source foods by poor children (panel 1).

Information derived from efficacy trials that attempted to improve complementary feeding through nutrition education, food supplementation, or both, can provide a perspective on the importance of suboptimum complementary feeding as a determinant of stunting. The effects on linear growth seem to be best with interventions that use specific educational messages—eg, on consumption of animal-source foods emphasise energy density of the diet, and, in areas with food insecurity or low consumption of sources of micronutrients, provide food supplements with micronutrient fortification.[98,99]

Contribution of infectious diseases to stunting and intrauterine growth restriction

Infectious diseases are important determinants of stunting.[100] Although there can be contributions to growth faltering from respiratory illnesses[101] or malaria,[102] the role of diarrhoea seems to be particularly important,[103–106] perhaps because of its association with malabsorption of nutrients, as well as anorexia and catabolism.[107]

To quantify the contribution of diarrhoea to the occurrence of stunting, data sets from Bangladesh (1),[104] Brazil (2),[103,108] Guinea-Bissau (2),[109–111] Ghana (1),[112,113] and Peru (3)[105,114,115] were analysed. Data were pooled to estimate the effects of diarrhoeal incidence on the odds of stunting at 24 months of age. All were longitudinal studies that enrolled children at or near birth and followed them with regular anthropometric measurements and daily records of diarrhoeal surveillance. Because children were measured at different ages, the measurement of height-for-age Z score at the oldest date in the interval between 18 and 24 months of age was accepted as the Z score at 24 months. Logistic regression was used to model the stunting at 24 months as a function of diarrhoeal incidence. Children were only included if they contributed at least 250 days of follow-up, up to the date when the outcome was measured. The effect of diarrhoeal incidence on stunting did not differ by study (p=0·409; likelihood ratio test), allowing us to pool across studies (webfigure). By contrast, our analysis required study-specific intercepts and study-specific gender effects. The odds of stunting increased multiplicatively with each episode of diarrhoea. The adjusted odds of stunting at 24 months of age increased by a factor of 1·05 (odds ratio 1·05, 95% CI 1·03–1·07) with each episode of diarrhoea in the first 24 months. The magnitude of this effect was not affected when the children who were stunted in the first 6 months of life were excluded.

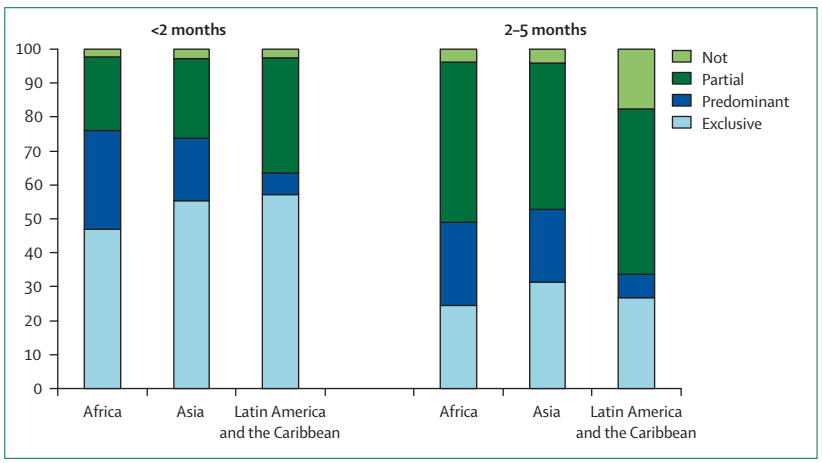

Figure 7: **Percentage of children by breastfeeding pattern, age group, and region**

See Online for webfigure

Malaria in pregnancy is associated with intrauterine growth restriction which increases the risk of death in infancy.[116] Infection at the end of pregnancy seems to be particularly harmful.[117]

Global and regional disease burden from undernutrition

The global burden of disease project

The global burden of disease project reports mortality and burden of disease for 136 comprehensive categories of specific diseases and injuries, and their sequelae.[54] The burden of disease measures the gap between the current health of a population and an ideal situation where everyone in the population lives into old age in full health, in DALYs. DALYs combine years of life lost due to premature death and years of life lived with disabilities (YLD) into one indicator allowing assessment of the total loss of health from different causes. One DALY can be

regarded as roughly 1 lost year of so-called healthy life. Methods and data for estimating mortality and DALYs in the global burden of disease project are described elsewhere.[54]

WHO has made an incremental revision of the global burden of disease for 2004, which included updating mortality and causes of death, and revising YLD estimates for selected causes if new data were available. Estimates of child deaths by cause have been revised to take into account new estimates of the total numbers of neonatal, infant, and child deaths for 2004,[118] updated country-specific estimates of deaths in children younger than 5 years by cause based on models developed by the WHO Child Epidemiology Reference Group,[119,120] and updated UNAIDS and WHO estimates for HIV/AIDS, tuberculosis, and vaccine-preventable child deaths.[121,122] YLD estimates for protein-energy malnutrition have been updated to take into account latest WHO estimates of stunting and wasting according to the new WHO standards,[23] and YLD estimates for iron deficiency anaemia have been updated using the most recent data from the WHO Global Database on Anaemia.[123] All estimates of death and disease burden attributable to undernutrition in this analysis are for the year 2004.

The 136 diseases and injuries in the global burden of disease project follow the rules of the international classification of disease (ICD) system. The ICD considers four groups of nutritional deficiencies, and their sequelae, as possible direct causes of death: protein-energy malnutrition, iron deficiency anaemia, vitamin A deficiency, and iodine deficiency. For this reason, estimates were made of the number of deaths and amount of disability that could be directly attributed to these conditions. As described above, in addition to these direct deaths, undernourished children are at an increased risk of illness and death from many infectious diseases, also included in the global burden of disease categories. Indeed, substantially more children die as a result of the synergy between infectious diseases and undernutrition than from the direct sequelae of the nutritional conditions themselves.[11] Like the ICD, global burden of disease also includes low birthweight as a direct cause of death; nearly all of these deaths in developing countries are due to preterm births, not intrauterine growth restriction among births at term.[119]

Panel 2: Specific assumptions for calculating the population attributable fraction for multiple nutritional risks

The hazardous effects of one risk are not mediated through other risks

This assumption might not hold for zinc deficiency because some of its hazardous effects are mediated through reducing growth. On the basis of the effects of zinc supplementation on linear growth,[127] and the model used to estimate intervention effects,[28] it is estimated that around 46% of the excess risk for zinc deficiency is mediated through stunting. There would be no mediation via stunting for vitamin A deficiency[128] or iron deficiency,[129] because of their lack of effects on growth.

The proportional risks for one risk do not depend on exposure to other risks

This assumption seems to be valid in that there has been no effect modification found in factorial design trials of vitamin A, zinc supplementation, or both,[130,131] and no difference in effect of vitamin A supplementation by baseline nutritional status by various anthropometric measures.[37,132] Likewise, no significant differences have been seen with the effects of zinc supplementation on infectious disease morbidity in children with better or worse nutritional status.[133]

Exposures to these risks are uncorrelated

The data from the cohort studies used to estimate odds ratios show that there was a small positive correlation between severe wasting and stunting (the prevalences of severe wasting in children with height-for-age *Z* scores below and above –2 were 4·7% and 2·9%, respectively). There was also a positive correlation between stunting and zinc deficiency, but this is accounted for in the mediated effect mentioned above. Correlation was not incorporated in the calculations, which results in a slight underestimation of the combined effects, but previous sensitivity analyses have shown that the underestimation is small for these risks.[126]

Estimating deaths and burden of disease attributable to nutritional risk factors

To estimate the number of deaths from various infectious diseases attributable to different forms of undernutrition, the methods of the comparative risk assessment project were used.[124,125] In brief, for each risk factor and for each of the diseases that are affected by it, population attributable fractions were computed using the following equation, which is for a risk factor with n levels of exposure. Population attributable fractions estimate the proportional reduction in mortality that would be seen if risk factor exposure had been reduced to an alternative (counterfactual) distribution that would result in the lowest population risk, irrespective of whether currently attainable in practice. This optimum exposure, referred to as the theoretical-minimum-risk exposure distribution, results in estimates of deaths and disease burden that could be avoided if all levels of suboptimum nutrition were addressed, in a consistent and comparable way across risk factors.

$$PAF = \frac{\sum_{i=1}^{n} P_i RR_i - \sum_{i=1}^{n} P'_i RR_i}{\sum_{i=1}^{n} P_i RR_i}$$

PAF=population attributable fractions. RR_i=relative risk of disease or mortality for the ith exposure category. P_i=proportion of children/women of child-bearing age in the ith exposure category. P'_i=proportion of children/women of child-bearing age in the ith exposure

category in alternative/counterfactual exposure scenarios. *n*=number of exposure categories.

Deaths and disease burden associated with protein-energy malnutrition (an ICD condition), and its direct sequelae as estimated in global burden of disease,[54] were added to the burden associated with underweight. In estimating the disease burden for stunting and wasting it is appropriate to add the direct protein-energy malnutrition burden to only one; it was added to wasting (or severe wasting) because this condition is most consistent with mortality from severe acute malnutrition, even though YLDs for chronic effects were attributed to both stunting and wasting.

The nutritional status measures—underweight, stunting, and wasting—were treated as risk factors whose exposures and relative risks applied to all children in the age group 1–59 months, and intrauterine growth restriction-low birthweight only for the first month of life. The analyses for vitamin A and zinc deficiencies and suboptimum breastfeeding, for which either exposure or increased risk were age-dependent, had to be done for age groups other than all children under 5 or neonatal, the two groups that are readily available from global burden of disease databases. The division of cause-specific deaths between 4 weeks and 59 months by age (eg, for the interval 1–5 months, 6–11 months, 12–23 months) were from data for total (all-cause) deaths by month of age estimated using demographic techniques from complete birth histories in demographic and health surveys.

Exposures and relative risks for the calculation of infectious disease deaths and burden from nutrition-related risk factors were largely newly derived, as described in this paper; however, the estimation of the direct sequelae was done using previous methods with the results updated to 2004. A summary of the source of the inputs is provided in webtable 7.

Cause-specific deaths can be caused by multiple risk factors acting simultaneously, and hence can be prevented by intervention on each of the risks. For example, some deaths from diarrhoea could be prevented by removing exposure to stunting, zinc deficiency, vitamin A deficiency, or suboptimum breastfeeding. Such deaths are attributable to all four risks when considered individually. As a result of multi-causality, the population attributable fractions for multiple risk factors that affect the same disease outcome overlap and cannot be combined by simple addition; rather their combined effect is generally less than the crude sum of individual ones, because some deaths are attributed to multiple exposures.[126] Under specific assumptions (panel 2), the combined (joint) population attributable fraction that avoids double-counting can be estimated from those of individual risks.[126]

Deaths and burden of disease attributable to nutritional risk factors

Of the nutritional status measures for children, underweight was responsible for the largest disease burden (table 5). The burden due to severe wasting from infectious diseases is modest compared with the other measures, largely because most children with non-optimum weight for height have a *Z* score of –1 to –3 and substantially fewer have a score less than –3. The burden associated with all levels of wasting was slightly less than that of stunting.

	Deaths	Percentage of deaths in children under 5 years	Disease burden (1000 DALYs)	Percentage of DALYs in children under 5 years
Underweight*	1 957 530	19·0	81 358	18·7
Stunting	1 491 188	14·5	54 912	12·6
Wasting*	1 505 236	14·6	64 566	14·8
Severe wasting*†	449 160	4·4	25 929	6·0
Intrauterine growth restriction-low birthweight	337 047	3·3	13 536	3·1
Total of stunting, severe wasting, and intrauterine growth restriction-low birthweight‡	2 184 973	21·4	90 962	21·2

*Deaths (138 739) and DALYs (14 486 400) directly attributed to protein energy malnutrition included· †Included in wasting. ‡Total takes into account the joint distribution of stunting and severe wasting.

Table 5: **Global deaths and disease burden measured in disability-adjusted life-years (DALYs) in children under 5 years of age attributed to nutritional status measures in 2004**

	Deaths	Percentage of deaths in children under 5 years	Disease burden (1000 DALYs)	Percentage of DALYs in children under 5 years
Vitamin A deficiency	667 771	6·5	22 668	5·3
Zinc deficiency	453 207	4·4	16 342	3·8
Iron deficiency	20 854	0·2	2 156	0·5
Iodine deficiency	3 619	0·03	2 614	0·6

Table 6: **Global deaths and disability-adjusted life-years (DALYs) in children under 5 years of age attributed to micronutrient deficiencies in 2004**

Stunting, severe wasting, and intrauterine growth restriction-low birthweight together were responsible for 2·1 million deaths (21% of worldwide deaths in children under 5) and 91·0 million DALYs (21% of global DALYs for children under 5; 7% of global total DALYs). Of the UN subregions, the disease burden attributed to these anthropometric measures is highest in south-central Asia (webtable 8), where India alone has 0·6 million deaths and 24·6 million DALYs attributed to stunting, severe wasting, and intrauterine growth restriction-low birthweight. The undernutrition burden is also high in eastern, middle and western Africa; these subregions, which together have an under-5 population of 111 million (93% of India), 1·1 million deaths, and 42·3 million DALYs, showing higher relative and absolute effects among African children.

See Online for webtable 7

See Online for webtable 8

Among the deficiencies of vitamins and minerals examined, the largest disease burdens were attributed to vitamin A and zinc deficiencies (table 6). Vitamin A deficiency in newborn babies, infants, and children resulted in about 6% of under-5 deaths, 5% of under-5 DALYs, and 1·7% of total DALYs. Zinc deficiency resulted in about 4% of under-5 deaths and DALYs and 1% of total

DALYs. The regional patterns for disease burden attributed to vitamin A and zinc deficiencies are similar. The highest burden for each is in South-central Asia, followed by several subregions of Africa (webtable 9).

See Online for webtable 9

Iron deficiency resulted in a relatively small number of under-5 deaths and DALYs (table 6). This burden is directly attributed to the sequelae of iron deficiency anaemia in children including cognitive impairment.[76] In addition, iron deficiency anaemia in pregnancy is considered a risk factor for maternal mortality; 115 000 deaths per year from maternal causes, resulting in 3·4 million DALYs, have been attributed to this risk factor.[12] Iodine deficiency results in a very small number of deaths, which is attributed to an excess risk of death with congenital hypothyroidism, and a modest number of DALYs that primarily result from multiple sequelae from iodine deficiency, including cognitive and motor impairment and hearing loss.[79]

In an analysis taking into account the joint distribution of nutritional status risk factors (intrauterine growth restriction, stunting, severe wasting, and deficiencies of vitamin A or zinc) and the fact that some of the effect of zinc deficiency is mediated through stunting, it is estimated that there were 2·8 million child deaths (28% of under-5 deaths) and 114·0 million DALYs (27% of under-5 DALYs) attributable to these forms of childhood undernutrition. This constitutes 8·5% of the total global disease burden.

There was a large disease burden attributed to suboptimum breastfeeding, including 1·4 million deaths (12% of under-5 deaths) and 43·5 million DALYs, which is 10% of global under-5 DALYs and 3% of total DALYs. Most of the attributable deaths (1·06 million) and DALYs (37·0 million) were due to non-exclusive breastfeeding in the first 6 months of life, accounting for 77% and 85%, respectively, of deaths and DALYs attributed to suboptimum breastfeeding. Again the highest disease burden estimates are for south-central Asia and several sub-regions of Africa (webtable 10). This risk factor was combined with anthropometric status and deficiencies of vitamin A and zinc in an analysis allowing for co-exposure and avoiding double counting of disease burden. If one assumes that the risks of suboptimum breastfeeding and other nutritional factors are independent, the combined mortality effects of all risk factors were 3·6 million child deaths (35% of under-5 deaths) and 140·5 million DALYs (35% of under-5 DALYs); this is 10% of the total global disease burden. These estimates change only slightly if the burden of disease directly attributed to iron and iodine deficiencies are added. These results are robust to assumptions about some of the effects of suboptimum breastfeeding being mediated through other nutritional exposures. For example, if 25% of the hazardous effects of suboptimum breastfeeding are mediated through other nutritional risks, the total number of attributable child deaths is reduced to 3·5 million, still about 35% deaths and DALYs in this age group. Adding the maternal deaths and DALYs due to iron deficiency anaemia increases the total global disease burden attributed to undernutrition to 11%.

See Online for webtable 10

Discussion

The attribution of more than a third of child deaths and more than 10% of total global disease burden to maternal and child undernutrition demonstrates the importance of these prevalent risk factors. The 21% of global deaths and DALYs in children younger than 5 years old attributed to stunting, severe wasting, and intrauterine growth restriction-low birthweight, largely because of their synergistic relationship with infectious diseases, constitutes the largest percentage for any risk factor in this age group.[125]

The estimated total burden attributed to the combination of underweight and intrauterine growth restriction-low birthweight is about the same—ie, 22% of deaths, and disease burden in children younger than 5 years—as the burden attributed to stunting, severe wasting, and intrauterine growth restriction-low birthweight. This result is lower than our previous estimate that indicated that 35% of child deaths could be attributed to childhood underweight and maternal low body-mass index operating through intrauterine growth restriction to affect low birthweight.[11] There are several reasons for this difference. The new estimates were done for a different base year (2004 *vs* 2000) with modest reductions in overall child mortality and in some major causes of death, such as diarrhoea, malaria, and measles, that are affected by the nutritional risk factors. Further, there have been declining trends in the prevalence of stunting in most regions.[134] More importantly the current estimates used the new WHO growth standards for all nutritional status prevalence and mortality and morbidity risk estimates. These factors, along with the use of different data sets for much of the risk analysis, resulted in somewhat lower relative risks of mortality than in previous analyses,[10,11] especially for children with *Z* scores between –1 and –2. Thus, some of the difference in estimated disease burden is due to changes in methods, but it also is likely to indicate progress in preventing and managing undernutrition and reducing some important causes of death.

The methods used in these analyses indicate several advances from those used previously.[11,12,56,73] Most of the risk relations were re-examined, as were the exposure definitions and prevalences, with the most current evidence. The latest information on total and cause-specific child mortality was used. The new WHO growth standards were used for all analyses. Importantly, the prevalence of stunting is about 15% higher with the new standards than with the previous growth reference.[135] The attributable deaths and DALYs were estimated for intrauterine growth restriction, stunting, and severe wasting, separately and together, as well as for all wasting and underweight. Co-exposures were considered, and the resulting estimate

for the anthropometric and micronutrient factors, as well as suboptimum breastfeeding, provides a total disease burden without double counting that results from simple addition of the burdens from individual factors.

These estimations using a risk factor method show that 449 000 child deaths can be attributed to severe wasting. Estimates by others[136] have ranged up to 1·7 million deaths using a methodology based on actual mortality rates in studies done an average 18 years (maximum 25 years) ago, when overall child mortality rates were much higher than today. The case fatality rates implied by these two calculations would be 2% versus 9%. True case-fatality rates for all cases of severe wasting identified in a cross-sectional population survey are unknown, but are almost certainly lower than these of severely malnourished children presenting to hospitals or feeding centres in emergency settings. Futhermore, over time case fatality rates have decreased because of better treatment. Since the prevalence of HIV infection has increased in some populations, some of the deaths reported to have been due to protein-energy malnutrition in civil registration systems could actually have been due to AIDS, but the magnitude of this possible misclassification is unknown. Finally, direct application of case fatality (versus proportional risk) overlooks the fact that some of the exposed children would have non-zero risk of death regardless of their severe wasting status. Irrespective of whether the true number of deaths attributable to severe wasting is closer to a half million or to 1·5 million a year, therapeutic feeding interventions are important components of nutrition programmes in settings where severe wasting is common.

Deficiencies of vitamin A and zinc were confirmed to be important risk factors in terms of their effects on total child mortality. The current estimate of disease burden due to vitamin A deficiency is similar to previous estimates despite increases in the population coverage with vitamin A supplementation, because of inclusion of risk in the 0–5 month age group for the first time. In other words, the true decline in the burden in children above 6 months of age has been numerically compensated by the finding that vitamin A is important in an even younger age group. That the estimates of disease burden due to zinc deficiency are about 40% lower than previously reported[73] is because of the lower relative risks based on analysis of additional studies.[72] The WHO/UNICEF recommendation that zinc be used along with oral rehydration therapy for all childhood diarrhoea is just beginning to be implemented in many countries, and preventive use of zinc supplementation or fortification is uncommon. The high residual burden of those micronutrient deficiencies indicates that interventions need to be expanded, especially in south-central Asia and Africa.

Iodine and iron deficiencies currently result in only small disease burdens. For iodine deficiency, there has been substantial success with promotion of the use of iodised salt; this and other interventions should be continued to prevent resurgence of the related disease burden. For iron deficiency the disease burden in children is relatively small, accounting for only 0·5% of under-5 DALYs, despite inclusion in the calculations of life-long developmental disability in 20% of children who have ever had severe anaemia.[76] This postulated permanent disability has not been seen in all studies and its existence might need to be reconsidered in the future.[137] Nevertheless, children with iron deficiency anaemia should be treated to prevent any possible current and future adverse effects. Iron deficiency anaemia is an important contributor to maternal mortality, increasing the risk of dying with blood loss during delivery.[12]

Suboptimum breastfeeding has large mortality consequences worldwide, similar to those of stunting. The estimate reported here is the same (1·4 million deaths) as a previous estimate using a different categorisation of breastfeeding practices (combining partial and predominant breastfeeding) and different mortality risks.[94,138] The timing of initiation of breastfeeding was not considered in these estimates. There is epidemiological evidence to suggest that beginning breastfeeding within the first day post partum would have additional benefit with regard to mortality even in exclusively breastfed infants, reaffirming recommendations to begin breastfeeding immediately after delivery.[89] More than three quarters of the burden attributed to suboptimum breastfeeding is due to non-exclusive breastfeeding in the first 6 months of life when even provision of water or teas leads to an increased risk of death. These estimates do not consider the adverse effect of transmission of HIV in breast milk. Recent evidence indicates that conditions in which breast milk substitutes are recommended for babies of HIV-positive mothers are rarely met, and there is a net benefit of breastfeeding in terms of HIV-free survival even in populations with a high prevalence of HIV infection.[139–141] Exclusive breastfeeding results in lower rates of HIV transmission than partial breastfeeding with rates of 1%[142,143] and 4%[140] being reported from studies in Africa. With around 2 million babies born to HIV-positive mothers every year,[144] these transmission rates would result in 20 000–80 000 HIV-infected infants in the first 6 months of life. Antiretroviral treatment for pregnant or lactating women will substantially reduce these resulting infections, and such treatment is increasing in Africa.[144] Because HIV transmission continues with partial breastfeeding after the first 6 months of life,[145] early breastfeeding cessation has been considered an option. Evidence is still incomplete; however, a recent trial found no difference in HIV-free survival at 24 months of age in children who were randomly assigned to abrupt weaning at 4 months of age or continued breastfeeding.[146]

Inadequate complementary feeding contributes to stunting as do infectious diseases, especially repeated episodes without adequate case management. These

exposures, which are arguably the key determinants of stunting, were not modelled as risk factors in this paper. However, the effects on stunting and related disease burden of interventions to improve complementary feeding and to reduce diarrhoea incidence are calculated in a subsequent paper in the Series.[28] Results presented here on the effects of diarrhoea on the risk of stunting are incorporated in these calculations of intervention effects, but other infectious diseases and perhaps asymptomatic infections are also likely to contribute to stunting.

The nutrition-related risk factors individually result in large disease burdens, but often coexist both in individuals and in populations. Stunting and severe wasting in children 1–59 months of age are largely uncorrelated, and the estimation of the joint effects of these two risk factors resulted in a slightly smaller total disease burden than simply adding their effects because even in the absence of statistical correlation, some children would be exposed to both conditions. Intrauterine growth restriction-low birthweight was considered for these estimations to affect only infants younger than 1 month, but in reality could affect later ages. Vitamin A, zinc, iron, and iodine deficiencies and the anthropometric measures as risk factors are largely uncorrelated, but there is still overlap in their risk because there is multicausality, such as diarrhoea for vitamin A, zinc, and stunting. In addition to simple multicausality, about half of the effect of zinc deficiency is mediated through stunting; the rest is a more direct effect on morbidity and mortality, probably as a result of reduced immune function.[147] The risk related to suboptimum breastfeeding might in part be due to micronutrient deficiencies resulting from inadequate dietary intake, but is also due to avoidance of infection. Calculating the combined effects of suboptimum breastfeeding and the other nutrition-related risk factors found that, even after accounting for overlapping effects from multicausality of diarrhoea and pneumonia, about half of the disease burden attributable to suboptimum breastfeeding was added to the other risk factors. Therefore, even if all other nutritional risks were addressed, a substantial number of child deaths would still require interventions related to breastfeeding practices.

Additional research will be important for improving understanding of the distribution of nutritional deficiencies in populations and their risk relations. Some specific research topics are listed in panel 3. Despite the remaining research needs, these results, which show the high prevalence of various forms of maternal and child undernutrition and their health consequences, present a compelling justification for implementation of effective nutrition-related interventions. The potential effects of these interventions are considered in the third paper in this Series, with particular attention to their contribution to achievement of MDG 1 with reduced undernutrition and also MDGs 4 and 5 regarding child and maternal mortality.

***Panel 3:* Research needs**

- Development of methods to assess nutritional status and its determinants
- Prevalence of deficiencies of vitamin A, zinc, iron, and iodine in subnational populations
- Consequences of nutritional deficiencies for mortality from HIV/AIDS, malaria, and other important infectious diseases
- Consequences of nutritional deficiencies for immune competence, brain development, cognitive ability, and other possible effects
- Overlap of micronutrients and their joint effects on mortality and morbidity
- Development of international fetal and newborn growth standards

Contributors

RB conceptualised and coordinated the analyses and preparation of the paper. Primary responsibility for specific topics were as follows: LHA, maternal undernutrition and consequences of selected micronutrient deficiencies; ZB, complementary feeding; LEC, analysis of intrauterine growth restriction-low birthweight and childhood undernutrition risks for mortality; MdO, stunting, wasting and low birthweight prevalence by country and region; ME, analysis of risk factor attributable mortality and disease burden; CM, update of country, regional, and global disease-specific mortality and burden of disease for 2004; and JR, exposure to zinc deficiency by country. All authors contributed to the final paper.

Other contributors

Analyses of national surveys for prevalence of underweight, stunting and wasting based on new WHO Child Growth Standards: Monika Blössner, Yang Hong, Allen Shoemaker (WHO, Switzerland). Provision of estimates of prevalence of breastfeeding status: Ana Betrán, Jeremy Lauer, (WHO, Switzerland). Review of relative risks of suboptimum breastfeeding: Ai Koyanagi, Sunil Sazawal (Johns Hopkins Bloomberg School of Public Health, USA). Provision of panel 1 (equity gaps in regard to stunting and dietary diversity): Satoru Shimokawa (Cornell University, USA), Cesar Victora (University of Pelotas, Brazil). Provision of data for analysis of mortality risks related to anthropometric indicators: Keith West, Luke Mullany, Parul Christian, Larry Moulton, James Tielsch (Johns Hopkins Bloomberg School of Public Health, USA), Linda Adair (University of North Carolina School of Public Health, USA), Kåre Mølbak (Statens Serum Institut, Denmark), Zulfiqar A Bhutta (Aga Khan University, Pakistan), A M Menezes (University of Pelotas, Brazil), Michel Garenne (Institute Pasteur, France), Shams El Arifeen (International Centre for Diarrhoeal Diseases Research, Bangladesh), M Andersen (University of Copenhagen, Denmark). Provision of data for analysis of socioeconomic confounding: Saul S Morris (London School of Hygiene and Tropical Medicine, United Kingdom), Keith West (Johns Hopkins Bloomberg School of Public Health, USA). Review of risk related to maternal body-mass index: Anju Aggarwal (Johns Hopkins Bloomberg School of Public Health, USA). Provision of data on vitamin A supplementation coverage: Nita Dalmiya (UNICEF, USA). Assistance in classifying countries as vitamin A deficient: Keith West (Johns Hopkins Bloomberg School of Public Health, USA). Analysis of the contribution of diarrhoea to stunting: William Checkley, Gillian Buckley (Johns Hopkins Bloomberg School of Public Health, USA). Analyses of mortality and burden of disease attributable to nutrition risk factors: Rodrigo Dias (Harvard University Initiative for Global Health, USA). Analyses of age patterns of deaths in children younger than 5 years: Kenneth Hill, Thomas Laakso (Harvard University Initiative for Global Health, USA). Analyses of contribution of undernutrition to mortality by cause at birth and during childhood, confounding by socioeconomic factors and of correlation between stunting and wasting: Ping Chen, Carmen Carrillo (Johns Hopkins Bloomberg School of Public Health, USA).

Maternal and Child Undernutrition Study Group

Series steering committee—Robert E Black (Johns Hopkins Bloomberg School of Public Health, USA), Zulfiqar A Bhutta (Aga Khan University, Pakistan), Jennifer Bryce (Johns Hopkins Bloomberg School of Public Health, USA), Saul S Morris (London School of Hygiene and Tropical Medicine, UK), Cesar G Victora (Federal University of Pelotas, Brazil). *Other members*—Linda Adair (University of North Carolina, USA), Tahmeed Ahmad (ICDDR,B, Bangladesh), Lindsay H Allen (USDA ARS Western Human Nutrition Research Center, USA), Laura E Caulfield (Johns Hopkins Bloomberg School of Public Health), Bruce Cogill (UNICEF, USA), Denise Coitinho (WHO, Switzerland), Simon Cousens (London School of Hygiene and Tropical Medicine, UK), Ian Darnton-Hill (UNICEF, USA), Mercedes de Onis (WHO, Switzerland); Kathryn Dewey (University of California, Davis, USA), Majid Ezzati (Harvard School of Public Health, USA), Caroline Fall (University of Southhampton, UK), Elsa Giugliani (Federal University of Rio Grande de Sul, Brazil), Batool A Haider (Aga Khan University, Pakistan), Pedro Hallal (Federal University of Pelotas, Brazil), Betty Kirkwood (London School of Hygiene and Tropical Medicine, UK), Reynaldo Martorell (Emory University, Rollins School of Public Health, USA), Colin Mathers (WHO, Switzerland), David Pelletier (Cornell University, USA), Per Pinstrup-Andersen (Cornell University, USA), Linda Richter (Human Sciences Research Council, South Africa), Juan A Rivera (Mexico National Institute of Public Health), Harshpal Singh Sachdev (Sitaram Bhartia Institute of Science and Research, India), Meera Shekar (World Bank, USA), Ricardo Uauy (Institute of Nutrition, Chile).

Conflict of interest statement

We declare that we have no conflict of interest. As corresponding author, R Black states that he had full access to all data and final responsibility to submit for publication.

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