“The Series identifies a set of ten proven nutrition-specific interventions, which if scaled up from present population coverage to cover 90% of the need, would eliminate about 900 000 deaths of children younger than 5 years in the 34 high nutrition-burden countries —where 90% of the world’s stunted children live.”
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Nutrition: a quintessential sustainable development goal

In the final paper of our 2008 Lancet Series on maternal and child undernutrition, Saul Morris and colleagues wrote that, “The international nutrition system—made up of international and donor organisations, academia, civil society, and the private sector—is fragmented and dysfunctional”.1 They concluded that, incredibly, no evidence base existed to prioritise actions to improve nutrition. And they argued that the voice of countries must be better heard, felt, and reflected in global decision making. Too often country priorities to strengthen nutrition were ignored by donors and agencies alike. 5 years on, thanks to the work of a consortium of scientists led by Robert E Black from Johns Hopkins Bloomberg School of Public Health (the Maternal and Child Nutrition Study Group), we review the progress made against these findings and recommendations.2–6 Although some news is better than 5 years ago, there is still a deeply worrying gulf between country needs and global actions. But what is most different—an extraordinary opportunity as well as a severe challenge—is the political urgency of nutrition.

This latest Lancet Series updates, with extensive new data, the contribution undernutrition in its various forms makes to child mortality and morbidity. Compared with 2008, the result is a radically different picture of the relation between nutritional deficiencies and child health. The overall finding is that 3.1 million children younger than 5 years die every year from undernutrition; that is a staggering 45% of total child deaths in 2011.

To address this enormous and too often hidden cause of child mortality, the Maternal and Child Nutrition Study Group propose a new framework to optimise the delivery of priority evidence-based interventions to prevent and treat undernutrition across the whole life course. Unique to this Series is the systematic approach to both the timing of the interventions and to creating an enabling environment for nutrition. The Maternal and Child Nutrition Study Group emphasises ten interventions targeted to women of reproductive age, during pregnancy, and to infants and children. They calculate the effects of these interventions in 34 countries across Africa, Asia, and the Middle East, where 90% of the global burden of undernutrition resides. In doing so, they reinforce the importance of the first 1000 days from conception to 2 years. What goes right and what goes wrong for fetal and child nutrition during this period has lasting and irreversible consequences for later life.

There are several entirely new findings in this Series. First, the adolescent girl is identified as especially vulnerable to the effects of undernutrition. But that very predicament also makes adolescent girls a group with a special opportunity too.

Second, the importance of fetal growth restriction or being born small for gestational age is highlighted. According to new estimates, fetal growth restriction causes more than 800,000 neonatal deaths and 20% of stunting in children younger than 5 years worldwide. These findings are presented by Robert E Black and colleagues,2 and Joanne Katz and colleagues7 in the companion Article. Third, the Series is not only concerned with interventions. It also identifies delivery platforms for the implementation of those interventions, most promisingly in the community and in schools. Fourth, the Series costs these interventions and explains why those costs—an additional Int$9.6 billion annually for the 34 countries identified—are much less prohibitive than they might at first seem. And finally, the Series identifies a further threat to maternal and child nutritional status: overweight and obesity.

On June 8, 2013, the Governments of Brazil and the UK will co-host a Nutrition for Growth event. There is therefore an immediate opportunity to foster political
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International momentum is the Scaling Up Nutrition (SUN) movement—called for in 2008 focus on the first 1000 days of life—the period from pregnancy to a child’s second birthday—as called for in the 2008 Series. One of the main drivers of this new international momentum is the Scaling Up Nutrition movement. National commitment in low-income and middle-income countries (LMICs) is growing, donor funding is rising, and civil society and the private sector are increasingly engaged.

Despite this progress, improvements in nutrition still represent a massive unfinished agenda. The 165 million children with stunted growth in 2011 have still represent a massive unfinished agenda. The politics of reducing malnutrition: ways to seize the agenda for nutrition, how to create political momentum, and how to turn that momentum into results. This is the prize we have to grasp in the next 18 months.

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to achieve the nutritional security that is needed for a healthy and productive life. Undernutrition is estimated to reduce a nation’s economic advancement by at least 8% (direct productivity losses, losses via poorer cognition, and losses via reduced schooling).3,10

Although preventable child mortality continues to decrease, undernutrition is responsible for 45% of deaths of children younger than 5 years, amounting to more than 3 million deaths each year.1 Deficiencies of essential vitamins and minerals are widespread and have important adverse effects on child survival and development. Additionally, overweight in adults and increasingly in children constitutes an emerging burden that is quickly establishing itself globally, affecting both poor and rich populations.8

Evidence presented in the accompanying Series on Maternal and Child Nutrition8,10–12 shows the importance of adolescent and maternal nutrition for the health of the mother and for ensuring healthy fetal growth and development. Fetal growth restriction is a cause of 800,000 deaths in the first month of life each year, more than a quarter of all neonatal deaths.8 Newborn babies with fetal growth restriction have a substantially increased risk of developing stunting by 24 months of age. Furthermore, these adverse nutritional insults early in life, when coupled with rapid weight gain later in childhood, are important determinants of obesity and non-communicable diseases in adulthood. Thus, it is imperative to act as early as possible in the crucial window of opportunity of pregnancy and the first 2 years of life.8 The emerging platforms for adolescent health and nutrition might offer opportunities for enhanced benefits.10

According to our conservative estimates, we identify a set of ten proven nutrition-specific interventions, which if scaled up from present population coverage to cover 90% of the need, would eliminate about 900,000 deaths of children younger than 5 years in the 34 high nutrition-burden countries—where 90% of the world’s stunted children live—and reduce the prevalence of stunting by a fifth, reducing the number of children with stunted growth and development by 33 million.10 The interventions with the largest predicted effects on child mortality are treatment of severe acute malnutrition throughout childhood; promotion of infant and young child feeding, including breastfeeding and appropriate complementary foods; and zinc supplementation. It is, however, important that interventions that have so far contributed to reductions in child mortality, such as vitamin A supplementation, be continued where the need still exists. The cost of scaling up this set of needed nutrition interventions to 90% coverage is estimated at Int$9·6 billion per year.10

Additionally, nutrition-sensitive activities should be pursued in sectors that address the underlying determinants of nutrition. Some, but not all, programmes in agriculture, cash transfers, early child development, and schooling have been shown to improve nutrition and broader developmental outcomes for children.11 The studies with the most positive effects had strong designs (including nutrition goals and actions), reached mothers and children early (and for longer durations), and targeted the poorest and most undernourished groups. Many also included actions to empower women and enhance their social status. More evidence is needed from programmes that have good designs, strong implementation, and rigorous evaluation.

An enabling environment for nutrition requires empirically sound, timely data about the nature of the problem, evidence for what works and how, good coherence between sectors, good coordination between national and subnational levels, sufficient capacity to build commitment, implementation of programmes at scale, and sustainable public and private means to finance interventions.12

Countries that have managed to improve nutritional status in these contexts have adopted an approach that targets the whole of society.13 This approach requires a good understanding of the political economy of nutrition. Governments and other stakeholders in successful countries have built alliances, managed tensions, identified win-win outcomes, established strong

Panel: Global nutrition targets for 2025, endorsed by the World Health Assembly

- 40% reduction of the global number of children younger than 5 years who are stunted
- 50% reduction of anaemia in women of reproductive age
- 30% reduction of low birthweight
- No increase in childhood overweight
- Increase the rate of exclusive breastfeeding in the first 6 months to at least 50%
- Reduce and maintain childhood wasting to less than 5%
accountability mechanisms, and innovated in the mobilisation of resources for nutrition.11

The private sector is an important force in shaping nutrition outcomes and has the potential to do more. Much more needs to be known about how different forms of public policy, regulation, and financial incentives can support private organisations to do the right things to improve nutrition. Knowledge in this area is scarce and must be expanded rapidly.

The impetus for improving nutrition is stronger today than 5 years ago. The World Health Assembly nutrition targets14 for reduction of stunting, wasting, low birthweight, anaemia, and overweight, and increasing exclusive breastfeeding in the first 6 months of life (panel), can be achieved by 2025 with sufficient support. The costs of inaction are enormous. As economies grow and the rate of population growth slows, the returns to improved cognitive performance and psychological functioning in the workforce will expand substantially. Benefits will be greater where strategies integrate the promotion of nutrition and child development.15

The new evidence provided in the Maternal and Child Nutrition Series strengthens the case for a continued focus on the first 1000 days. Investments within this window can help meet crucial goals: the prevention of undernutrition, overweight, and poor child development outcomes with longlasting effects on human capital formation. Because many women do not access nutrition-promoting services until month 5 or 6 of pregnancy, we draw attention to the need to ensure women enter pregnancy in a state of optimum nutrition.

Nutrition is foundational to both individual and national development. The post-Millennium Development Goals agenda must put the resolution of all forms of malnutrition at the top of its aims. An increase in donor spending is crucial if nutrition targets are to be met or surpassed. Government spending in LMICs needs to match or exceed this rate of increase. Nutrition budget lines need to be established in all high-burden countries. Governments need to be supported to raise public resources for nutrition. The increased mobilisation of private resources from individuals, businesses, and new philanthropies needs to be incentivised towards the most effective ways of improving nutrition. Scaling Up Nutrition is a crucial driver of these needed actions and support for it must remain strong.

Many nutrition gains have been made, but they need to be protected in the face of new stressors such as climate change, humanitarian crises, and food price volatility. We need to encourage innovation in design and delivery of nutrition-specific interventions, to make them even more affordable at scale. New incentives need to be established that support innovations in nutrition-sensitive programme design and implementation—to unleash their potential to achieve their own goals by providing crucial additional support to efforts to reduce malnutrition. This Series strengthens the evidence that good nutrition is a fundamental driver of a wide range of development goals.

Investments need to be directed not only to interventions, but also to the creation of environments that enable them. This approach requires strategic investment in commitment building, capacity, and leadership; timely data describing the nature of the malnutrition problem and its causes; evidence for what works; accountability mechanisms; resource mobilisation; and building of institutions required for sustainable implementation. A political economy approach to prioritisation of such investments is crucial if viable enabling environments are to be created.

More research is needed to develop scalable interventions or improve the effectiveness of existing ones to have greater effects, especially by preventing fetal growth restriction and growth faltering in infancy. Although promising service delivery platforms exist in communities, evidence is needed about how to ensure that nutrition interventions reach the populations with greatest need. More research is needed into the barriers to effective implementation and into the costs and logistics of scaling up: into the crucial elements of capacity at different levels, into the development and assessment of financing mechanisms for nutrition, and into ways to reduce the costs of implementation. Rigorous evidence is needed to show how the private sector can best support optimum nutrition. Research is also needed into the drivers of country success, how to create enabling environments, and into the features of nutrition-sensitive programmes that improve nutrition.

This year, 2013, represents the best opportunity yet to make these proposed actions a reality. National and international momentum to address human nutrition and related food security and health needs is at a high level. Nutrition is now more prominent on the agendas
of the UN, G8, and G20, and supporting civil society, business, and academic organisations. We must work together to seize this opportunity.

Maternal and Child Nutrition Study Group
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Delivery platforms for sustained nutrition in Ethiopia

The 2013 Lancet Series on Maternal and Child Nutrition emphasises the crucial importance of scale-up of effective nutrition interventions through health and community delivery platforms. The Series acknowledges that strong health systems are central to achievement of this goal, and for progress towards the 2015 Millennium Development Goals (MDGs). A broad consensus exists about the need for strengthening of health systems to meet the goals of the health-related MDGs by 2015. Because disease-control programmes and general health services often share common service-delivery platforms, they are necessary and complementary in countries with a high disease burden, especially in sub-Saharan Africa. Some findings have suggested that health and nutrition programmes can strengthen health systems and, similarly, that health systems can strengthen programme implementation. Furthermore, for such strengthening to take place, a system or platform for service delivery should be country led and owned to ensure sustainability and effectiveness.
In the past few years, many countries have worked to develop systems and infrastructure at the most decentralised level of services, and these investments have enabled populations to access essential services in sectors such as health, agriculture, education, and social welfare. Ethiopia is exemplary in this regard in view of the country’s progress towards some of the key MDGs, which is mainly attributable to a decentralised service delivery platform—the Health Extension Programme.4 Launched in 2003, this programme was organised to provide universal access to primary health care, mainly preventive services,6 through more than 38 000 government-salaried female health extension workers. Two workers were placed in a health post to serve each kebele (the smallest administrative unit) of about 5000 people nationwide. Through this programme new vaccines were introduced and health services expanded, which improved health and nutrition care practices, and investments were made in education and social economic development, contributing to a reduction in the number of child deaths by nearly half.3,10

The present estimate (supported by the Central Statistical Agency) for the mortality rate in children younger than 5 years in Ethiopia is 77 per 1000 livebirths (compared with 166 in 2000 and 123 in 2005).11 On the basis of the present trend, Ethiopia is predicted to meet MDG 4, to reduce child mortality, by 2015, by having a mortality rate in children younger than 5 years of 68 per 1000 livebirths.12 Furthermore, a comparison of national levels of malnutrition in the 2000 and 2011 Ethiopia Demographic and Health Surveys (EDHS) shows that stunting has declined from 58% to 44%, underweight from 41% to 29%, and prevalence of wasting from 12% to 10%.13 Globally, the prevalence of stunting in children younger than 5 years has fallen by 36% in the past two decades, from an estimated 40% in 1990, to 26% in 2011.9

To consolidate the gains and enhance the effectiveness of the Health Extension Programme, the Government of Ethiopia has designed a scaling-up strategy, in the form of a so-called health development army, which will scale up documented best practices and use families as role models. Such a strategy is based on social learning theory whereby peer-to-peer modelling can disseminate emerging information and instil improved health-seeking behaviours at community level.

The Health Extension Programme plays a crucial part in the success of the national nutrition programme and strategy that was introduced in Ethiopia in 2008. The community-based management of acute malnutrition approach of the Health Extension Programme manages more than 300 000 children in more than 10 000 health posts annually, has provided vitamin A supplementation and deworming tablets to 11 million children and 700 000 pregnant and lactating women every 6 months since 2005–06, and distributes iron-folate supplementation targeted to reach 80% of pregnant women every year.13 Interventions of the community-based nutrition programme include infant and young child nutrition, and growth monitoring and promotion via the Triple A cycle (assess the problem, analyse its causes and possible solutions, and take appropriate action). The community-based nutrition programme is currently being supported in more than 300 food-insecure woredas (districts), reaching 1 500 185 (80%) children younger than 2 years. Efforts of the community-based nutrition programme have resulted in more than 50% of children in Ethiopia being exclusively breastfed (EDHS, 2011).14 However, the proportion of children receiving a minimum acceptable diet is only 4% in Ethiopia, showing the urgent need to finalise a national strategy for improvement of quantity and quality of complementary feeding.

The revised national nutrition programme spanning 2013–15 will address these challenges by emphasising the first 1000 days of life, with a focus on children younger than 2 years, pregnant and lactating women, and adolescent girls, to break the intergenerational cycle of malnutrition. Furthermore, the revised programme will emphasise actions for acceleration of stunting reduction by focusing on nutrition-sensitive interventions in other development sectors such as education, agriculture, social protection and women’s affairs, and civil society organisations and the private sector. The role of health extension workers and the health development army will continue to be central to achievement of equitable access of all vulnerable women and children to both curative and preventive services, and to ensure that targets specified in the health sector development plan IV of Ethiopia are met.15

Ethiopia’s actions have enabled development workers to engage people at risk in an integrated manner using a unified Health Extension Programme, enabling achievement of great gains in child survival and
nutrition. The Government of Ethiopia, on the basis of experiences in the past 10 years of this programme and the substantial improvements in nutritional status, believes that even greater efforts can be made to reduce stunting. The government will continue to optimise the revised national nutrition programme and the global efforts on nutrition such as Scaling Up Nutrition (SUN) and Renewed Efforts Against Child Hunger (REACH), which are mechanisms to catalyse further multisectoral nutrition-sensitive actions beyond the health sector. Nutrition, as one of many crucial indicators of health status, should be used for close programmatic linkages and synergies between targeted social protection interventions. These synergistic actions across social services will contribute towards increased resource allocation for the national nutrition programme, and ensure that sustainable interventions are scaled up to improve food and nutrition security.

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Only collective action will end undernutrition

We are in a race against time to eradicate the global scourge of undernutrition. Undernutrition cripples global economic growth and development, and future global prosperity and security are intimately linked with our ability to respond adequately to this urgent challenge. The new Series in The Lancet shows that undernutrition contributes to the deaths of about 3 million children each year—45% of the total. Its results stunt the physical growth and life chances of millions of people, and for Africa and Asia estimates suggest that up to 11% of national economic productivity is lost to undernutrition.

The evidence provided in this Series should act as a turning point to galvanise global action. The solution lies largely in the early years of life, when the foundations for human potential are laid—getting the right nutrients at the right time prevents undernutrition. The result is heightened educational attainment, adult wages, and economic productivity.

Women and girls are at the heart of this message. As the bearers and carers of children, their health and economic potential is entwined with that of future
generations. Unless girls grow well in early childhood and adolescence and enter into motherhood well nourished, are lent support during pregnancy, protected from heavy physical labour, and empowered to breastfeed and provide good food for their babies and toddlers, the intergenerational cycle of undernutrition will not be broken. This Series shows that poor maternal nutrition at conception and during pregnancy is a major contributor to undernutrition in childhood.¹ Empowering women to make the right choices for their health, and that of their children, is crucial to solving this challenge.

Why is this such an urgent issue? Important demographic changes are occurring in many countries with high levels of undernutrition. The ratio of the working age to non-working age population is rising and will peak in the next 20 years, and this increase in the available workforce has substantially boosted economic growth in many parts of the world.³ Any such demographic dividend will be even greater in well-nourished populations. Additionally, rapid urbanisation, increased sedentary behaviour, and a transition in dietary patterns has resulted in a fast rise of obesity in middle-income and even low-income countries. This Series emphasises that undernourished children are at increased risk of becoming overweight and developing non-communicable diseases such as diabetes in later life.⁴ Acting now brings a triple benefit: it saves lives today, maximises economic opportunity, and helps to reduce obesity and chronic disease in the future.

This Series shows that there are simple and proven interventions that can substantially reduce undernutrition and mortality in children. Many of these interventions deliver an excellent return on investment and should be delivered at scale without delay. However, making a lasting effect on the root causes of undernutrition will need more effort. Brazil’s remarkable experience during the past 20 years shows us that the right programmes need to be matched with strong political leadership and determination. Brazil’s success resulted from a whole-government response, a clear focus on groups at greatest risk, strong civil society engagement, and investments to track progress and use data to strengthen accountability and inform policy choices.⁴

In addition to strong national action on undernutrition, we need to take a hard look at our global agriculture and food system. As the global population rises, our food system needs to keep pace with the demand for both dietary energy and the essential vitamins and minerals needed for human health. Our agriculture and food system needs to be profitable for farmers and the wider food sector, environmentally sustainable, and directly supportive of the health and nutritional needs of populations.

Everyone is part of the solution. Governments need to lead; businesses need to identify how to improve nutrition through their business models and employment practice; civil society organisations need to help citizens to drive transparency and accountability; and the scientific community needs to keep us focused on evidence about what works. Policy commitments, capacity strengthening, and targeted financing are all essential.

Global efforts on food and nutrition will likewise be substantially boosted by a clear signal of nutrition priorities in the post-2015 development agenda. This agenda will do more than steer aid; it should provide direction on global investment, buy in support from the private sector, and encourage a coherent approach from international institutions. Nutrition should be centrally positioned in that agenda to ensure energy and nutrient needs are met at each stage of life.

The first Lancet Series on maternal and child undernutrition, published in 2008, helped to start the race to eradicate poor nutrition. In the past 5 years the governments of 35 countries have committed to do more to tackle undernutrition, and have joined the Scaling Up Nutrition movement. On the last day of the 2012 Olympics, the governments of the UK and Brazil co-hosted an event in London, UK, to generate political momentum in the fight against undernutrition. On June 8, 2013, the Nutrition for Growth high level event in London will help to secure a global response that will include financial, business, scientific, and political commitments matched to the scale of the challenge. Progress will be reviewed annually and again at the Olympics in Rio de Janeiro, Brazil, in 2016. We cannot afford to miss this opportunity to act together to beat undernutrition.

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For the first Lancet Series on maternal and child undernutrition see http://www.thelancet.com/series/maternal-and-child-undernutrition

For Scaling Up Nutrition see http://scalingupnutrition.org
Nutrition-sensitive food systems: from rhetoric to action

Action to improve the nutrition sensitivity of food systems—and thereby increase the nutritional value of food for people around the world—offers substantial but underused opportunities.1,2 The rhetoric about such opportunities brought about by the global food crisis in 2007–08 has not resulted in much new action, for at least two reasons. First, goals other than improved nutrition are pursued by strong economic and political interests in both the agricultural sector and the post-harvest value chain.3 Farmers and other economic agents in food systems aim to make money subject to reasonable levels of risk, and governments pursue policies that are compatible with the interests of politically powerful stakeholder groups.4 Malnourished populations are rarely among these interests.

The very high value of improved nutrition to societies should be supported by alignments to create compatibility between nutrition and economic goals for farmers and processors, and political momentum3 has to be created to foster policy interventions that make food systems nutrition sensitive. Governments could pursue two kinds of policy action: they could either change the behaviour of farmers, consumers, food processors, and other economic agents in the system through incentives, regulations, and knowledge; or they could accept present behaviours and introduce health-specific and nutrition-specific interventions to compensate for any nutritional damage done or improvements forgone. Although changing of behaviour is likely to be more cost-effective and sustainable, the second option is the most common. For example, food-system policies and the private sector promote inexpensive calories and expensive nutrients, resulting in overweight and micronutrient deficiencies. Health and nutrition-specific interventions, such as treatment of chronic diseases and micronutrient supplementation, are introduced to remedy problems that could have been avoided.

The appropriate policy interventions to change behaviour will be context specific and might include agricultural research to increase productivity of fruit and vegetable cultivation and reduce micronutrient deficiency; taxes on sugar, sweeteners, and fat to reduce the prevalence of obesity; regulations for advertising and promotion; and education about nutrition.5 In high-income and rapidly growing low-income countries, the agricultural sector has become or is rapidly becoming a supplier of raw materials for the food processing industry, rather than a provider of food for direct consumption. As this transition proceeds, the potential for improvements to nutrition through nutrition-sensitive food systems moves from agriculture to the post-harvest value chain. The transition amplifies health and nutrition risks by promotion of what Monteiro

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and colleagues call “ultra-processed” foods, resulting in unhealthy dietary patterns. However, policy action to regulate and incentivise the food industry to avoid such negative health and nutrition effects and change consumer preferences is very scarce.

A second reason for lack of action to improve nutrition is the fixation of the health and nutrition community on randomised controlled trials (RCTs) as the only legitimate source of evidence. Unfortunately, RCTs—the gold standard in health research—are generally impossible to apply to the food system except in small, usually unimportant, projects. Health and nutrition effects resulting from agricultural and other food-system policies and programmes are very difficult to assess with RCTs, partly because treatments cannot be randomised and because the effect pathway is long. Yet the most promising opportunities for improvement of health and nutrition are undoubtedly found in such policies, and not in home gardens and other minor projects which are amenable to study within the framework of randomised trials.

Although existing evidence obtained by other approaches is deemed inconclusive and does not support policy intervention, the pathways through which food systems can affect nutrition (positively or negatively) are well known. Furthermore, key components making up these pathways, such as incomes, prices, women’s time allocation, dietary diversity, advertising and promotion, and household and individual behaviour have a substantial effect on nutrition. Thus, if pathway analysis shows that changes in the food system improve one or more of these components—eg, dietary diversity or women’s time allocation—and such improvements reduce micronutrient deficiencies, is such evidence really acceptable for policy guidance only if it is derived from RCTs? If so, the evidence will be limited to small food-systems programs such as kitchen garden projects, whereas the really important changes for nutrition, such as prioritisation of agricultural research to enhance productivity in fruit and vegetable cultivation so as to reduce prices and improve micronutrient status, and various policies to change women’s time allocation or prices of various foods, will be ignored because they cannot be studied in RCTs.

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I declare that I have no conflicts of interest.


In April, 2010, a policy brief—Scaling Up Nutrition: A Framework for Action—was released at the spring meetings of the World Bank and International Monetary Fund. It was a collective effort stimulated by the publication in January, 2008, of The Lancet’s Series on undernutrition. The Lancet Series encouraged an emphasis on the 1000 day window from the start of pregnancy to a child’s second birthday, with interventions that are both cost-effective and yield high returns for cognitive development, individual adult earnings, and economic growth. A second Series on nutrition, published in The Lancet, now explicitly

Global child and maternal nutrition—the SUN rises

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shows that the solution to malnutrition relies on a collective effort in which all stakeholders—governments, academia, civil society, UN system organisations, foundations, development banks, and businesses—carry out specific roles in ensuring that interventions are delivered equitably and at scale.

The policy brief, which quickly became known as the SUN Framework, set the stage for the transformation that is now happening in global nutrition. It called for country-owned nutrition strategies and programmes; urgent scaling up of evidence-based and cost-effective interventions; integration of nutrition within national strategies for gender equality, agriculture, food security, social protection, education, water supply, sanitation, and health care; and a substantial increase in domestic support and external assistance for nutrition within the food security, social protection, and health sectors. The SUN Road Map, prepared later in 2010 and revised in 2012, set out ways for a wide range of groups to work together in sharpening, scaling up, and aligning their responses to people’s nutritional needs—and achieving results.

Alongside the 1000 days advocacy partnership, the SUN Movement was launched at the UN General Assembly in September, 2010. It takes forward the SUN Road Map by encouraging coherence and effectiveness among all groups working for better nutrition; it is not an initiative, project, or programme. By April, 2013, 35 countries had joined the SUN Movement with commitments that are in line with the SUN Framework and Road Map. These countries’ nutrition solutions show the commitments of political leaders, whole-of-society responses, careful tracking of progress, and the benefits of shared experience.

The second Lancet nutrition Series provides a range of valuable insights as the SUN Movement moves through 2013, a year dense with events that will move nutrition to the heart of the development agenda. It calls for a substantial increase of political commitment in responding to the complex causes of undernutrition. It recognises that the SUN Movement has the potential to harness such change and yield durable results.

The first paper1 of the Series leaves no doubt as to why nutrition is key for sustainable development and the wellbeing of entire populations. The second paper2 strengthens the arguments of the 2008 Lancet Series by bringing additional evidence to support the focus on ensuring that all women, girls, and young children are able to access specific interventions of good quality; they should be included in mainstream efforts for public health, family planning, and water and sanitation. The third paper3 sets the foundation for evidence-based research into achieving outcomes through nutrition-sensitive strategies in four key areas: agriculture and food, social security, early child development, and classroom education. It draws on the experience of countries that have made great progress when stressing that gender and social equality are the cornerstones of nutritional success.

By focusing on the political context for effective action, the fourth paper4 recalls that the realisation of human rights, a commitment to equity, and gender equality should be properly prioritised. It includes important proposals for ways in which business can best be engaged (and the challenges of doing so), and encourages increased involvement of civil society at all levels. It likewise underlines the need for governments to increase their own accountability for ensuring that people are able to achieve good nutrition and to ensure the existence of a fair and transparent framework for regulating any entity that might—even unwittingly—undermine nutritional justice.

At the May, 2012, World Health Assembly, government representatives agreed ambitious goals for reduction of all forms of malnutrition, including obesity. This Lancet Series points out that...
these goals can only be achieved through improved nutrition governance, more human resources, better demonstration of results, and increased investments from domestic and international sources. In the past 3 years the SUN Movement has provided a platform to enable leaders to pledge to intensify efforts for improved nutrition. 2013 provides a once-in-a-lifetime opportunity to strengthen worldwide resolve for improved nutrition, through commitments being made in a series of international and regional events.

The publication of the second Lancet Series is timely and reinforces the urgency for transformation of political commitment into actions that lead to improvements in nutrition. The Series brings scientific rigour to the challenge of equitable delivery of effective services at scale—both now and in the years to come.

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Early nutrition and adult outcomes: pieces of the puzzle

The association between nutrition in early life and long-term health has been of interest for decades. Since the articulation of the fetal origins hypothesis by David Barker and colleagues, there has been debate about the implications of fetal undernutrition and early childhood growth on outcomes of importance in adult health and risks of chronic diseases. Both epidemiological and animal studies have shown that the risk of metabolic syndrome is significantly increased after exposure to suboptimum nutrition during crucial periods of development. The importance of these findings greatly increased after reports about the global burden of non-communicable diseases and risk factors were published in December, 2012.

Evidence for the importance of early nutrition for adult outcomes was derived initially from observational cohort studies and was reaffirmed by analysis of outcome data from several cohort studies in 2008. This analysis was focused on a meta-analysis of coefficients from different sites: birthweight, weight and length Z scores, and stunting at age 2 years. In The Lancet, Linda Adair and colleagues report findings from a study in which they pooled data from five birth cohorts and investigated how linear growth and relative weight gain in several age ranges affected adult outcomes. They report that higher birthweight was associated with an adult body-mass index of greater than 25 kg/m² (odds ratio 1·28, 95% CI 1·21–1·35) and a reduced likelihood of short stature (0·49, 0·44–0·54) and of not completing secondary school (0·82, 0·78–0·87). Faster linear growth was also strongly associated with reduced likelihood of short adult stature (age 2 years: 0·23, 0·20–0·52; mid-childhood 0·39, 0·36–0·43) and of not completing secondary school (age 2 years: 0·74,
0·67–0·78; mid-childhood 0·87, 0·83–0·92). Faster relative weight gain was associated with an increased risk of adult overweight (age 2 years: 1·51, 1·43–1·60; mid-childhood 1·76, 1·69–1·91) and elevated blood pressure (age 2 years: 1·07, 1·01–1·13; mid-childhood: 1·22, 1·15–1·30).

Notwithstanding the key findings, several limitations of this pooled analysis should be recognised. The authors had to make do with disparate information about socioeconomic status and income, and impute some information that was missing. Although they adjusted for maternal education and socioeconomic status (largely assets rather than income), other potential confounding factors (eg, household and learning environment) could not be assessed in relation to attained schooling. Several additional limitations preclude firm conclusions. Little or no information was available about maternal nutrition and micronutrient status. Additionally, Adair and colleagues do not report any outcomes related to intrauterine growth retardation or gestational age at birth, and merely report association with birthweight, which might be oversimplified. Being small for gestational age at term, and especially preterm, has now been recognised as a major risk factor for excess newborn and infant mortality and accounts for a substantial proportion of child stunting. Prematurity is associated with increased risks of metabolic syndromes in later life. Potential variations in body composition of newborn babies might not be captured by mere measurement of birthweight or size. So-called thin-fat infants—ie, small newborn babies that have elevated body fat content—have been described and could be associated with increased risks of insulin resistance in childhood.

These limitations aside, Adair and colleagues’ findings are some of the most important from existing cohorts linking early childhood nutrition—especially birthweight and improved patterns of linear growth—with long-term outcomes. They have clear implications for public health policy and nutrition interventions. As shown by an analysis of evidence-based interventions, a focus on improvements in nutrition in pregnancy and linear growth in the first 2 years of life could lead to substantial reductions in stunting and improved survival. These improvements form the basis for the emphasis on the first 1000 days of life, which has been used effectively to scale up nutrition activities. However, this tenet could be too simplistic, because it focuses on care during pregnancy and ignores the vital contribution of maternal health and nutrition in the periods before and just after conception to intrauterine and postnatal growth. Evidence supports an association between micronutrient supplementation around the time of conception and DNA methylation and increased methylation of the IGF2 genes in childhood, indicating that these factors could affect linear growth postnatally. Although Adair and colleagues’ analysis of birth outcomes in the international cohorts does not shed light on the importance of maternal health and nutrition before conception, these factors might be just as important as postnatal factors and should be investigated.

What is the way forward? Although the evidence emerging from observational studies such as Adair and colleagues’ is important for policy, well designed prospective studies with appropriate interventions and follow-up are clearly needed. The outcomes should include elements of child development, education, employment, and earnings, which would allow improved estimation of effect on human capital. Although expensive and difficult to organise and implement, such cohort studies are a crucial investment for the future and, in view of the interest in human development in the post-2015 era, should be prioritised for funding.

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I declare that I have no conflicts of interest.

Comment


Maternal and Child Nutrition 1

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


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.

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† 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, wasting, stunting, 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

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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 Comment7 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](source: thelancet.com)
stunting from early childhood. 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 and children and poorer birth outcomes than pregnancies in older women. Furthermore, pregnancy in adolescence will slow and stunt a girl’s growth. 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; corresponding values for Guatemala were 21.0% and 20.4%, respectively.

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.

Few studies have examined the risk of maternal mortality in relation to maternal anthropometry with a prospective design. In one study in Nepal of about 22,000 women, mid upper arm circumference during pregnancy was not associated with maternal mortality risk.
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.25–27

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.28 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 lower risk of neonatal and infant death,29 birth trauma, and macrosomic infants.30–33 In the post-partum period, obese women are more likely to delay or fail to lactate and have more weight retention than women of normal weight.34 Obese women with a history of gestational diabetes have an increased risk of subsequent type two diabetes, metabolic syndrome, and cardiovascular disease.35 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.36–38

**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.16 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.16 The corresponding figure for children was 8.0 g/L.77 We applied these shifts to the present distributions of haemoglobin estimated by Stevens and colleagues38 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 analyses39 showed that anaemia in pregnancy increased the risk of maternal mortality. An updated analysis40 with ten studies (four more than the

<table>
<thead>
<tr>
<th>Vitamin A deficiency40</th>
<th>Iodine deficiency40</th>
<th>Zinc deficiency40</th>
<th>Iron deficiency anaemia (haemoglobin &lt;110 g/L)</th>
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<td><strong>Children &lt;5 years</strong></td>
<td><strong>Pregnant women</strong></td>
<td><strong>Children &lt;5 years</strong></td>
<td><strong>Pregnant women</strong></td>
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<td>Night blindness</td>
<td>Serum retinol &lt;0.70 µmol/L</td>
<td>Night blindness</td>
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<td>0.9% (0.1–1.8)</td>
<td>33.3% (29.4–37.1)</td>
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<td>15.3% (6.0–24.6)</td>
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<td>Africa</td>
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<td>2.1% (1.0–3.1)</td>
<td>41.6% (34.4–44.9)</td>
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<td>Americas and the Caribbean</td>
<td>0.6% (0.0–1.3)</td>
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<td>Asia</td>
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<td>0.5% (0.0–1.3)</td>
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<td>2.9% (1.2–4.6)</td>
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<td>0.5% (0.1–1.0)</td>
<td>12.6% (6.9–19.2)</td>
<td>9.2% (0.3–18.2)</td>
<td>1.4% (0.0–4.0)</td>
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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.60–62 A meta-analysis61 that included 11 trials identified 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 review60 had much the same findings. Dibley and colleagues62 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 trial63 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.64

Randomised controlled trials from high-income countries have shown benefits of iron supplementation for improved maternal mental health and reduced fatigue.65 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,66 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.67 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).68

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.69 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.60

**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).62 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.64,65 Maternal night blindness has been associated with increased low birthweight66 and infant mortality,67 yet trials of vitamin A in pregnancy have not showed significant effects on these outcomes.68–71

**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.68 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.69,70 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.71–73 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.74

**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),77 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 of 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 μg/L).

Severe iodine deficiency in pregnancy causes cretinism, which can be eliminated with iodine supplementation before conception or in the first trimester of pregnancy.5 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.78,79 A review of the effects of iodine supplementation in deficient populations showed a small increase in birthweight.79 Effects of mild or moderate iodine deficiency on brain development are not well established.76,79 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 folic acid during critical periods in children associated with iodine deficiency of their mothers in pregnancy; however, they controlled for only a limited number of socioeconomic confounders.78,79 A review of the effects of iodine supplementation in deficient populations showed a small increase in birthweight.79 Effects of mild or moderate iodine deficiency on brain development are not well established.76,79 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.

**Calcium and vitamin D**

Calcium is an essential nutrient for several body functions, including enzymatic and hormonal homeostasis. 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 prospective 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.91 The effects of calcium supplementation interventions are described in the accompanying report by Zulfiqar A Bhutta and colleagues.92

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.96–101

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.99,104–106 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.93,99,102 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).99,103 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).104 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
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. Through recent analyses, we now have estimates of SGA prevalence from 22 population-based cohort studies and 23 countries with facility-based data, 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. 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 risk of dying among children younger than 5 years born 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 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 0·072 (95% CI 0·070–0·074) 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 0·324 (0·321–0·327) for the shortest mothers. The association with wasting was significant but much weaker.

Fetal growth restriction

Maternal stunting is a composite indicator representing genetic and environmental effects on the growing period of childhood. In a study 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 0·072 (95% CI 0·070–0·074) 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 0·324 (0·321–0·327) for the shortest mothers. The association with wasting was significant but much weaker.

Fetal growth restriction

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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,\textsuperscript{166} we estimated that the number of deaths attributed to SGA in 2011 was 817 000 in Asia (appendix p 22). The largest number of attributed deaths were in Africa (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).

**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\textsuperscript{144} 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.\textsuperscript{15} A meta-analysis of zinc supplementation trials\textsuperscript{144} 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\textsuperscript{146} 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.\textsuperscript{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,\textsuperscript{146,149} 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.\textsuperscript{3}

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.\textsuperscript{150–151}
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\textsuperscript{60} 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.\textsuperscript{61,62} A study\textsuperscript{63} 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.\textsuperscript{64}

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;\textsuperscript{58} however, this was unadjusted for gestational age. Size at birth was not related to women’s educational achievement in Guatemala\textsuperscript{65} and term low birthweight was not associated with IQ and behaviour in school-aged children in Brazil\textsuperscript{66} and Jamaica,\textsuperscript{67} or behaviour in South Africa.\textsuperscript{68} In Taiwan, term infants of low birthweight had lower academic achievement at age 15 years than did infants of normal birthweight,\textsuperscript{69} and in Thailand birthlength was associated with IQ at age 9 years independent of postnatal growth to age 1 year,\textsuperscript{70} however, in both cases effect sizes were small.

### Childhood nutrition

**Stunting, underweight, and wasting**

Panel 1\textsuperscript{155–157} describes the determinants of stunting and wasting, underweight, and severe wasting for children younger than 5 years had a height-for-age score (HAZ) of –2 or lower (stunted) on the basis of

<table>
<thead>
<tr>
<th>Stunting (HAZ &lt;–2)</th>
<th>Wasting (WHZ &lt;–2)</th>
<th>Severe wasting (WHZ &lt;–3)</th>
<th>Underweight (WAZ &lt;–2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UN\textsuperscript{157}</strong></td>
<td><strong>NIMS\textsuperscript{158}</strong></td>
<td><strong>UN</strong></td>
<td><strong>NIMS</strong></td>
</tr>
<tr>
<td>Proportion (millions)</td>
<td>Proportion (millions)</td>
<td>Proportion (millions)</td>
<td>Proportion (millions)</td>
</tr>
<tr>
<td>Africa</td>
<td>56.3</td>
<td>35.5</td>
<td>13.4</td>
</tr>
<tr>
<td>(52.5–58.0)</td>
<td>(34.4–36.6)</td>
<td>(7.3–9.6)</td>
<td>(7.3–9.6)</td>
</tr>
<tr>
<td>Asia</td>
<td>29.5</td>
<td>19.2</td>
<td>10.7</td>
</tr>
<tr>
<td>(26.4–31.3)</td>
<td>(20.2–29.8)</td>
<td>(7.9–12.3)</td>
<td>(8.2–11.4)</td>
</tr>
<tr>
<td>Latin America and the Caribbean</td>
<td>7.1</td>
<td>14.6</td>
<td>7.8</td>
</tr>
<tr>
<td>(9.4–17.7)</td>
<td>(13.6–19.4)</td>
<td>(7.3–8.2)</td>
<td>(0.9–1.9)</td>
</tr>
<tr>
<td>Oceania</td>
<td>0.8</td>
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<td>0.4</td>
</tr>
<tr>
<td>(16.0–61.4)</td>
<td>(27.8–33.5)</td>
<td>(0.3–0.5)</td>
<td>(3.0–6.2)</td>
</tr>
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<td>159.7</td>
<td>25.9</td>
</tr>
<tr>
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<td>(145.9–173.4)</td>
<td>(27.9–31.0)</td>
<td>(7.4–10.3)</td>
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<tr>
<td>High-income countries</td>
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<td>(2.9–8.9)</td>
<td>(0.8–3.5)</td>
<td>(0.0–0.3)</td>
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<tr>
<td>Global</td>
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<td>7.2</td>
</tr>
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<td>(150.8–22.8)</td>
<td>(6.8–9.3)</td>
<td>(43.3–59.6)</td>
</tr>
</tbody>
</table>

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 annual average rate of reduction of 2·1% per year (figure 4\textsuperscript{a}). 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).\textsuperscript{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.\textsuperscript{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,\textsuperscript{154} 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 (1·34 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.\textsuperscript{154} Estimated prevalences in NIMS were slightly higher at

![](https://www.thelancet.com)
110 million (19·4%). 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. 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

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**Figure 5: Prevalence of stunting (HAZ <–2 Z scores below median) and overweight (BMI for age >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. BMI=body-mass index. DHS=Demographic and Health Survey. MICS=Multiple Indicator Cluster Survey.
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.162 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 1,315 deaths in children younger than 5 years.164 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 underweight were associated with increased hazards of death from diarrhea, pneumonia, and measles; the association was also noted for other infectious diseases, but not malaria. We calculated the population attributable fractions for stunting, underweight, 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 deaths163 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.11 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.111,114 Effect sizes for the longitudinal studies comparing children with HAZ of −2 or lower with non-stunted children (HAZ ≥1) are moderate to large.168 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.141 Associations with underweight have also been reported.169

Stunted children show behavioural differences in early childhood including apathy, more negative affect, and reduced activity, play, and exploration.150,164 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,169 and weight gain in the first 2 years predicted school outcomes in five cohorts.168 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.169 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.164 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 1·31–3·60 (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.\textsuperscript{121} Childhood overweight is also a strong risk factor for adult obesity and its consequences.\textsuperscript{1,222}

**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.\textsuperscript{123–125} 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.\textsuperscript{126} 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.\textsuperscript{127} To further assess this scientific literature, we identified seven double-blind randomised controlled trials\textsuperscript{128–132} of iron lasting at least 8 weeks in children younger than 4 years. Five trials\textsuperscript{128–130,132} showed benefits in motor development and two did not.\textsuperscript{129,131} Only one showed benefits in language,\textsuperscript{129} and a small study showed benefits in mental development.\textsuperscript{132} In an eighth randomised controlled trial,\textsuperscript{133} children given iron in infancy showed no cognitive benefit when followed up at age 9 years. Four additional randomised controlled trials\textsuperscript{134–137} examined the combined effects of iron and folate supplementation in children younger than 36 months of age. One showed benefits to motor milestones,\textsuperscript{135} others showed no benefits to motor\textsuperscript{136,137} or language\textsuperscript{136} milestones, and one showed no benefit to cognitive function.\textsuperscript{134} 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.
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. 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, 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. Meta-analyses of these trials show a mortality reduction of 23%, 30%, and 24% 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. 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

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**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.
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; 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. 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 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. 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. 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. 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). 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. 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. 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. 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. Updated systematic reviews of these risks have results that are much the same as our previous estimates (appendix p 21). 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. 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, 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, 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. 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 suboptimum 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. For the assessment the following formula was used:

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

For the purpose of this analysis, RR equals the RR of mortality for the ith exposure category, associated with specific UN regions. P 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 \( PAF = 1 - \text{product} (1 - PAF_i) \), where PAF equals the population attributable fraction of the different risk factors. 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, 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. 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. 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, increased depression in adolescents who had severe acute malnutrition in infancy, increased risk of suicidal ideation associated with lower HAZ at 24 months, and higher levels of hyperactivity in late adolescence and attention deficit in adults. 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, and wages. Effects of improved nutrition in the first several years of life on risk factors for chronic diseases were minor but in some cases beneficial. Exposure to improved nutrition during childhood affected the growth of the next generation in girls and their future children.

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. 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 inter-generational effects on birthweight. Surprisingly, some findings suggest protective effects of famine exposure, which might be explained by high mortality and intense selection of the hardiest.

**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 having fetal growth restriction. The use of more appropriate methods than those in our previous review 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 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 WHIZ, 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. 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. 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). 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 confirmed previous estimates 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). 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 nearby 157 000 child deaths attributed to vitamin A deficiency is smaller than our previous estimate (668 000). 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 diarrhoeal 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.

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. Our number is higher than the estimated 545 000 deaths attributed to suboptimum breastfeeding in the GBD Study. 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.

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—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 (370 000 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 bodyweight 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). Studies show that the trend toward childhood obesity can start as early as age 6 months. In LMICs, rapid weight gain after 2 years of age is particularly associated with adult fat mass. Intrauterine, infant, and preschool periods are deemed to be crucial periods for programming long-term regulation of energy balance.
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).221 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).221 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 sub-national 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 co-author for this paper. SPW contributed sections on the effects of child development of maternal IDA, fetal growth restriction, and childhood undernutrition, maternal IDA, and mental health and served as a co-author for this paper. ZAB assisted with conceptualising the paper and contributed sections on micronutrients and adolescent nutrition. FC contributed to writing the sections on maternal and childhood outcomes, 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, 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. 5G-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.

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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. Alhissio Barros, Giovanny França, and Maria Clara Restrepo contributed to the analyses of inequalities and of breastfeeding patterns. Anne CC Lee and Naoko Kazuki contributed to analyses on fetal growth restriction. Monika Bösner 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 Nestlé Creating Shared Value Advisory Committee. VM serves on the Nestlé Creating Shared Value Advisory Committee. MGdO is a staff member of the World Health Organization. MGdO 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 noted that he had full access to all data and final responsibility for the decision to submit for publication.

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Maternal and Child Nutrition 2

Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost?

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Maternal undernutrition contributes to 800 000 neonatal deaths annually; stunting, wasting, and micronutrient deficiencies are estimated to underlie nearly 3·1 million child deaths annually. Progress has been made with many interventions implemented at scale and the evidence for effectiveness of nutrition interventions and delivery strategies has grown since The Lancet Series on Maternal and Child Undernutrition in 2008. We did a comprehensive update of interventions to address undernutrition and micronutrient deficiencies in women and children and used standard methods to assess emerging new evidence for delivery platforms. We modelled the effect on lives saved and cost of these interventions in the 34 countries that have 90% of the world’s children with stunted growth. We also examined the effect of various delivery platforms and delivery options using community health workers to engage poor populations and promote behaviour change, access and uptake of interventions. Our analysis suggests the current total of deaths in children younger than 5 years can be reduced by 15% if populations can access ten evidence-based nutrition interventions at 90% coverage. Accelerated gains are possible and about a fifth of the existing burden of stunting can be averted using these approaches, if access is improved in this way. The estimated total additional annual cost involved for scaling up access to these ten direct nutrition interventions in the 34 focus countries is Int$9·6 billion per year. Continued investments in nutrition-specific interventions to avert maternal and child undernutrition and micronutrient deficiencies through community engagement and delivery strategies that can reach poor segments of the population at greatest risk may make a great difference. If this improved access is linked to nutrition-sensitive approaches—ie, women’s empowerment, agriculture, food systems, education, employment, social protection, and safety nets—they can greatly accelerate progress in countries with the highest burden of maternal and child undernutrition and mortality.

Introduction

Stunting prevalence has been decreasing slowly and 165 million children were stunted in 2011.1 Undernutrition, consisting of fetal growth restriction, stunting, wasting, and deficiencies of vitamin A and zinc, along with suboptimum breastfeeding, underlies nearly 3·1 million deaths of children younger than 5 years annually worldwide, representing about 45% of all deaths in this group.2 Maternal and child obesity have also increased in many low-income and middle-income countries.1

In a comprehensive review of nutrition interventions, we previously assessed 43 nutrition-related interventions in detail and reported estimates of efficacy and effect for 11 core interventions.4 Much progress has been made since with many interventions implemented at scale, assessments of promising new interventions, and new delivery strategies. We used standard methods to do a comprehensive review of potential nutrition-specific interventions to address undernutrition and micronutrient deficiencies in women and children. We modelled the potential effect of delivery of these interventions on lives saved in the 34 countries with 90% of the global burden of stunted children, and estimated the effect of various delivery platforms that could enhance equitable scaling up of nutrition-specific interventions.

Selection of interventions for review

We selected several nutrition-specific interventions across the lifecycle for assessment of evidence of benefit (figure 1); these interventions included those affecting adolescents, women of reproductive age, pregnant women, newborn babies, infants, and children. We also reviewed the evidence for delivery platforms for nutrition interventions and other emerging interventions of interest for nutrition of women and children.

We identified and relied on the most recent reviews with good quality methods for all interventions and updated the evidence by incorporating newer studies, when available. For other identified interventions, when we did not find any relevant review, we did a de-novo review using the methodology described in panel 1.5 Additionally, we consulted the electronic library on nutrition actions (eLENA) for existing evidence used by WHO for development of guidelines and policies for action (appendix p 2).

Interventions to address adolescent health and nutrition

There is growing interest in adolescent health as an entry point to improve the health of women and children, especially because an estimated 10 million girls younger than 18 years are married each year.6 A range of interventions exist in relation to adolescent health and

See Online for appendix
nutrition, which could also affect the period before first pregnancy or between pregnancies. Evidence supporting reproductive health and family planning interventions in this age group suggests that it might be possible to reduce unwanted pregnancies and optimise age at first pregnancy. These aims might be important to reduce the risk of small-for-gestational age (SGA) births in populations in which a substantial proportion of births occur in adolescents. Opportunities might also exist to address micronutrient deficiencies and emerging issues of overweight and obesity in adolescents through community and school-based education platforms. Although evidence from robust randomised controlled trials is scarce, we identified a range of interventions in the adolescent period affecting maternal, newborn, and child health and nutrition outcomes (panel 2).

**Key messages**

- Globally, 165 million children are stunted; undernutrition underlies 3·1 million deaths in children younger than 5 years.
- A clear need exists to introduce promising evidence-based interventions in the preconception period and in adolescents in countries with a high burden of undernutrition and young age at first pregnancies; however, targeting and reaching a sufficient number of those in need will be challenging.
- Promising interventions exist to improve maternal nutrition and reduce fetal growth restriction and small-for-gestational-age (SGA) births in appropriate settings in developing countries, if scaled up before and during pregnancy. These interventions include balanced energy protein, calcium, and multiple micronutrient supplementation and preventive strategies for malaria in pregnancy.
- Replacement of iron-folate with multiple micronutrient supplements in pregnancy might have additional benefits for reduction of SGA in at-risk populations, although further evidence from effectiveness assessments might be needed to guide a universal policy change.
- Strategies to promote breastfeeding in community and facility settings have shown additional benefits for enhancing exclusive breastfeeding rates; however, evidence for long-term benefits on nutritional and developmental outcomes is scarce.
- Evidence for the effectiveness of complementary feeding strategies is insufficient, with much the same benefits noted from dietary diversification and education and food supplementation in food secure populations and slightly greater effects in food insecure populations. Further effectiveness trials are needed in food insecure populations with standardised foods (pre-fortified or non-fortified), duration of intervention, outcome definition, and cost effectiveness.
- Treatment strategies for severe acute malnutrition with recommended packages of care and ready-to-use therapeutic foods are well established, but further evidence is needed for prevention and management strategies for moderate acute malnutrition in population settings, especially in infants younger than 6 months.
- Data for the effect of various nutritional interventions on neurodevelopmental outcomes are scarce; future studies should focus on these aspects with consistency in measurement and reporting of outcomes.
- Conditional cash transfers and related safety nets can address the removal of financial barriers and promotion of access of families to health care and appropriate foods and nutritional commodities. Assessments of the feasibility and effects of such approaches are urgently needed to address maternal and child nutrition in well supported health systems.
- Innovative delivery strategies, especially community-based delivery platforms, are promising for scaling up coverage of nutrition interventions and have the potential to reach poor populations through demand creation and household service delivery.
- Nearly 15% of deaths of children younger than 5 years can be reduced (ie, 1 million lives saved), if the ten core nutrition interventions we identified are scaled up.
- The maximum effect on lives saved is noted with management of acute malnutrition (435 000 [range 285 000–482 000] lives saved), 221 000 (135 000–293 000) lives would be saved with delivery of an infant and young child nutrition package, including breastfeeding promotion and promotion of complementary feeding; micronutrient supplementation could save 145 000 (30 000–216 000) lives.
- These interventions, if scaled up to 90% coverage, could reduce stunting by 20·3% (33·5 million fewer stunted children) and can reduce prevalence of severe wasting by 61·4%.
- The additional cost of achieving 90% coverage of these proposed interventions would be Int$9·6 billion per year.

**Interventions in women of reproductive age and during pregnancy**

**Folic acid supplementation**

Neural tube defects can be effectively prevented with periconceptional folic acid supplementation. A review of five trials of periconceptional folic acid supplementation suggested a 72% reduction in risk of development of neural tube defects and a 68% reduction in risk of recurrence compared with either no intervention, placebo, or micronutrient intake without folic acid (table 1). A review of folic acid supplementation during pregnancy showed that folic acid supplementation improved mean birthweight, with a 79% reduction in the incidence of megaloblastic anaemia (table 1). Furthermore no evidence of adverse effects was noted from folic acid supplementation in programme settings. Despite
strong evidence of benefit, reaching women of reproductive age in the periconceptual period to provide folic acid supplements through existing delivery platforms remains a logistical challenge. Fortification of cereals and other foods might be a feasible way to reach the population in need.

**Iron or iron and folic acid supplementation**

A review of iron supplementation in non-pregnant women of reproductive age showed that intermittent iron supplementation (alone or with any other vitamins and minerals) reduced the risk of anaemia by 27% (table 1)\(^\text{19–26}\). A Cochrane review of daily iron supplementation to women during pregnancy reported a 70% reduction in anaemia at term, a 67% reduction in iron deficiency anaemia (IDA), and 19% reduction in the incidence of low birthweight. Another review further suggests that the effects were much the same in women receiving intermittent iron therapy in non-anaemic populations, WHO recommends daily iron supplementation during pregnancy as part of the standard of care in populations at risk of iron deficiency.\(^\text{28}\)

**Maternal multiple micronutrient supplementation**

Multiple-micronutrient deficiencies often coexist in low-income and-middle-income countries (LMICs) and can be exacerbated in pregnancy with potentially adverse
maternal outcomes. A Cochrane review of multiple micronutrient supplementation in pregnant women assessed 23 trials and reported an 11–13% reduction in low birthweight and SGA births, whereas effects on anaemia and IDA were much the same when compared with iron and folate acid supplements (table 1). Despite earlier concerns about potential excess neonatal mortality with multiple micronutrient use, present analyses suggest no adverse effects on maternal mortality, stillbirths, perinatal, and neonatal mortality with insufficient data for neurodevelopmental outcomes. Although scarce, there are interesting data for benefits of maternal multiple micronutrient supplementation on growth in early childhood. Preliminary data from a large trial comparing multiple micronutrient with iron-folate supplementation in pregnancy in Bangladesh show a significant reduction in preterm births with no adverse effects. Inclusion of this study in our meta-analysis confirms the reduction in low birthweight (relative risk [RR] 0·88, 95% CI 0·85–0·91) and SGA (0·89, 0·83–0·96) and is also indicative of a small effect on preterm births (0·97, 0·94–0·99). These findings support the potential replacement of iron-folate supplements in pregnancy with multiple micronutrient supplements in populations at risk.

Maternal calcium supplementation
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. Calcium supplementation during pregnancy in women at risk of low calcium intake has been shown to reduce maternal hypertensive disorders and preterm birth. A Cochrane review by Hofmeyr and colleagues assessed 13 trials and showed that calcium supplementation during pregnancy reduced the incidence of gestational hypertension by 35%, preeclampsia by 55%, and preterm births by 24% (table 1). These estimates have been updated in a review of 15 randomised controlled trials, which also showed a 52% reduction in the incidence of preeclampsia and confirmed that these effects were only noted in populations at risk of low calcium intake.

Maternal iodine supplementation or fortification
In nearly all regions affected by iodine deficiency, use of iodised salt is the most cost-effective way to avert deficiency. A Cochrane review suggests that although iodised salt is an effective means to improve iodine status, no conclusions can be drawn about physical and mental development in children and mortality. In some regions of the world with severe iodine deficiency, salt iodisation alone might not be sufficient for control of iodine deficiency in pregnancy; in these circumstances iodised oil supplementation during pregnancy can be a viable option (table 1). A review of five randomised trials of iodised oil supplementation in pregnancy in iodine-deficient populations showed a 73% reduction in cretinism and a 10–20% increase in developmental scores in children. Existing evidence supports continued focus on effective universal salt iodisation for women of reproductive age and those who are pregnant. Further high-quality controlled studies are needed to address dosage and alternative strategies for iodine supplementation in different population groups and settings.

Addressing maternal wasting and food insecurity with balanced energy and protein supplementation
Maternal undernutrition is a risk factor for fetal growth restriction and adverse perinatal outcomes. Several nutritional interventions have been assessed in such situations, including dietary advice to pregnant women,
provision of balanced energy protein supplements, and high protein or isocaloric protein supplementation. In other contexts, prescription and promotion of low energy diets to pregnant women who are either overweight or exhibit high weight gain in early gestation have been assessed.29 Balanced energy protein supplementation, providing about 25% of the total energy supplement as protein, is deemed an important intervention for prevention of adverse perinatal outcomes in malnourished women.29–31 A Cochrane review31 concluded that balanced energy protein supplementation reduced the incidence of SGA by 32% and risk of stillbirths by 45% (table 1). An updated meta-analysis showed that balanced energy protein supplementation increased birthweight by 73 g (95% CI 30–117) and reduced risk of SGA by 34%, with more pronounced effects in malnourished women.32

### Nutrition interventions in neonates

#### Delayed cord clamping

Early clamping of the umbilical cord after birth is a common practice and permits immediate transfer of the baby for care as required, whereas delaying of clamping allows continued blood flow between the placenta and the baby for a longer duration. A Cochrane review33 suggested that delayed cord clamping in term neonates led to significant increase in newborn haemoglobin and higher serum ferritin concentration at 6 months of age (table 2).33

### Table 1: Review of nutrition interventions for women of reproductive age and during pregnancy

<table>
<thead>
<tr>
<th>Evidence reviewed</th>
<th>Setting</th>
<th>Estimates</th>
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<td><strong>Folic acid supplementation</strong></td>
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<td>Women of reproductive age</td>
<td>Systematic review of five trials34 of periconceptual folic acid supplementation</td>
<td>Developing and developed countries</td>
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<td>Systematic review of 31 trials35</td>
<td>Mostly developed countries</td>
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<td><strong>Iron and iron-folate supplementation</strong></td>
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<td>Women of reproductive age</td>
<td>Systematic review of 21 RCTs and quasi-experimental studies36</td>
<td>Mostly developed countries</td>
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<tr>
<td>Pregnant women</td>
<td>Systematic review of 43 RCTs and quasi-experimental studies37 (34 iron alone, eight iron-folate)</td>
<td>Mostly developed countries</td>
</tr>
<tr>
<td><strong>MMN supplementation</strong></td>
<td></td>
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<tr>
<td>Pregnant women</td>
<td>Systematic review of 21 RCTs38</td>
<td>Mostly effectiveness studies</td>
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<tr>
<td><strong>Calcium supplementation</strong></td>
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<tr>
<td>Pregnant women</td>
<td>Systematic review of 15 RCTs39</td>
<td>Mostly effectiveness trials</td>
</tr>
<tr>
<td><strong>Iodine through iodisation of salt</strong></td>
<td></td>
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<tr>
<td>Pregnant women</td>
<td>Systematic review of five RCTs40</td>
<td>Mostly effectiveness trials</td>
</tr>
<tr>
<td><strong>Maternal supplementation with balanced energy protein</strong></td>
<td></td>
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<tr>
<td>Pregnant women</td>
<td>Systematic review of 16 RCTs and quasi-experimental studies41</td>
<td>Mostly effectiveness trials</td>
</tr>
</tbody>
</table>

NDT=neural tube defects. RR=relative risk. MD=mean difference. RCT=randomised controlled trial. MMN=multiple micronutrient. SGA=small-for-gestational age.
Neonatal vitamin K administration

Vitamin K deficiency can result in bleeding in the first weeks of life and vitamin K is commonly given prophylactically after birth for prevention of bleeding. In the absence of vitamin K prophylaxis there is a 0.4–1.7% risk of development of clinically significant bleeding. A Cochrane review suggested that one dose of intramuscular vitamin K, when compared with placebo, reduced clinical bleeding at 1–7 days of life, including bleeding after circumcision (table 2). Oral and intramuscular vitamin K had much the same effects on improved biochemical indices of coagulation status at 1–7 days. Currently, vitamin K administration after birth is largely restricted to births in health facilities; no information is available on the public health significance of vitamin K deficiency-related bleeding in LMICs or population-based programmes for prevention.

Neonatal vitamin A supplementation

A Cochrane review of oral or intramuscular vitamin A supplementation to very low birthweight infants showed reduced mortality and oxygen requirement at 1 month of age compared with placebo (table 2). Although neonatal vitamin A supplementation has also been shown to be effective in reduction of all-cause mortality by 6 months of age, evidence is conflicting, and might be related to maternal vitamin A status. A Cochrane review did report a 14% reduction in the risk of infant mortality at 6 months of age, four more trials are currently underway in Asia and Africa, and researchers agree that these additional data will be needed before development of recommendations for neonatal vitamin A supplementation.

Kangaroo mother care

Kangaroo mother care denotes early skin-to-skin contact between mother and baby at birth or soon thereafter, plus early and continued breastfeeding, parental support, and early discharge from hospital. A Cochrane review of 34 randomised controlled trials of early skin-to-skin care in healthy neonates showed a significant 27% increase in breastfeeding at 1–4 months of age and increased duration of breastfeeding (table 2). In a Cochrane review of 16 randomised trials, kangaroo mother care in preterm neonates was associated with a 40% reduction in the risk of mortality, a 58% reduction in nosocomial infection or sepsis, and a 77% reduction in prevalence of hypothermia. The trials included in these analyses were done in health facilities; although kangaroo mother care might also be useful for home deliveries, there is not yet evidence of effectiveness in community settings. Kangaroo mother care was also shown to increase some measures of infant growth, breastfeeding, and mother-infant attachment, but few studies provide objective evidence of any effect on early child development.
Nutrition interventions in infants and children
Promotion of breastfeeding and supportive strategies
WHO recommends initiation of breastfeeding within 1 h of birth, exclusive breastfeeding of infants till 6 months of age, and continued breastfeeding until 2 years of age or older. However, global progress on this intervention is both uneven and suboptimum. The exact scientific basis for the absolute early time window of feeding within the first hour after birth is weak. A systematic review suggests that breastfeeding initiation within 24 h of birth is associated with a 44–45% reduction in all-cause and infection-related neonatal mortality, and is thought to mainly operate through the effects of exclusive breastfeeding. We updated the previous review by Imdad and colleagues, which assessed the effect of promotion of dietary diversity and complementary feeding practices and height-for-age Z scores (WAZ; 0·12; 95% CI 0·01–0·43, four studies), whereas the effect on stunting was not statistically significant (RR 0·70, 95% CI 0·49–1·01, four studies). We identified a significant effect on weight gain (SMD 0·40, 95% CI 0·02–0·78, four studies), whereas no effects were noted for weight-for-age Z scores (WAZ; 0·12; 95% CI 0·02 to 0·26, four studies). Studies of nutrition education in food insecure populations (with an average daily per person income of less than US$1·25) showed significant effects on HAZ (SMD 0·25, 95% CI 0·09–0·42, one study), stunting (RR 0·68, 95% CI 0·60–0·76, one study), and WAZ (SMD 0·26, 95% CI 0·12–0·41, two studies). The review did not find any eligible study that provided complementary feeding (with or without education) in a food secure population. Overall, the provision of complementary foods in food insecure populations was associated with significant gains in HAZ (SMD 0·39; 95% CI 0·05–0·73, seven studies) and WAZ (SMD 0·26, 95% CI 0·04–0·48, three studies), whereas the effect on stunting did not reach statistical significance (RR 0·33, 95% CI 0·11–1·00, seven studies).

Promotion of dietary diversity and complementary feeding
Complementary feeding for infants refers to the timely introduction of safe and nutritionally rich foods in addition to breast-feeding at about 6 months of age and typically provided from 6 to 23 months of age. Different approaches have been used to create indicators of dietary diversity and to study its association with child malnutrition. In seven Latin American surveys, Ruel and Menon noted significant associations between complementary feeding practices and height-for-age Z scores (HAZ). Similarly, analysis of Demographic Health Survey data to create a dietary diversity score based on seven food groups showed that increased dietary diversity was positively associated with height-for-age HAZ in nine of 11 countries. More recently, WHO infant and young child feeding indicators were studied in 14 Demographic Health Survey datasets from low-income countries; consumption of a minimum acceptable diet with dietary diversity reduced the risk of both stunting and underweight whereas minimum meal frequency was associated with lower risk of underweight only.

In an update of a previous review of complementary feeding, we assessed 16 randomised and non-randomised controlled trials and programmes of moderate quality (table 3). We identified ten studies that assessed the effect of nutrition education and seven studies that assessed the effect of provision of additional complementary foods (one trial with three intervention groups was in both these categories). Studies of nutrition education in food secure populations showed a significant increase in height (standard mean difference [SMD] 0·35, 95% CI 0·08–0·62, four studies), and HAZ (0·22, 0·01–0·43, four studies), whereas the effect on stunting was not statistically significant (RR 0·70, 95% CI 0·49–1·01, four studies). Studies of nutrition education in food insecure populations (with an average daily per person income of less than US$1·25) showed significant effects on HAZ (SMD 0·25, 95% CI 0·09–0·42, one study), stunting (RR 0·68, 95% CI 0·60–0·76, one study), and WAZ (SMD 0·26, 95% CI 0·12–0·41, two studies). The review did not find any eligible study that provided complementary feeding (with or without education) in a food secure population. Overall, the provision of complementary foods in food insecure populations was associated with significant gains in HAZ (SMD 0·39; 95% CI 0·05–0·73, seven studies) and WAZ (SMD 0·26, 95% CI 0·04–0·48, three studies), whereas the effect on stunting did not reach statistical significance (RR 0·33, 95% CI 0·11–1·00, seven studies).

Vitamin A supplementation in children
A Cochrane review of 43 randomised trials showed that vitamin A supplementation reduced all-cause mortality by 24% and diarrhoea-related mortality by 28% in children aged 6–59 months (table 3). Vitamin A supplementation also reduced the incidence of diarrhoea and measles in this age group but there was no effect on mortality and morbidity related to respiratory infections. Although a large effectiveness study from India assessing the effect of vitamin A supplementation and deworming over several years did not show a significant effect on mortality from vitamin A supplementation (mortality ratio 0·96, 95% CI 0·89–1·03), inclusion of these data with previous results still shows a significant, albeit lower, effect on mortality (RR 0·88, 95% CI 0·84–0·94). We believe that vitamin A supplementation continues to be an effective intervention in children aged 6–59 months in populations at risk of vitamin A deficiency.

Iron supplementation in infants and children
A Cochrane review of 33 studies showed that intermittent iron supplementation to children younger than 2 years reduced the risk of anaemia by 49% and iron
deficiency by 76% (table 3). The findings also suggested that intermittent iron supplementation could be a viable public health intervention in settings in which daily supplementation had not been implemented or was not feasible. A review\(^{[77]}\) of the effect of iron supplementation in children on mental and motor development showed only small gains in mental development and intelligence scores in supplemented school-age children who were initially anaemic or iron-deficient. There was no convincing evidence that iron treatment had an effect on mental development in children younger than 27 months.

Since the demonstration of increased risk of admission to hospital and serious illnesses with iron supplementation,\(^{[78]}\) there has been concern about administration of iron supplements in malaria endemic areas. WHO currently recommends administration of iron supplements in malaria endemic areas on the stipulation that malaria prevention and treatment is made available.\(^{[79]}\)

<table>
<thead>
<tr>
<th>Setting</th>
<th>Estimates</th>
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</thead>
<tbody>
<tr>
<td><strong>Breast feeding promotion in infants</strong></td>
<td></td>
</tr>
<tr>
<td>Systematic review of 110 RCTs and quasi-experimental studies(^{[54]})</td>
<td>Developing and developed countries</td>
</tr>
<tr>
<td><strong>Complementary feeding promotion in children 6-24 months of age</strong></td>
<td></td>
</tr>
<tr>
<td>16 RCTs and quasi-experimental studies(^{[57]})</td>
<td>Mostly from food secure populations. Various foods used</td>
</tr>
<tr>
<td><strong>Preventive vitamin A supplementation in children 6 months to 5 years of age</strong></td>
<td></td>
</tr>
<tr>
<td>Systematic review of 13 trials(^{[58]})</td>
<td>Developing and developed countries</td>
</tr>
<tr>
<td><strong>Iron supplementation in children</strong></td>
<td></td>
</tr>
<tr>
<td>Systematic review of 33 RCTs and quasi-experimental studies(^{[59]})</td>
<td>LMICs. Participant’s ages ranged from neonates to 19 years</td>
</tr>
<tr>
<td>Systematic review of 17 RCTs(^{[60]})</td>
<td>Developing and developed countries. In children aged 6 months to 15 years</td>
</tr>
<tr>
<td><strong>MMN supplementation including iron in children</strong></td>
<td></td>
</tr>
<tr>
<td>Systematic review of 10 RCTs(^{[61]})</td>
<td>Mostly developing countries. In children aged 6 months to 16 years</td>
</tr>
<tr>
<td>Systematic review of 10 RCTs(^{[62]})</td>
<td>Developing countries. Mostly effectiveness studies. In children aged 6 months to 11 years</td>
</tr>
<tr>
<td><strong>Zinc supplementation in children</strong></td>
<td></td>
</tr>
<tr>
<td>Systematic review of 18 RCTs(^{[63]})</td>
<td>Mostly developing countries. In children younger than 5 years</td>
</tr>
<tr>
<td>Systematic review of 13 trials(^{[64]})</td>
<td>Developing and developed countries. In children younger than 5 years</td>
</tr>
</tbody>
</table>

Table 3: Review of evidence for nutrition interventions for infants and children
Multiple micronutrient supplementation in children

Although the theoretical benefits of strategies to improve diet quality and micronutrient density of foods consumed by small children are well recognised, few resource-poor countries have clear policies in support of integrated strategies to control micronutrient deficiencies in young children.9 Available options include the provision of multiple micronutrients via supplements, micronutrient powders, or fortified ready-to-use foods including lipid-based nutrient supplements. A comprehensive review of the effects of multiple micronutrients compared with two or fewer micronutrients showed small benefits on linear growth (mean difference [MD] 0·13, 95% CI 0·06–0·21) and weight gain (0·14, 0·03–0·25) but with little evidence of effect on morbidity outcomes as suggested by individual studies (table 3).58 Another review59 of the effect of multiple micronutrient supplementation on improvement of cognitive performance in children concluded that multiple micronutrient supplementation might be associated with a marginal increase in reasoning abilities but not with acquired skills and knowledge.

Micronutrient powders are increasingly in use at scale in programmes to address iron and multiple micronutrient deficiencies in children. We reviewed 16 randomised controlled trials to assess the effectiveness of micronutrient powders and estimated that they significantly improved haemoglobin concentration and reduced IDA by 57% and retinol deficiency by 21%.39 We noted no evidence of benefit on linear growth. However, in-line with findings from an earlier review of liquid iron supplementation trials,90 use of micronutrient powders was shown to be associated with a significant increase in the incidence of diarrhoea (RR 1·04, 95% CI 1·01–1·06), largely because of results from a recent large cluster-randomised controlled trial of micronutrient powders in Pakistan in malnourished children.71 These findings underscore the need for further assessment of micronutrient powder programmes in varying contexts for safety and benefits.

Preventive zinc supplementation in children

Preventive zinc supplementation in populations at risk of zinc deficiency reduces the risk of morbidity from childhood diarrhoea and acute lower respiratory infections and might increase linear growth and weight gain in infants and young children.47,21 A review by Yakoob and colleagues48 assessed 18 studies from developing countries and showed that preventive zinc supplementation reduced the incidence of diarrhoea by 13% and pneumonia by 19%, with a non-significant 9% reduction in all-cause mortality (table 3). However, subgroup analysis showed that there was a significant 18% reduction in all-cause mortality in children aged 12–59 months. A daily dose of 10 mg zinc per day over 24 weeks in children younger than 5 years could lead to an estimated net gain of 0·37 cm (SD 0·25) in height in zinc-supplemented children compared with placebo.30 There is no convincing evidence that zinc supplementation in infants or children results in improved motor or mental development.29

Disease prevention and management

Several interventions have the potential to affect health and nutrition outcomes through reduction in the burden of infectious diseases. Table 4 summarises the evidence for interventions for disease prevention and management.

Prevention and treatment of severe acute malnutrition

A substantial global burden of wasting exists, especially severe acute malnutrition (SAM; weight-for-height Z score [WHZ] <-3), which coexists with moderate acute malnutrition (MAM; WHZ <-2). In stable non-emergency situations with endemic malnutrition, MAM can often present in combination with stunting. Most of the interventions previously discussed should be implemented to prevent the development of SAM in food insecure populations. Several approaches for prevention and treatment are in use. Although the provision of complementary and supplementary foods could be considered in targeted food distribution programmes, other ways to stimulate access and purchasing power can be conceived. Where markets are fragmented or food access is constrained, appropriate food supplements might be considered as in-kind transfers. WHO recommends inpatient treatment for children with complicated SAM, with stabilisation and appropriate treatment of infections, fluid management, and dietary therapy and also supports community-based care for uncomplicated SAM.68 Although facility-based treatment of SAM remains important, community management of SAM continues to grow rapidly globally. This shift in treatment norms from centralised, inpatient care towards community-based models allows more affected children to be reached and is cost effective. Up to an estimated 15% of cases of SAM will need initial facility-based care, whereas the rest can receive only community-based treatment.86

Facility-based management of SAM according to the WHO protocol

A scientific literature review by Schofield and Ashworth80 showed that between the 1950s and 1990s, case fatality rates were typically 20–30% in children with SAM treated in hospitals or rehabilitation units, and rates were higher (50–60%) for oedematous malnutrition. A previous review of existing studies had estimated that following the WHO protocol, as opposed to standard care, would lead to a 55% reduction in deaths (RR 0·40, 95% CI 0·32–0·62; random effects).

In view of the limitations of analysis and variable quality of studies in the previous review, we updated the review to assess the effect of the WHO protocol or adaptations thereof on recovery and case fatality of children with SAM.
Case fatality rates ranged from 3·4% to 35%. The highest case fatality rate stemmed from a cohort of children with HIV infection. However, a clear need exists for continued work to improve staff training and quality to achieve high rates of survival across various resource-constrained settings.

**Community-based management of SAM**

The products used to deliver nutrients for management of SAM and MAM, and the approaches used to target and deliver these products, evolved rapidly during the past decade. Innovations include new formulations and packaging and a shift from institutional to community-based management.

We reviewed interventions to treat SAM in community settings, and were largely able to pool studies comparing

**Table 4: Review of evidence for disease prevention and management**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Settings</th>
<th>Estimates</th>
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<td><strong>WASH interventions</strong></td>
<td></td>
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</tr>
<tr>
<td>Overview of three systematic reviews</td>
<td>Developing countries</td>
<td>Significant effects: reduced risk of diarrhoea with hand washing with soap (RR 0·52, 95% CI 0·34–0·65), with improved water quality, and with excreta disposal</td>
</tr>
<tr>
<td>DHS data from 65 countries</td>
<td>Developing countries</td>
<td>Significant effects: a recent World Bank report based on analysis of trends in DHS data suggests that open defecation explained 54% of international variation in child height by contrast with GDP, which only explained 29%. A 20 percentage point reduction in open defecation was associated with a 0·1 SD increase in child height A Cochrane review of the effect of WASH interventions on nutrition outcomes is underway</td>
</tr>
<tr>
<td><strong>Deworming in children (for soil-transmitted intestinal worms)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systematic review of five RCTs</td>
<td>Developing countries</td>
<td>Non-significant effects: one dose of anthelmintic in second trimester of pregnancy had a non-significant effect on maternal anaemia, low birthweight, premature births, and perinatal mortality</td>
</tr>
<tr>
<td>Systematic review of 34 RCTs</td>
<td>Developing countries</td>
<td>Non-significant effects: one-dose deworming had a non-significant effect on haemoglobin and weight gain. For multiple doses at 1 year follow up, there was a non-significant effect on weight, haemoglobin, cognition, and school attendance Treatment after confirmed infection Significant effects: one-dose deworming drugs increased weight (0·58 kg, 95% CI 0·40–0·76) and haemoglobin (0·37 g/dL, 95% CI 0·1·0·64). Evidence on cognition was inconclusive These analyses are corroborated by the large-scale DEVTA trial of regular deworming and VAS over 5 years, which also did not show any benefits on weight gain or mortality</td>
</tr>
<tr>
<td><strong>Feeding practices in diarrhoea</strong></td>
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<tr>
<td>Review of 29 RCTs</td>
<td>Developing countries</td>
<td>Significant effects: in acute diarrhoea, lactose-free diets, when compared with lactose-containing diets, significantly reduced incidence of diarrhoea (SMD -0·36, 95% CI -0·62 to -0·10) and treatment failure (RR 0·53, 95% CI 0·40–0·70) Non-significant effects: weight gain</td>
</tr>
<tr>
<td><strong>Zinc therapy for diarrhoea</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systematic review of 13 studies</td>
<td>Mostly Asia</td>
<td>Significant effects: reduced all-cause mortality reduced by 46% (95% CI 12–68), diarrhoea-related admissions to hospital by 23% (95% CI 15–31) Non-significant effects: diarrhoea-specific mortality, diarrhoea-prevalence Zinc reduced duration of acute diarrhoea by 0·50 days and persistent diarrhoea by 0·68 days</td>
</tr>
<tr>
<td><strong>IPTp/ITN for malaria in pregnancy</strong></td>
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<tr>
<td>Systematic review of 16 RCTs</td>
<td>Mostly Africa</td>
<td>Significant effects: Anti-malarials to prevent malaria in all pregnant women reduced antenatal parasitemia (RR 0·53, 95% CI 0·33–0·86), increased birthweight (MD 126·7 g, 95% CI 88·64–164·75), reduced low birthweight by 43% (RR 0·57, 95% CI 0·46–0·72) and severe antenatal anaemia 38% (RR 0·62, 95% CI 0·50–0·78) Non-significant effects: perinatal deaths</td>
</tr>
<tr>
<td>Systematic review of six RCTs</td>
<td>Developing countries</td>
<td>Significant effects: ITNs in pregnancy reduced low birthweight (RR 0·77, 95% CI 0·61–0·98) and reduced fetal loss (first to fourth pregnancy: RR 0·67, 95% CI 0·47–0·97) Non-significant effects: anaemia and clinical malaria</td>
</tr>
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<td><strong>Malaria prophylaxis in children</strong></td>
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<tr>
<td>Systematic review of seven RCTs</td>
<td>Developing countries of West Africa</td>
<td>Significant effects: Reduced clinical malaria episodes (RR 0·26, 95% CI 0·17–0·38), reduced severe malaria episodes (RR 0·27, 95% CI 0·10–0·76). IPTc also reduced risk of moderately severe anaemia (RR 0·71, 95% CI 0·52–0·98) Non-significant effects: all-cause mortality</td>
</tr>
<tr>
<td>Systematic review of 22 RCTs</td>
<td>Developing countries in Africa</td>
<td>Significant effects: ITNs improved packed cell volume of children by 1·7 absolute packed cell volume percent. When the control group used untreated nets, the difference was 0·4 absolute packed cell volume percent. ITNs and IRS reduced malaria-attributable mortality in children (1–59 months) by 55% (95% CI 49–61) in Plasmodium falciparum settings</td>
</tr>
</tbody>
</table>

WASH=water, sanitation, and hygiene. RCT=randomised controlled trial. DHS=Demographic and Health Survey. GDP=gross domestic product. RR=relative risk. MD=mean difference. SMD=standard mean difference. WAZ=weight-for-age Z score. HAZ=height-for-age Z score. DEVTA=de-worming and enhanced vitamin A. IPTp=intermittent preventive treatment of malaria in pregnancy. IPTc=IPT in children. ITN=insecticide-treated bednets. IRS=indoor residual spraying.
ready-to-use therapeutic foods (RUTF) with standard care, as opposed to rigorous evaluation of effectiveness of the approach in programme settings. We identified no significant differences in mortality; however, children who received RUTF had faster rates of weight gain and had 51% greater likelihood to recover (defined as attaining WZH ≥ –2) than did those receiving standard care.

Notably, a new randomised controlled trial compared standard RUTF with RUTF and additional 7 day course of antibiotics, either amoxicillin or cefdinir, in children with uncomplicated SAM. This trial showed that the children receiving an antibiotic had a lower mortality rate, faster recovery rate, and higher weight gain compared with children receiving placebo. Although further research on this topic is needed, especially in children with HIV infection, this study shows that effective community management of SAM might require an approach that goes beyond merely the choice of specially formulated foods to the entire package of care.

Substantial programmatic evidence supports use of RUTF for community-based treatment, which has substantially changed the approach to treatment of SAM. Yet because of the nature of the evidence, establishing effect estimates for the overall approach to community management has proved challenging. Available evidence shows some positive effects with the use of RUTF compared with standard care for the treatment of SAM in community settings, yet the differences were for the most part small and several outcomes had substantial heterogeneity. An emphasis not only on the choice of commodities, but also on the quality of programme design and implementation is crucial to improvement of outcomes for children with SAM, as is research to fill information gaps, such as optimum treatment methods and approaches for treatment of breastfed infants younger than 6 months.

Interventions for prevention and management of obesity

Obesity is increasing in many populations and is one of the most important challenges of the 21st century. Obese women are at an increased risk of adverse pregnancy outcomes. A Cochrane review assessed the effectiveness of interventions (eating, exercise, behaviour modification, or counselling) that reduce weight in obese pregnant women and identified no evaluable trials. Some studies assessed the effect of diet, exercise, or both for weight reduction in women after childbirth, and showed that women who exercised did not lose significantly more weight, but women who took part in a diet (MD –1.70 kg, 95% CI –2.08 to –1.32), or diet plus exercise programme (–2.89 kg; –4.83 to –0.95), did so. These interventions did not seem to adversely effect breastfeeding performance in any setting.

We identified six reviews that examined breastfeeding in infancy and its association with obesity prevalence or average body-mass index (BMI) in childhood or adulthood. All studies suggested a small protective effect of breastfeeding on obesity later in life, although the magnitude of the effect varied between reviews and the strength of the affect of confounding was unclear. The largest prospective follow up study in healthy term infants in Belarus showed that improving the duration and exclusivity of breastfeeding did not prevent overweight or obesity in children, nor did it affect insulin-like growth factor I concentrations at age 11–5 years. These findings suggest that despite the myriad advantages of breastfeeding, population strategies to increase the duration and exclusivity of breastfeeding are unlikely to curb the obesity epidemic.

A Cochrane review examined the effects of obesity prevention interventions delivered for more than 12 weeks on changes in BMI and BMI Z scores in children and suggested a significant beneficial effect across age groups with a SMD of –0·15 kg/m (95% CI –0·21 to –0·09). The subgroup analysis showed significant effects for children aged 6–12 years with non-significant effects in younger children and adolescents. Interventions that combined physical activity and diet were more effective than either delivered alone. Findings suggested that short-term interventions (<12 months duration) were more effective than were those delivered over a longer duration (SMD –0·17, 95% CI –0·25 to –0·09 and SMD –0·12, 95% CI –0·21 to –0·03, respectively); however, there was substantial heterogeneity in all pooled estimates. Another review of interventions to treat obesity in children showed that combined behavioural and lifestyle interventions or self-help could benefit overweight children and adolescents. Overall the evidence of effectiveness of all obesity prevention and therapeutic interventions is weak, underscoring the need for high-quality research in this discipline.

Delivery platforms and strategies for implementation of nutrition-specific interventions

Delivery strategies are crucial to achieve coverage with nutrition-specific interventions and to reach populations in need. A range of channels can provide opportunities for scaling up and reaching large segments of the population.

Fortification of staple foods and specific foods

A detailed discussion of fortification strategies is beyond the scope of this review. As supported by the Copenhagen consensus, fortification is one of the most cost-effective strategies to reach populations at large. Further discussion of fortification as a means for delivery of key micronutrients is provided in panel and the accompanying report by Stuart Gillespie and colleagues.

Cash transfer programmes

Financial incentives are widely used as policy strategies to ameliorate poverty, reduce financial barriers, and improve
Community-based platforms for nutrition education and promotion

Community-based interventions to improve maternal, newborn, and child health are now widely recognised as important strategies to deliver key maternal and child survival interventions and have been shown to reduce inequities in childhood pneumonia and diarrhoea deaths. These interventions are delivered by health-care personnel or lay individuals, and implemented locally in homes, villages, or any defined community group. A full spectrum of promotive, preventive, and curative interventions can be delivered via community platforms,
including provision of basic antenatal, natal, and postnatal care; preventive essential newborn care; breastfeeding counselling; management and referral of sick neonates; development of skills in behaviour change communication; and community mobilisation strategies to promote birth and newborn care preparedness. For example, a review of community-based packages of care suggested that these interventions can improve rates of facility births by 28% (RR 1.28, 95% CI 1.04–1.59) and result in a doubling of the rate of initiation of breastfeeding within 1 h (RR 2.23, 95% CI 1.70–2.97). Lewin and colleagues reviewed 82 studies with lay health workers and showed moderate quality evidence of effect on initiation of breastfeeding (RR 1.36, 95% CI 1.14–1.61), any breastfeeding (1.24, 1.10–1.39), and exclusive breastfeeding (2.78, 1.74–4.44) when compared with usual care. Although much of the evidence from large-scale programmes using community health workers is of poor quality, process indicators and assessments do suggest that community health workers are able to implement many of these projects at scale, and have substantial potential to improve the uptake of child health and nutrition outcomes among difficult to reach populations. It is important to underscore the crucial importance of community engagement and buy-in to ensure effective community outreach programmes, behaviour change, and access.

**Integrated management of childhood illnesses**

WHO, in collaboration with UNICEF and other agencies, developed the Integrated Management of Childhood Illness (IMCI) strategy in the 1990s. IMCI includes both curative and preventive interventions targeted at improvement of health practices at health facilities and at home. The strategy includes three components: improvements in case management; improvements in health systems; and improvements in family and community practices. Assessments of IMCI in Uganda, Tanzania, Bangladesh, Brazil, Peru, South Africa, China, Armenia, Nigeria, and Morocco have shown various benefits in health service quality, mortality reduction, and health-care cost savings. In Tanzania, implementation of IMCI was associated with significant improvements in equity differentials for six child health indicators, with the largest improvements noted for stunting in children between 24 and 59 months of age. Much the same findings were reported from Bangladesh, where implementation of IMCI was associated with a significant

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**Panel 4: Nutrition in emergencies**

Irrespective of the underlying cause, humanitarian emergencies are often characterised by high and rising rates of severe acute malnutrition (SAM), moderate acute malnutrition (MAM), and micronutrient deficiencies in children (and sometimes adults). The foremost intent of nutrition-specific interventions in such situations is to prevent mortality, and involves management of wasting and resolution of specific nutrient deficiencies, and ensuring adequate food consumption. The humanitarian community largely agrees that emergency nutrition interventions have improved in the past 10–15 years in terms of coverage, scale of operations, reporting standards, and effectiveness (assessed by Sphere and other standards of practice). Until the early 2000s, nutrition programming in emergencies was dominated by facility-based therapeutic care, targeted or blanket supplementary feeding, and provision of micronutrient supplements. More recently, the focus has widened, with attention being given to both short-term and longer-term concerns, and to a choice of actions from a more comprehensive range of interventions. The options for effective management for both SAM and MAM in emergencies have improved in the past 10–15 years as products used have been improved and coverage has increased through community-based treatment. Potential alternatives to the use of food to address seasonal or emergency-driven peaks in wasting are being explored, including combinations of food plus cash, cash alone, or vouchers; however, cost-effectiveness studies of various strategies are scarce. There is evidence that in contexts in which markets have not been seriously disrupted, appropriate foods are readily accessible, and rates of undernutrition are not dangerously high, alternatives or complements to food-based rations might be viable and potentially cost-effective.

Concern has also grown about the potential trade-offs between long-term versus short-term objectives of emergency nutrition interventions. Although life-saving actions are justifiably prioritised over the prevention of chronic diseases, food assistance programmes suitable for acute emergencies might be less appropriate for protracted situations. This has important implications when thinking through seasonal blanket distribution of ready-to-use foods to prevent a worsening of levels of acute malnutrition. As a result of the difficulty of generating experimental data specific to programming in emergencies, the discipline has evolved relying less on randomised controlled trials and more on the sharing of lessons learned, which are used to inform technical or operational guidelines disseminated by WHO and UN bodies. Although practice must still be improved in many areas, and outcomes better documented, it remains crucially important to secure appropriate resources to support nutrition actions in this most challenging of disciplines and to assess outcomes for future learning. The nutritional status of individuals assessed and treated in emergency contexts overlaps substantially with non-emergency settings. Although high-quality programmatic research can and must help improve the design and outcome of effective emergency nutrition interventions, these interventions should be seen as entry points that support, rather than supplant, longer-term actions seeking to address underlying causes of poor nutrition.
increase in exclusive breastfeeding and comparatively faster reduction in the prevalence of stunting in children aged 24–59 months.\textsuperscript{119}

**School-based delivery platforms**

Many countries have school feeding programmes targeting children who are older than 5 years. The main purpose of such programmes is to provide incentives for school enrolment and evidence of nutrition benefits is scarce. A Cochrane review\textsuperscript{130} of 18 relevant studies of the effectiveness of school feeding programmes in improving physical and psychosocial health for disadvantaged school pupils reported an increase in school attendance by 4–6 days annually and weight gains averaging 0·39 kg (95% CI 0·11–0·67) over 11 months and 0·71 kg (0·48–0·95) over 19 months. The results were inconclusive for height gain, so there must be caution that these programmes do not lead to obesity. A detailed discussion of school feeding programmes is provided in the accompanying report by Stuart Gillespie and colleagues.\textsuperscript{119} Notwithstanding the scarce evidence, schools offer an enormous opportunity for promotion of health and nutrition for older children and adolescents and could have an important role in future.

**Child health days**

Child health days have been introduced in weak health systems to rapidly enhance coverage of essential child survival interventions. There are few robust assessments or reported experiences with child health days, which commonly include delivery of vitamin A supplements, immunisations, insecticide-treated nets, and deworming drugs. Available evidence suggests that these days can achieve greater coverage than stand-alone campaigns in previously low-coverage countries.\textsuperscript{111} A descriptive review\textsuperscript{111} of scale-up of child health days from 1999 to 2009 suggests that these days were more effective than stand-alone campaigns, provided that the number of interventions did not exceed four. The overall equity effect of these approaches are uncertain and further studies are needed to establish how best to integrate this approach within routine health-care services.

**Delivery of nutrition interventions in humanitarian emergency settings**

Delivery strategies for nutrition interventions in humanitarian emergencies necessitate a different approach to what might be deemed optimum in stable circumstances. In view of variability in the characteristics of emergencies and protracted population displacement, humanitarian emergencies might closely mirror situations of endemic malnutrition in food insecure settings. Hence prevention and health promotion strategies, such as breastfeeding and complementary feeding education and support, should also become essential parts of the packages of interventions in emergency contexts (panel 4\textsuperscript{133–144}).

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**Panel 5: Evidence for emerging interventions**

**Household air pollution**

Household air pollution (HAP) from solid fuels used in simple stoves for cooking and heating, is recognised as a risk factor for several health outcomes with important consequences for child survival, including pneumonia,\textsuperscript{144} low birthweight, and stillbirths.\textsuperscript{145} A review of observational studies\textsuperscript{146} shows significant risk reduction estimates for HAP for low birthweight (29%), stillbirth (34%), stunting (21%), and all-cause mortality (27%). Reduction of exposure to HAP could substantially reduce risk of several important outcomes for child survival. One randomised controlled trial in rural Guatemala,\textsuperscript{147} with an improved stove intervention, reduced average exposure to indoor air pollution by 50% and resulted in a reduction in physician-diagnosed pneumonia (relative risk [RR] 0·84, 95% CI 0·63–1·13) although this difference was not statistically significant. However, this finding was supported by the results of an exposure-response analysis which showed a statistically significant reduction in the same outcome (0·82, 0·70–0·98). This intervention also resulted in a reduction in low birthweight (0·74, 95% CI 0·23–1·66), with babies weighing 89 g more (95% CI 27 to 204) than those in the control group.\textsuperscript{148} A range of interventions, including both clean fuels and improved solid fuel stoves are available, but substantial challenges remain in achieving sustained use of low-cost low-emission technologies at scale in low-income households.

**Maternal vitamin D supplementation**

Vitamin D is an essential requirement of the body at any age. Vitamin D can be acquired through three main channels: through the skin via exposure to sunlight, from the diet, and from supplements or fortified foods. However, natural low-cost sources of dietary sources of vitamin D are very scarce. A systematic review\textsuperscript{149} assessing the association of vitamin D status in pregnancy, suggests that women with circulating 25-hydroxyvitamin D (25[OH]D) concentrations of less than 50 nmol/L in pregnancy have an increased risk of preeclampsia (odds ratio [OR] 2·09, 95% CI 1·50–2·90), gestational diabetes mellitus (1·38, 1·12–1·70), preterm birth (1·58, 1·08–2·31) and small-for-gestation age ([SGA] 1·52, 1·08–2·15). A long-term cohort study\textsuperscript{150} did not find any association of low maternal vitamin D concentrations with bone mineral content in late childhood. Similarly, a Cochrane review\textsuperscript{151} assessed the effectiveness of vitamin D supplementation in pregnancy and revealed little evidence of benefits on functional pregnancy outcomes, although significant increase in serum vitamin D concentrations at term were noted and borderline reduction in low birthweight was reported in three trials (RR 0·48, 95% CI 0·23–1·01). The number of high-quality trials with maternal vitamin D supplementation is too small to draw conclusions on its usefulness and safety.

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**Maternal zinc supplementation**
A Cochrane review suggests that zinc supplementation in pregnancy results in a 14% reduction in preterm birth (RR 0.86, 95% CI 0.76–0.97). This decrease was not accompanied by a similar reduction in stillbirths, neonatal death, SGA, or low birthweight. No subgroup differences were identified in women with low versus normal zinc nutrition levels or in women who complied with their treatment versus those who did not. We conclude that there is presently insufficient evidence for a beneficial role of isolated zinc supplementation in pregnancy.

**Omega-3 fatty acid supplementation**
Several reviews have been done to assess the effectiveness of maternal supplementation with omega-3 fatty acids during pregnancy and its effects on various outcomes including nutritional, morbidity, mortality, cognitive, and neurodevelopmental measures. Findings from these reviews, consisting of studies done in developed countries and of variable quality, suggest that marine omega-3 fatty acids administered in pregnancy reduce the rate of preterm birth and increase birthweight. However, a Cochrane review suggests that there is not enough evidence to support the routine use of marine oil supplements or other prostaglandin precursors during pregnancy to reduce the risk of pre-eclampsia, preterm birth, low birthweight, or SGA. A review of the intake of omega-3 and omega-6 fatty acids in low-income countries showed that the total omega-3 fatty acid supply was below the recommended intake range for infants and young children, and below the minimum recommended level for pregnant and lactating women, in the nine countries with the lowest gross domestic product. The review noted that supply of omega-3 fatty acids could be increased by using vegetable oils with higher alpha-linolenic acid and by increasing fish production through fish farming. Another review on the effect of fatty acid status on immune function of children in low-income countries suggested that fatty acid interventions could yield immune benefits in children in poor settings, especially in non-breastfed children and in relation to inflammatory disorders, such as persistent enteropathy, although more trials are needed for a conclusive association.

**Antenatal psychosocial assessment and mental health support**
Stable maternal mental health during pregnancy is crucial for the development of the early mother–child relationship and for health. Although there is ample evidence of the link between maternal mental health and child health and growth, there is insufficient evidence to support routine psycho-social screening for all pregnant women. There is promising evidence that cognitive-behaviour therapy-based interventions provided by community health workers to pregnant women, can effectively reduce depression at 3 months post-partum (adjusted OR 0.22, 95% CI 0.14–0.36) and at 1-year follow-up (0.23, 0.15–0.36). However, there was no effect on weight gain or linear growth in infancy. There is a need for further robust trials of maternal mental health interventions with longer term follow up.

**Role of massage for promoting growth in preterm Infants**
Preterm infants have been noted to benefit from massage therapy and the suggested mechanisms include increased vagal activity and gastric motility, which leads to increased concentrations of insulin and insulin-like growth factor 1. A Cochrane review of the effect of massage in preterm infants showed that massage increased daily weight gain by 5 g, reduced the length of hospital stay by 4.5 days, and had a slight effect on development and weight gain at 4–6 months, although the evidence was of weak quality. A more recent review of the effects of massage therapy for preterm infants showed that 5–10 days of moderate pressure massage, typically 15 min three-times daily, resulted in improved weight gain (mean for studies 28–48%) and bone density, and reduced length of hospital stay. Related evidence from studies of emollient therapy in preterm infants from the developing world suggest potential synergistic benefits of skin barrier protection, thermoregulation, and light massage.

**Vitamin D supplementation in children**
In view of the widespread deficiency of vitamin D and associated health consequences and rickets, preventive vitamin D supplementation to high-risk populations, including infants and toddlers, might be a useful strategy. A Cochrane review of vitamin D supplementation in children in at-risk populations is underway, and an existing review of postnatal supplementation shows relatively few studies assessing effects on bone density, growth, and other functional outcomes.

**Zinc supplementation for treatment of newborn infections and childhood pneumonia**
A Cochrane review suggests that zinc supplementation in addition to antibiotics in children with severe and non-severe pneumonia did not have a significant effect on clinical recovery or duration of hospital stay. Other recent studies show mixed effects across a range of severity of disease, showing the need for larger well-powered studies for the treatment of severe pneumonia with zinc in populations at-risk of deficiency. Two trials of adjunctive zinc supplementation in presumed serious infections in neonates and young infants show disparate findings, underscoring the need for further well-designed and adequately powered studies of zinc as an adjunct to the treatment of serious infections in infancy.

**Lipid-based nutrient supplementation**
Lipid-based nutrient supplements (LNS, in the form of vegetable oil, peanut butter, milk powder, sugar, vitamins, and minerals) are used in small quantities (20 g) to meet micronutrient requirements in children, in combination with a normal diet. Randomised controlled trials in Malawi and Ghana have shown significant benefits on iron status and linear growth. Further evidence of benefits and absence of adverse effects are needed to assess the feasibility of use of LNS in programme settings and randomised controlled trials are underway—three in Africa and one in Asia—which should provide more information.
Emerging interventions that need further evidence

We also reviewed interventions that are not currently recommended but that have potential and future prospects for inclusion in regular programmes. These interventions, which have possible effects on nutritional outcomes in women and children, include strategies to reduce household air pollution, maternal vitamin D supplementation, maternal zinc supplementation, omega 3 fatty acids supplementation in pregnancy, antenatal psychosocial assessment and cognitive behaviour therapy for depression, emollient and massage therapy for preterm infants, vitamin D supplementation in children, zinc therapy for pneumonia, and lipid-based nutrient supplements. Some of the existing evidence around these interventions is summarised in panel 5.186–188

Modelling the effect of scaling up coverage of nutrition interventions in countries with the highest burden

We used the Lives Saved Tool (LiST) to model the potential effect on child health and mortality in 2012 of scaling up a set of ten nutrition-specific interventions that could affect stunting and severe wasting159 (panel 6; figure 2). For modelling, we selected 34 countries with more than 90% of the burden of
stunting (figure 3; appendix pp 8–12) and took 2011 as the base year. The present coverage level for each intervention was taken from the latest available estimates from large-scale surveys and effectiveness of interventions (see LiST for details). We modelled the effect of scaling up the following ten nutrition interventions: periconceptional folic acid supplementation or fortification, maternal balanced energy protein supplementation, maternal calcium supplementation, multiple micronutrient supplementation in pregnancy, promotion of breastfeeding, appropriate complementary feeding, vitamin A and preventive zinc supplementation in children 6–59 months of age, management of SAM, and management of MAM, from their present level of coverage to 90% (or retention of present coverage when higher than 90%). Appendix pp 13–16 list the estimates of effect considered for each intervention. The conversion of intervention effects of preventive zinc supplementation and complementary feeding strategies from linear growth to stunting effects in LiST is detailed in appendix pp 17–22. We assessed the effect of this scale up scenario on mortality in children younger than 5 years, rates of breastfeeding, stunting, and wasting.

Our model suggested that if these ten nutrition interventions were scaled up to 90% coverage, mortality in children younger than 5 years could be reduced by 15% (range 9–19), with a 35% (19–43) reduction in diarrhoea-specific mortality, a 29% (16–37) reduction in pneumonia-specific mortality, and a 39% (23–47) reduction in measles-specific mortality (figure 4). The analysis also showed fewer deaths attributable to congenital anomalies and birth asphyxia related to periconceptional folic acid use and a reduction in SGA (figure 4; appendix pp 23–24). This scale up had a little effect on maternal mortality (data not shown). Scaling up of all ten interventions to 90% coverage was also associated with a mean 20.3% (range 11.1–28.9) reduction in stunting and a 61.4% (35.7–72) reduction in severe wasting. The maximum effect for severe wasting was noted in children in the 12–23 months age group (appendix p 25).

The analysis suggested that the interventions with the largest potential affect on mortality in children younger than 5 years are management of SAM, preventive zinc supplementation, and promotion of breastfeeding (figure 5). Analysis of community support strategies for breastfeeding suggested that achieving 90% coverage of breastfeeding promotion could increase exclusive breastfeeding by 15% (7–22) in children younger than 1 month and by 20% (13–26) in children aged 1–5 months.
Implementation of nutrition-specific packages of care

We also assessed the potential effect of nutrition-specific packages of care by scaling up these interventions to 90% coverage. Four packages were assessed for effect on child survival: optimum maternal nutrition during pregnancy (maternal multiple micronutrients, use of iodised salt, calcium, and balanced energy protein supplementation), an infant and young child nutrition package (breastfeeding promotion and appropriate complementary feeding education or provision), micronutrient supplementation (preventive zinc and vitamin A supplementation), and management of acute malnutrition (management of MAM, management of SAM). Analysis of these nutrition-specific packages showed that the most lives could be saved by the therapeutic feeding for severe acute malnutrition, followed by the infant and young child nutrition package (table 5).

Can these interventions promote equitable access?

To assess the potential benefit of community-based delivery strategies on reaching and engaging poor and marginalised populations, we assessed the effect of community-based promotion and delivery of seven nutrition-specific interventions (multiple micronutrient supplementation in pregnancy, promotion of breastfeeding, appropriate complementary feeding, management of SAM, vitamin A supplementation, preventive zinc and vitamin A supplementation, and treatment of diarrhoea with zinc) across various wealth quintiles in three target countries—Pakistan, Bangladesh, and Ethiopia (figure 6). Baseline data were stratified by wealth quintiles by reanalysing the most recently available Demographic Health Survey for each country. Since no recent estimates existed for cause-specific mortality across wealth quintiles for Bangladesh and Ethiopia, we used LiST to recompute the cause of death structure using the procedures described by Amouzou and colleagues. For Pakistan, we used the recent national verbal autopsy study for the cause of death structure and distribution of deaths by asset quintiles from a recent analysis. As shown in figure 6 and appendix p 26, the effect of this scale up is greatest in the poorest quintiles, suggesting that scaling up these interventions through community-based approaches would not only reduce the overall burden of childhood mortality but also substantially reduce existing disparities in access and mortality.

Cost analysis

We used a so-called ingredients approach to work out the cost of nutrition interventions, based on the UN One Health Tool, which allows for regional variation due to personnel costs. We constructed cost estimates as add-ons to existing antenatal, postnatal, and standard infant
visits as part of WHO’s Expanded Program on Immunisation, plus five stand-alone nutrition visits between 6 and 35 months of age. The few interventions targeted at children between 36 and 59 months of age were assumed to be delivered opportunistically (at clinic visits, or during outreach visits for younger siblings). The base delivery platform assumed was outreach programmes for sub-Saharan Africa, and primary health-care clinics elsewhere (appendix pp 27–28 provides details). We compared the unit costs from the ingredients method with actual costs as used in the Scaling up Nutrition (SUN) costing. Although the ingredients method allows greater detail than an actual costs method such as SUN for planning purposes, the comparison to actual costs serves as a useful check on the appropriateness of assumptions made. Costs were estimated for ten nutrition interventions (one population-wide, three in pregnancy, and six after birth; intervention definitions and assumptions are provide in appendix pp 29–30).

We calculated unit costs separately for WHO subregions (appendix p 31). Unit costs were higher in Africa compared with elsewhere, because of higher labour costs and the extra travel time required for delivery using outreach (associated with lower population density in many areas, and also the lower coverage of primary care facilities). The unit costs for interventions were much the same between the ingredients and SUN approaches, allowing for some difference in interventions based on updated recommendations.

Our analysis shows that the estimated total additional cost involved to achieve 90% coverage of the population in need in the 34 focus countries with the selected set of ten nutrition interventions is Int$9·6 billion per annum (table 6). Of this $9·6 billion, $3·7 billion (39%) is for micronutrient interventions, $0·9 billion (9%) for educational interventions, and $2·6 billion (27%) for SAM management. The amount required for provision of supplementary food for pregnant women and for children aged 6–23 months in poor households (those with <$1·25 per person per day) constitutes the remaining $2·3 billion (24%). When these costs are broken down by region, $3·4 billion is needed in the 20 countries included from sub-Saharan Africa, $4·8 billion in the four in south Asia plus Myanmar (Burma), $1·0 billion for the six in eastern Mediterranean, and $0·5 billion for the three remaining countries (Vietnam and the Philippines in western Pacific region, plus Guatemala; appendix p 32). The $9·6 billion estimate for the nutrition interventions is lower than the 2008 SUN estimate of $11·8 billion. The SUN figure included $1·2 billion for capacity building and monitoring and assessment, which we excluded from the present analysis because we do not have a mechanism to allocate this cost by region or country and category.
There are differences in the details of our results compared with the earlier SUN estimates. Unit costs are similar but not identical. The list of focus countries is likewise similar but not identical (using 2005 data, Turkey, Peru, Cambodia, and Burundi were included in the list of countries with 90% of the world’s stunted children, but not with 2010 data; Rwanda and Chad entered this list with 2010 data). Some interventions are excluded from the new total (deworming, therapeutic zinc for diarrhoea), whereas some new ones are included (calcium supplements and balanced energy protein supplements in pregnancy). Complementary food supplementation is targeted only to the 6–23 month age group in this new analysis. Population in need has changed since the SUN estimates were calculated, with changes in coverage of some interventions (notably, management of SAM has begun to scale up).

Discussion

This update of nutrition interventions differs from past exercises in several ways. First, we included a wider range of nutrition-specific interventions and applied more stringent assessment criteria, using the Grades of Recommendation Assessment, Development and Evaluation system and Child Health Epidemiology Reference Group criteria for most interventions. Second, in view of emerging evidence of the importance of maternal nutrition, SGA, and early stunting; we specifically focused on interventions that might affect prevalence and outcomes in SGA births and early stunting. We also reviewed and modelled a range of delivery strategies and platforms and specifically explored the potential of reaching poor and disadvantaged populations through community platforms and outreach services, an approach used to assess the effect of interventions to address childhood diarrhoea and pneumonia. Finally, the LiST model was substantially updated to include age-specific effects and the inter-relationship of new interventions and their effect on maternal and child undernutrition, a much more complex exercise than what was undertaken previously. To undertake this exercise we substantively updated LiST in a way that more accurately captures the role of undernutrition and the effect of proven interventions on maternal and child health.

Several limitations should be recognised in considering our findings. A large proportion of the evidence on interventions is still derived from efficacy trials as opposed to effectiveness studies and hence variations exist in estimates of effect size for various interventions. Few robust assessments have been done in programme settings and available data from observational studies do not permit ready assessment of intervention effectiveness. There are also very few studies that report morbidity and neurodevelopmental outcomes. We reviewed the available evidence of effects on neurodevelopmental outcomes from studies of maternal and child nutrition interventions and identified little data with evaluation methodologies for assessment. We are therefore greatly limited in the inferences that can be drawn on neurodevelopment and long-term outcomes from nutrition interventions.

Notwithstanding these limitations, our estimates of the effect of nutrition-specific interventions, though more conservative than previous findings, still suggest great benefits from a core set of interventions delivered antenatally or postnatally. Our assessments of benefits from interventions to reduce SGA are hindered by the limited range of interventions in pregnancy. Even though antenatal care services offer a unique opportunity for maternal screening and interventions, the difficulty of reaching women early enough in pregnancy is a major limitation in ensuring adequate uptake of interventions for a reasonable length of time. In parts of the world with high rates of maternal malnutrition, micronutrient deficiencies, and SGA births, these factors remain major determinants of stunting in early childhood. This finding underscores the need to address determinants of undernutrition early in the lifecycle through appropriate strategies, such as enhancing adolescent nutrition and family planning to delay the age of first pregnancy or increase spacing between births. Achieving high coverage of multiple micronutrient supplementation in pregnancy offers a new avenue to reduce SGA births and their consequences for mortality and growth in early childhood. The absence of appreciation of the crucial links of maternal and fetal nutrition to fertility and repeated pregnancies has been a major barrier in targeting of interventions to address these factors appropriately.

Although the overall effect on stunting alleviation seems modest, the rate of decline suggested from the package of nutrition-specific interventions is plausible and within the broad range of observed effects across countries. A review of global stunting trends by Stevens and colleagues showed average rates of reduction in stunting in the best performing countries ranging from 21–42% over the past decade, broadly consistent with what our model predicts from scaling up a core set of nutrition-specific interventions. Importantly, the countries that have made tremendous strides in improving nutrition and health outcomes (such as Brazil, China, Saudi Arabia, Kuwait, and Chile) have implemented nutrition-specific interventions, but also have been settings with exceptional economic growth, and investments in nutrition-sensitive interventions to address population health, education, and social sector development. Much the same conclusions were drawn by UNICEF in a report on undernutrition. A major advance on our previous review of interventions is the addition of delivery platforms that allow us to assess strategies to reach populations who are not being reached currently. Our findings suggest that community platforms offer a unique opportunity to engage and reach poor and difficult to access populations through communication and outreach strategies. These strategies could also lead to potential integration of nutrition with maternal, newborn, and child health interventions. Since several countries are investing in
community health worker programmes to address maternal, newborn, and child health, much potential exists for scaling up nutrition promotion and therapeutic interventions through such platforms and hence integrating the two at point-of-service delivery. This integration could also help achieve reductions in inequities in the short term as has been noted by universal scaling up of selected maternal and child survival interventions. However, importantly, implementation of such programmes involves unique combinations and sequencing of health system policies, actions, and advocacy. Community-based nutrition programmes need meticulous planning, a rights-based framework for engagement of communities and other sectors, and piloting. Other health system pillars are crucial to success, including training and support for community health workers, strengthening of the supply chain, simplified information systems, monitoring, and regular feedback.

The model used in this review estimates feasible reductions in mortality and stunting with enhanced investments. The same investments that can achieve these results will also lead to other improvements in cognitive and socioemotional development. Although these outcomes are not included in the model, partly because the costing database differs (i.e., LiST mainly addresses mortality), substantial evidence from a range of models and longitudinal studies confirms that the benefits in terms of overall development on human capacity are appreciable.

In terms of cost, an annual outlay of an additional $9·6 billion to bring to scale a range of nutrition interventions that would save nearly 1 million lives is reasonable since many interventions would be scaled up from negligible coverage rates. The cost per (discounted) life-year saved is about $370 for a set of interventions that could effectively deliver optimum nutrition to pregnant women, infants, and children, and manage SAM. These figures suggest that the nutrition interventions are well within the cost-effectiveness benchmark (less than three-times per person income) for all countries. More than half of the $9·6 billion is accounted for by two large countries that could rely heavily on domestic resources (India and Indonesia). Consumables (whether drugs, or other items such as for transport or administration) account for slightly less than half the $9·6 billion, and all but the poorest countries can be expected to cover most of the expenditures on personnel; $3–4 billion from external donors could make a substantial difference to child nutrition. What proportion of development assistance for health is earmarked for nutrition is unclear. Global tracking data from the Institute for Health Metrics and Evaluation were unable to disaggregate nutrition-related funding from the annual funding of $5·17 billion for maternal, newborn, and child health programmes. The Countdown collaboration estimates nutrition-specific funding for the same year (2012) at $324·5 million. Much funding for nutrition-related programmes probably overlaps with existing programmes for maternal, newborn, and child health and health systems strengthening and there might also be potential synergies, making it possible to share costs.

The evidence from carefully conducted cohort studies of benefits of higher birthweight and early linear growth on education and improved health outcomes is convincing and consistent with the overall message from our review and modelling exercise. As the world moves towards the post-2015 development agenda, it is important to draw attention to the unfinished agenda of maternal and child undernutrition and to the emerging issues of obesity. Our review reconfirms the existence of feasible and low cost evidence-based interventions and the fact that coverage rates for many of these interventions remain poor and for some, non-existent. In view of the importance of fetal nutrition and poverty alleviation strategies to reach those in greatest need, priority must be given to scaling up nutrition specific and sensitive interventions in some of the highest burden countries. At the same time, in view of the increasing importance of non-communicable diseases, concerted efforts must be made to develop and implement interventions to reduce the risk of obesity.

Contributors
ZAB conceptualised the review in consultation with the coordinators (PW, AL, SH, and REB) and wrote the first draft of the paper with substantial inputs from JKD, NW, YT, and AR developed the modification of LiST for assessment of effect and equity. Costing for selected interventions was done by MFG and SH. YW contributed to the scientific literature search, screening, collection, and analysis of data for the deworming review. LL led the review of severe and moderate acute malnutrition. KW led the obesity prevention review and contributed to the severe and moderate acute malnutrition reviews. CM and SZ oversaw the obesity reviews. BAH assessed the effect of maternal multiple micronutrient supplements, neonatal vitamin A supplementation, and deworming in pregnant women. ZL contributed to reviews of complementary feeding strategies and community platforms. RAS contributed to reviews of micronutrient powders and breastfeeding. AI contributed to the reviews of calcium, balanced protein supplementation in pregnancy, and vitamin A supplementation. All authors and members of the review groups (below) saw successive drafts of the paper and provided input. ZAB finalized the paper and is the overall guarantor.

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Maternal and Child Nutrition 3

Nutrition-sensitive interventions and programmes: how can they help to accelerate progress in improving maternal and child nutrition?

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Acceleration of progress in nutrition will require effective, large-scale nutrition-sensitive programmes that address key underlying determinants of nutrition and enhance the coverage and effectiveness of nutrition-specific interventions. We reviewed evidence of nutritional effects of programmes in four sectors—agriculture, social safety nets, early child development, and schooling. The need for investments to boost agricultural production, keep prices low, and increase incomes is undisputable; targeted agricultural programmes can complement these investments by supporting livelihoods, enhancing access to diverse diets in poor populations, and fostering women’s empowerment.

However, evidence of the nutritional effect of agricultural programmes is inconclusive—except for vitamin A from biofortification of orange sweet potatoes—largely because of poor quality evaluations. Social safety nets currently provide cash or food transfers to a billion poor people and victims of shocks (eg, natural disasters). Individual studies show some effects on younger children exposed for longer durations, but weaknesses in nutrition goals and actions, and poor service quality probably explain the scarcity of overall nutritional benefits. Combined early child development and nutrition interventions show promising additive or synergistic effects on child development—and in some cases nutrition—and could lead to substantial gains in cost, efficiency, and effectiveness, but these programmes have yet to be tested at scale. Parental schooling is strongly associated with child nutrition, and the effectiveness of emerging school nutrition education programmes needs to be tested. Many of the programmes reviewed were not originally designed to improve nutrition yet have great potential to do so. Ways to enhance programme nutrition-sensitivity include: improve targeting; use conditions to stimulate participation; strengthen nutrition goals and actions; and optimise women’s nutrition, time, physical and mental health, and empowerment. Nutrition-sensitive programmes can help scale up nutrition-specific interventions and create a stimulating environment in which young children can grow and develop to their full potential.

Introduction

The food system is threatened by food and oil price volatility, diversion of resources from production of food to biofuels, climate change and related water shortages, persistent conflicts and emergencies, and natural disasters affecting agriculture production and yields.1–4 These challenges are compounded by changes in demand for food that are brought about by growing populations, increasing incomes, and urbanisation—shifts that raise concerns about diet quality and food safety, while threatening water, land, and other finite natural resources.5–8 In view of these challenges, protection of nutrition, let alone acceleration of progress, will entail more than bringing nutrition-specific interventions to scale. It will require a new and more aggressive focus on coupling effective nutrition-specific interventions (ie, those that address the immediate determinants of nutrition) with nutrition-sensitive programmes that address the underlying causes of undernutrition (panel 1).9

Nutrition-sensitive programmes draw on complementary sectors such as agriculture, health, social protection, early child development, education, and water and sanitation to affect the underlying determinants of nutrition, including poverty; food insecurity; scarcity of access to adequate care resources; and to health, water, and sanitation services.10 Key features that make programmes in these sectors potentially nutrition-sensitive are: they address crucial underlying determinants of nutrition; they are often implemented at large scale and can be effective at reaching poor populations11 who have high malnutrition rates; and they can be leveraged to serve as delivery platforms for nutrition-specific

Key messages

• Nutrition-sensitive interventions and programmes in agriculture, social safety nets, early child development, and education have enormous potential to enhance the scale and effectiveness of nutrition-specific interventions; improving nutrition can also help nutrition-sensitive programmes achieve their own goals.
• Targeted agricultural programmes and social safety nets can have a large role in mitigation of potentially negative effects of global changes and man-made and environmental shocks, in supporting livelihoods, food security, diet quality, and women’s empowerment, and in achieving scale and high coverage of nutritionally at-risk households and individuals.
• Evidence of the effectiveness of targeted agricultural programmes on maternal and child nutrition, with the exception of vitamin A, is limited; strengthening of nutrition goals and actions and rigorous effectiveness assessments are needed.

(Continues on next page)
interventions. Nutrition-sensitive programmes might therefore help to accelerate progress in improving nutrition by enhancing the household and community environment in which children develop and grow, and by increasing the effectiveness, coverage, and scale of nutrition-specific interventions.

Nutrition-sensitive programmes can help protect poor populations from the negative consequences of global food security threats and mitigate the effects of financial, weather-related, and man-made shocks (eg, conflicts). Such shocks make poor populations increasingly vulnerable to undernutrition, as shown by food and fuel price crises in the past 6 years,1 and documented effects of conflicts on morbidity and mortality among affected populations.2,3 Climate change and the expected increased frequency of droughts and flooding are likely to reduce food availability and dietary diversity, and increase rates of infectious diseases such as diarrhoea or malaria.4 Under these circumstances, nutrition-sensitive programmes can help to protect the assets and welfare of poor people and their investments in the health, nutrition, and development of their children.

Nutrition-sensitive programmes are likely to affect nutrition through changes in food and non-food prices and income, and through women’s empowerment. Panel 2 and figures 1 and 2 show results of analyses of the links between income growth and maternal and child anthropometry and anaemia (appendix p 1). Appendix p 2 summarises evidence regarding the association between women’s empowerment and child nutrition.

We review evidence of the nutritional effect of programmes from different sectors, and discuss how such investments could be made more nutrition-sensitive. We selected sectors on the basis of: relevance for nutrition (eg, address crucial underlying determinants of nutrition); availability of assessments of their nutritional effect; high coverage of poor populations; and targeting (programmes are, or could be, targeted to reach nutritionally vulnerable groups). The two sectors that most closely meet these criteria are agriculture and social safety nets. Early child development programmes do not meet the high coverage criteria but they are included because child development and nutrition outcomes share many of the same risk factors, and there is a growing interest in examination of potential integration and synergies in programming and outcomes.5,6,7 Schooling is also included, despite failing to meet all criteria, because of the importance of parental education for child nutrition and development. Health, water and sanitation, and family planning are covered in the accompanying report by Zulfiqar Bhutta and colleagues.8 Investments and policies in several other sectors (eg, transportation; communication and information technology; and global food, agriculture, and trade) have the potential to affect nutrition, as do more targeted policies (eg, maternity leave); however,

(Continued from previous page)

• The feasibility and effectiveness of biofortified vitamin A-rich orange sweet potato for increasing maternal and child vitamin A intake and status has been shown; evidence of the effectiveness of biofortification continues to grow for other micronutrient and crop combinations.
• Social safety nets are a powerful poverty reduction instrument, but their potential to benefit maternal and child nutrition and development is yet to be unleashed; to do so, programme nutrition goals and interventions, and quality of services need to be strengthened.
• Combinations of nutrition and early child development interventions can have additive or synergistic effects on child development, and in some cases, nutrition outcomes. Integration of stimulation and nutrition interventions makes sense programmatically and could save cost and enhance benefits for both nutrition and development outcomes.
• Parental schooling is consistently associated with improved nutrition outcomes and schools provide an opportunity, so far untapped, to include nutrition in school curricula for prevention and treatment of undernutrition or obesity.
• Maternal depression is an important determinant of suboptimum caregiving and health-seeking behaviours and is associated with poor nutrition and child development outcomes; interventions to address this problem should be integrated in nutrition-sensitive programmes.
• Nutrition-sensitive programmes offer a unique opportunity to reach girls during preconception and possibly to achieve scale, either through school-linked conditions and interventions or home-based programmes.
• The nutrition-sensitivity of programmes can be enhanced by improving targeting; using conditions; integrating strong nutrition goals and actions; and focusing on improving women’s physical and mental health, nutrition, time allocation, and empowerment.

See Online for appendix

Panel 1: Definition of nutrition-specific and nutrition-sensitive interventions and programmes

Nutrition-specific interventions and programmes
• Interventions or programmes that address the immediate determinants of fetal and child nutrition and development—adequate food and nutrient intake, feeding, caregiving and parenting practices, and low burden of infectious diseases
• Examples: adolescent, preconception, and maternal health and nutrition; maternal dietary or micronutrient supplementation; promotion of optimum breastfeeding; complementary feeding and responsive feeding practices and stimulation; dietary supplementation; diversification and micronutrient supplementation or fortification for children; treatment of severe acute malnutrition; disease prevention and management; nutrition in emergencies

Nutrition-sensitive interventions and programmes
• Interventions or programmes that address the underlying determinants of fetal and child nutrition and development—food security; adequate caregiving resources at the maternal, household and community levels; and access to health services and a safe and hygienic environment—and incorporate specific nutrition goals and actions
• Nutrition-sensitive programmes can serve as delivery platforms for nutrition-specific interventions, potentially increasing their scale, coverage, and effectiveness
• Examples: agriculture and food security; social safety nets; early child development; maternal mental health; women’s empowerment; child protection; schooling; water, sanitation, and hygiene; health and family planning services

Adapted from Scaling Up Nutrition9 and Shekar and colleagues, 2013.10
Panel 2: How responsive is nutrition to income growth?

As economies grow, stunting rates typically decrease, but the predicted decrease is far slower than the corresponding poverty reduction associated with economic growth (figure 1). Country fixed-effects regressions show that a 10% increase in gross domestic production (GDP) per person predicts a 5.9% (95% CI 4.1–7.6) reduction in stunting and an 11% (8.6–13.4) decrease in the World Bank’s poverty measure of individuals living on $1.25 per person per day. The effect of growth in gross national product on nutrition comes from a combination of increased household resources, and improved infrastructure and nutrition-relevant services. Much unexplained variability exists in the effect of national income on stunting. As shown in figure 1, countries such as Guatemala, South Africa, and India have higher stunting rates than expected for their income levels. By contrast, the Dominican Republic, Senegal, Ghana, China, and Sri Lanka are among the best performers.

The association between prevalence of child underweight and GDP growth is stronger than for stunting, with the rate of decrease with 10% GDP growth being 7.0% (95% CI 5.3–8.8; appendix p 1). This estimate is larger than reported with earlier datasets. Anaemia—defined as haemoglobin concentrations below 109 g/L—decreases at a slower rate; a 10% improvement in income would decrease child anaemia by only 2.4% (1.3–3.6) and maternal anaemia by 1.8% (0.4–3.1). However, severe anaemia—defined as haemoglobin below 70 g/L—decreases at a much higher rate with income growth for both mothers (6.5%; 95% CI 4.2–8.8) and children (9.0%; 5.1–12.9). Although data for low birthweights are not as reliable as those for other nutritional indicators, estimates using World Bank data suggest that a 10% increase in GDP per person typically reduces low birthweight prevalence by only 2.3% (95% CI 0.8–4.1). Bangladesh, India, Sudan, and Haiti have particularly high rates of low birthweight prevalence relative to their national levels of income. For women underweight (body-mass index <18.5 kg/m²), a 10% growth in national income results in a 4.0% (95% CI 1.7–5.8) decrease in underweight prevalence, a rate substantially lower than the reduction in child underweight.

The association between national income growth and women overweight and obesity is much stronger than for women underweight: a 10% increase in GDP per person typically reduces low birthweight prevalence by only 2.3% (95% CI 0.8–4.1). Bangladesh, India, Sudan, and Haiti have particularly high rates of low birthweight prevalence relative to their national levels of income. For women underweight (body-mass index <18.5 kg/m²), a 10% growth in national income results in a 4.0% (95% CI 1.7–5.8) decrease in underweight prevalence, a rate substantially lower than the reduction in child underweight.

Cost effectiveness studies cannot be easily applied to assess or rank these programmes. Similarly, although cost–benefit analysis can be used in principle, this analysis needs a common metric for all outputs, generally in monetary terms. However, a conversion of a death averted into monetary values requires an arbitrary assessment of the value of premature deaths averted. Similarly, although equity is usually deemed socially desirable, its value cannot be easily quantified.

Therefore, the nutrition outcomes in the programmes we discuss cannot be directly compared with those in the accompanying report by Zulfiqar Bhutta and colleagues. However, as we explain, the programmes we review are an integral component of an overall strategy to improve global nutrition.

Agriculture

Agriculture systems have a crucial role in provision of food, livelihoods, and income. Agriculture is the main occupation of 80% of poor populations in rural areas, including women. In Africa, women account for 70% of agricultural labour and 80% of food processing labour. Growing concerns about how to meet the food needs of an estimated global population of 9 billion by 2050 have spurred renewed efforts to boost agriculture production and productivity in the face of increasing threats that affect the global food system. Agriculture growth has been shown to reduce undernutrition; an additional investment of US$8 billion per year globally would reduce the number of underweight children by 10 million and of hungry people by 201 million by 2050, and raise the income of many of the world’s poorest people. Moreover, the economic returns to investments in agriculture are high compared with many other economic investments.

Although investments to enhance agriculture productivity and boost global food supply are crucial for long-term reductions in poverty, hunger, and malnutrition, they might not solve the problem of scarcity of access to nutritious and diverse diets (as opposed to scarcity of calories) that poor people face. A new emphasis on making agricultural systems and food and agriculture policies more nutrition-sensitive is called for and several reports discuss approaches and instruments to do so. An approach that can complement efforts to raise agricultural productivity and food supply globally is targeted agricultural programmes aimed at enhancing poor households’ income and access to high-quality diets. Our review focuses on these types of programmes, most specifically homestead food production systems, and the biofortification of staple crops, because they both meet our selection criteria, with the exception of scale.

Targeted agricultural programmes can affect nutrition through several pathways (panel 3). Despite variations in the way researchers use these pathways, all concur that women—their social status, empowerment, control over resources, time allocation, and health and nutritional status—are key mediators in the pathways...
between agriculture inputs, intra-household resource allocation, and child nutrition.\textsuperscript{25,32,34–35} The recognised importance of development of new approaches to stimulate agriculture’s contribution to nutrition has led to an increased interest in examination of the so far untapped potential of leveraging value chains to improve nutrition. Since this approach is still at a nascent stage, experience and evidence of effectiveness are scarce. Panel 4\textsuperscript{36–39} provides a brief overview of the approach.

Home gardens and homestead food production systems

Several scientific literature reviews of homestead food production systems have been done in the past decade.\textsuperscript{34,38,47–52} These reviews focused on different types of programmes and nutritional outcomes and used different search strategies and inclusion and exclusion criteria. Despite these differences, key conclusions were largely consistent across all reviews (appendix pp 3–4). First, these reviews note that there is little evidence of effectiveness of homestead food production programmes on maternal or child nutritional status (anthropometry or micronutrient status), with the possible exception of vitamin A status. For child anthropometry, a few studies reported an effect on at least one indicator,\textsuperscript{35–37} but effects were generally small. Although meta-analysis might not be the method of choice for synthesis of evidence from such diverse programmes, the results of a four-study meta-analysis\textsuperscript{52} showed no overall effect of targeted agricultural programmes on underweight, wasting, or stunting. Another four-study meta-analysis\textsuperscript{51} for vitamin A status, however, reports a small overall difference in serum retinol between intervention and control areas (0.08 μmol/L); a cluster-randomised effectiveness assessment of a biofortified orange sweet potato intervention in Uganda also showed a 9.5 percentage point reduction in the prevalence of low serum retinol (≤1.05 μmol/L) in intervention compared with control children aged 3–5 years at baseline.\textsuperscript{38} The second consistent message is that nutritional effect is more likely when agriculture interventions target women and include women’s empowerment activities, such as improvement in their knowledge and skills through behaviour-change communications or promotion of their increased control over income from the sale of targeted commodities. No studies, however, have specifically compared targeting of men versus women, or mainstreaming gender versus not doing so in the programmes reviewed. The third key message is that, with the exception of two studies of biofortified orange sweet potato,\textsuperscript{38,51} impact evaluation studies have generally been too poor and sample sizes often too small to draw definite conclusions about effects on nutritional status.

One review,\textsuperscript{39} which specifically looked at effects of homestead food production systems on intermediary outcomes along the impact pathway, concluded that, when measured, positive effects are shown for several underlying determinants of nutrition, including household production and consumption, maternal and child outcome along the impact pathway, concluded that, when measured, positive effects are shown for several underlying determinants of nutrition, including household production and consumption, maternal and child nutritional status, and demand for targeted commodities. No studies, however, have specifically compared targeting of men versus women, or mainstreaming gender versus not doing so in the programmes reviewed.

Figure 1: Prevalence of stunting in children aged 0–5 years and GDP per person

Most observations for prevalence of stunting are from 2000–08. The fitted curves are locally weighted regressions of prevalence of stunting in children aged 0–5 years and poverty (≤$1.25 per person, per day), against GDP per person. The adjustment to international dollar units converts income expressed in nominal dollars to one that is expressed in terms of international dollars, which have the same estimated purchasing power as a dollar in the USA, accounting for local prices. The size of the circles represents the estimated population of stunted children aged 0–5 years, in about 2005, on the basis of multiplication of stunting prevalence by UN estimates of the population of children aged 0–5 years. Data are sourced principally from the Demographic and Health Surveys,\textsuperscript{16} with observations for some countries sourced from WHO.\textsuperscript{15} GDP=gross domestic product. BGD=Bangladesh. CIV=Côte d’Ivoire. DOM=Dominican Republic. DRC=Democratic Republic of the Congo. ETH=Ethiopia. IDN=Indonesia. IRQ=Iraq. MDG=Madagascar. MMR=Myanmar (Burma). KEN=Kenya. NGA=Nigeria. PAK=Pakistan. PHN=Philippines. SDN=Sudan. VTN=Vietnam.

Figure 2: Prevalence of women overweight (BMI>25) and GDP per person, for low-income and middle-income countries

Most observations for prevalence of women overweight are from 2000–10. The fitted curve is a locally weighted regression of prevalence of women overweight against GDP per person. The correlation between prevalence of women underweight and the log of GDP per person is 0.71 and is significant at the 1% level. The size of the circles represents the estimated population of overweight women aged 15–49 years, in about 2005, on the basis of multiplication of prevalence of women overweight by the UN population estimates of the female population aged 15–49 years. Data are sourced principally from the Demographic and Health Surveys\textsuperscript{16} and WHO.\textsuperscript{15} DRC=Democratic Republic of the Congo. GDP=gross domestic product. PPP=purchasing power parity.
In the past 5 years, value chains have been singled out as one potential strategy to leverage steps along the chain. Distribution, retailing, promotion, labelling, and consumption. The concept of value as waste. Broadly defined steps along the supply chain include production, processing, and nutrition linkages, value chain concepts and analysis might provide a useful framework and platform to achieve these goals. Coordination between actors, because all value chain processes and actors are tightly linked by each action affecting the others along the chain; they are analytical, versatile, and solution-oriented and can therefore be used to assess the constraints that affect availability, affordability, acceptability, or quality of nutritious foods in a given context, and identify and test solutions that can be implemented at specific leverage points along the chain. They focus on addition of economic value, and could therefore be used to identify points before, during, and after production at which nutritional (and economic) value could be added, or losses in nutrients prevented. In view of the importance of coordination across sectors and of development of joint solutions to stimulate agriculture and nutrition linkages, value chain concepts and analysis might provide a useful framework and platform to achieve these goals.

Panel 4: Value chains for nutrition

Food supply chains are defined as the series of processes and actors that take a food from its production—including inputs into production—to consumption and disposal as waste. Broadly defined steps along the supply chain include production, processing, distribution, retailing, promotion, labelling, and consumption. The concept of value chain refers to the addition of value (usually economic) for chain actors at different steps along the chain.

In the past 5 years, value chains have been singled out as one potential strategy to leverage agriculture to improve nutrition. The approach could be particularly relevant for traditional value chains for micronutrient-rich foods such as dairy, meat, fish, poultry, and fruits and vegetables, which are generally lacking in the diets of low-income households because of scarce availability, perishability, and high prices often compounded by a scarcity of information and knowledge about their health and nutritional benefits. Food value chains are therefore a possible entry point to stimulate both supply and demand (especially among poor populations) for micronutrient-rich foods.

Value chain concepts and analysis have unique features that make them a promising approach for tackling both undernutrition and overnutrition: 1) they focus on coordination between actors, because all value chain processes and actors are tightly linked by each action affecting the others along the chain; 2) they are analytical, versatile, and solution-oriented and can therefore be used to assess the constraints that affect availability, affordability, acceptability, or quality of nutritious foods in a given context, and identify and test solutions that can be implemented at specific leverage points along the chain; 3) they focus on addition of economic value, and could therefore be used to identify points before, during, and after production at which nutritional (and economic) value could be added, or losses in nutrients prevented. In view of the importance of coordination across sectors and of development of joint solutions to stimulate agriculture and nutrition linkages, value chain concepts and analysis might provide a useful framework and platform to achieve these goals.

Three broad milestones need to be achieved for biofortification to succeed: 1) breeding objectives (minimum target concentration for each micronutrient) must be met; 2) retention and bioavailability of micronutrients must be satisfactory so that intake leads to expected improvements in status; and 3) farmer adoption rates and intakes by target populations must be adequate. HarvestPlus, a programme that has led a global effort to breed and disseminate biofortified staple food crops since 2003, has made substantial progress in research to test these three steps for vitamin A, zinc, and iron in seven crops: cassava, biofortification. Biofortification is a uniquely nutrition-sensitive agriculture intervention because it focuses on breeding of staple crops that are rich in essential micronutrients. The many advantages of the approach are well documented. Biofortification, however, cannot achieve the high concentrations of micronutrients needed to treat severe deficiencies or to fulfil the high requirements (eg, for iron and zinc) of pregnant and lactating women and infants; it is more suited for provision of a daily dose of micronutrients (about 50% or more of daily needs) to help prevent deficiencies in individuals throughout the lifecycle, outside of the 1000 days window. As is true for all approaches, biofortification should be considered as one component of a larger strategy to eliminate micronutrient deficiencies, and the optimum mix of supplementation, dietary diversification, fortification, biofortification, and health services should be defined depending on local context.
maize, sweet potato, bean, pearl millet, rice, and wheat (table). In addition to achieving major progress in breeding and releasing crops, the programme will complete all planned retention and bioavailability studies in 2013, and 11 efficacy trials in 2014. Two effectiveness trials,58,59 which assessed the rollout of orange sweet potato in Uganda and Mozambique (milestone three), have been completed. They showed high farmer adoption and significant increases in vitamin A intakes in both countries and in child vitamin A status in Uganda.58,59 Effectiveness trials for the other target crops are expected to be completed by 2018.

Thus, present evidence regarding biofortification is concentrated on the first two milestones—proof of concept that breeding for micronutrient-rich crops is feasible and that micronutrients are retained and bio-available—and a growing evidence of efficacy. Results on bioconversion of β-carotene to retinol in humans and bioavailability of zinc and iron from biofortified compared with common varieties are very encouraging, suggesting that extra minerals will lead to net increases in quantities absorbed. Efficacy studies also confirm that intakes of iron-biofortified rice60 and beans61,62 improve iron status, and that all biofortified crops released so far have favourable agronomic qualities, including equal or higher yields than common varieties, and greater disease resistance and drought tolerance. Evidence regarding the effectiveness of biofortification, however, is still confined to vitamin A in orange sweet potato, and the scalability of delivery is yet to be shown.

Social safety nets

Social safety nets are programmes that distribute transfers to low-income households. These programmes raise income among vulnerable groups and enhance resilience by preventing destitution brought about by loss of assets or reduced investment in human capital during times of crises. Transfers can be in the form of cash or food, although with improved technology for tracking income transfers, cash transfers are increasingly the preferred means to support chronically poor households. Between 0·75 and 1·0 billion people in low-income and middle-income countries currently receive cash support.73 Although many transfer programmes reach only a small share of the vulnerable population, some have extensive coverage, such as Ethiopia’s Productive Safety Net Programme, which reaches 10% of the country’s population,74 and transfer programmes in Brazil and Mexico that reach 25%, and in Ecuador 40%, of their populations.75 The generosity of transfers varies widely, ranging from transfers that increase total income marginally to those that boost income by up to a third for the poorest recipients.75

(Continued from previous page)

Value chains also have important limitations. First, they focus on one food at a time, as opposed to the whole diet and the many nutrients required for healthy living. Efforts to integrate nutrition into value chains should therefore focus on complementary value chains to fill the specific dietary and nutrient gaps identified in target populations. Second, the focus on addition of economic value plus incorporation of nutrition goals might create insurmountable trade-offs for value chains actors. Third, although they might be well-suited to enhance access to micronutrient-rich foods for girls and women during the reproductive period, their role for addressing the special needs of young children might be limited to fortified complementary foods or products, and a few target foods such as dairy products and biofortified crops (eg, biofortified orange sweet potatoes).

Case studies40–42 and a review of on-going programmes44 suggest that several research initiatives and value chain actors are currently exploring the potential of value chains to improve nutrition. One such initiative is homegrown school feeding programmes, which use value chains to link agriculture and nutrition, with potential livelihood and income benefits for farmers and nutrition benefits for young children and their families.65,66 Existing efforts to incorporate nutrition in value chains should also consider addressing food safety issues, especially since most of the micronutrient-rich foods of interest are also highly perishable and susceptible to food safety problems. Tackling of food-borne diseases would improve nutrition.

<table>
<thead>
<tr>
<th>Country (year of first release)*</th>
<th>Status of nutrition studies†</th>
<th>Dietary intake and retention</th>
<th>Bio-availability</th>
<th>Efficacy</th>
<th>Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A crops (released)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Iron crops (released)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Bean Rwanda (2012)</td>
<td>✓</td>
<td>✓</td>
<td>Continuing</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Pearl Millet India (2012)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>2013–15</td>
<td></td>
</tr>
<tr>
<td>Zinc crops (under development—to be released in 2013)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Rice Bangladesh and India (2013)</td>
<td>✓</td>
<td>2013</td>
<td>2013–14</td>
<td>2014–16</td>
<td></td>
</tr>
</tbody>
</table>

References are provided in appendix pp 5–6. *Approved for release by National Governments after intensive multi-location testing for agronomic traits and micronutrient performance. †Completed though not necessarily reported.

Table: Release schedule for biofortified crops and status of related nutrition studies
The main goal of social transfers is to augment income, but programmes sometimes include additional interventions or conditions that can enhance their nutrition sensitivity such as: linking of transfers to health and nutrition services (eg, through conditionality); targeting of households with nutritionally vulnerable members, on the basis of age or physiological status; inclusion of nutrition-specific interventions for selected individuals within the household (eg, nutrition behaviour-change communications or distribution of fortified foods or supplements); administration of transfers in a sex-sensitive manner (eg, by directing transfers to women or designing them to accommodate time constraints of caregivers); and targeting of populations facing climatic or economic stress related to seasonality or other shocks, or focusing on emergencies.

**Conditional cash transfers**
Conditional cash transfers aim to stimulate households to invest in the health, nutrition, and education of their children (enhancing human capital) by promotion of the use of these services as conditions (conditionality) for receipt of transfer. Most conditional cash transfers target transfers to women, on the premise that increasing women’s control over resources will lead to greater investments in children (appendix p 2). Although conditional cash transfers are implemented worldwide, experimental evidence of effectiveness comes mostly from Latin America. In addition to their positive effects on poverty reduction, household food consumption, and dietary diversity, almost all programmes assessed increased the use of preventive and curative health and nutrition services. The Mexico, Brazil, and Nicaragua programmes also showed improvements in women’s control over additional resources, enhanced self-esteem, heightened knowledge and awareness of health and nutrition, and increased opportunities for women to strengthen their social networks.

Despite the many benefits of conditional cash transfers for households and women, evidence of effects on nutritional outcomes is mixed. A review using pooled estimates shows that, overall, conditional cash transfers have had a small, but not statistically significant, effect on child anthropometry. A forest plot analysis of 15 programmes, combining conditional cash transfers and unconditional cash transfers, shows an average effect of 0.04 in height-for-age Z score, an effect size that is neither statistically significant nor biologically meaningful; similarly, no significant effect was identified for conditional cash transfers only. In view of the heterogeneity of populations and programme designs and methods, meta-analyses might not be the most appropriate approach for assessment of effect, but analyses of individual studies are consistent with the findings. Only a few conditional cash transfer studies show effects on anthropometry, and these effects are shown in the youngest or poorest children, or those exposed to the programme for long durations. Evidence of effects on micronutrient nutrition is equally scant and comes from only a few studies that have looked at these outcomes. The Mexico conditional cash transfer programme, which distributed a micronutrient-fortified food to beneficiary mothers and children, showed a positive effect on child intake of iron, zinc, and vitamin A among those who consumed the product, but only a small effect on mean haemoglobin or anaemia reduction. Two other programmes, in Honduras and Nicaragua, that assessed effect on haemoglobin showed no effect. The Mexico programme showed reductions in low birthweight attributed to changes in women’s empowerment, which in turn were attributed to women’s increased demand for better quality prenatal care as a result of participation in the programme. Evidence is also emerging of small effects of conditional cash transfers on child development outcomes.

**School feeding programmes**
School feeding programmes are a type of conditional transfer, albeit in kind. Similar to other transfers, they are mainly a form of social assistance for consumption. The links to nutrition are less direct than transfers targeted to mothers and children during the first 1000 days, but school feeding can reduce hunger and stimulate learning. These programmes, however, are implemented in nearly every country in the world. Results from a meta-analysis show that school feeding programmes have small effects on school-age children’s anthropometry, particularly in low-income settings. Major effects on height are not expected in school-age children and weight gains can be either positive (in underweight populations) or negative (when risks of obesity are high). In middle-income countries, school meals might also serve as an opportunity to combat obesity; Brazil and Chile have redesigned their programmes with this risk in mind.

School meals might also benefit other members of the household when the food provided is shared or when the school-aged child’s intake at home is reduced. Randomised controlled trials in Burkina Faso and Uganda showed effects on weight among preschool-aged boys (ie, <5 years) whose siblings received school meals or take-home rations compared with a control group (Gilligan D, International Food Policy Research Institute, personal communication). Another opportunity offered by school feeding programmes is to affect iron nutrition, especially for adolescent girls. A review of randomised evaluations of iron-rich school meals (fortified or providing animal-source foods) documents that three of four studies improved iron status, irrespective of initial status. The addition of a micronutrient mix to school meals in India improved total body iron, but not anaemia, possibly because of worm loads. Deworming can, however, be included as part of a larger school health programme, although the timing of
delivery differs from the daily meal programme. Since school-aged children are the main reservoir of worm loads in a population, such an intervention could benefit younger children as well.

**Unconditional transfers**
Unconditional transfers, either as cash or in kind, have also been popular, particularly outside of Latin America. Households commonly spend more on food and health with cash transfers—even when they are only indirectly linked to nutrition and health—than they spend out of other increases in income.\(^5\)\(^6\) Moreover, some unconditional cash transfers use so-called soft conditions in the form of broadly targeted behaviour-change communications or social marketing to encourage health-seeking behaviour. In Africa, soft conditions or unconditional cash transfers are more common than conditional cash transfers.\(^8\) One randomised trial showed that a conditional cash transfer with health conditionality increased clinic visits in Burkina Faso, whereas an unconditional cash transfer did not,\(^9\) showing the importance of the condition for achieving health-seeking behaviour changes in this setting. Evidence, however, shows an absence of overall effect of both unconditional cash transfers and conditional cash transfers on child nutritional status.\(^7\) Costs will differ between the two approaches as will the distribution of benefits for different outcomes; as such, no method dominates in all situations.

**In-kind household food distributions**
In-kind household food distributions are currently less prominent than they were in previous decades, mostly because of cost considerations. They are now largely used as part of an emergency response or in places where the logistics of cash transfers are constrained. Evidence from Mexico suggests that in-kind food transfer programmes might have unintended effects on overweight and obesity when the energy contribution of the food basket exceeds the energy gap in the targeted population (panel 5,\(^9\)\(^9\)\(^9\)\(^9\)\(^9\)\(^9\) figure 3). In addition to general family rations, food distribution programmes often provide micronutrient-fortified foods (eg, corn-soy or wheat-soy blend) to pregnant and lactating women and their young child with family rations or cash. Disasters, particularly sudden onset emergencies such as earthquakes and hurricanes, often disrupt normal market channels, which might dampen the logistical advantages of cash compared with food transfers. Although food aid deliveries overall declined from 15 million metric tonnes (t) in 1999 to 4-1 million t in 2011, emergency deliveries have remained almost constant; they now account for more than 67% of total food aid.\(^7\) Even when targeted towards overall household subsistence, aid during disasters can prevent major deteriorations in child undernutrition.\(^9\)\(^9\)\(^9\) Age-based targeting of fortified foods can help prevent undernutrition and complement efforts to tackle cases of severe acute malnutrition with specially formulated products. The nutritional effects of emergency deliveries can be

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**Panel 5: Unintended, negative effects of in-kind and cash transfers in Mexico**
Social safety nets can reduce poverty and increase use of health and education services.\(^7\) Depending on their target populations, however, these interventions can have unintended negative consequences. The effects of Mexico’s Programa de Apoyo Alimentario (PAL; Food Support Programme) on excess weight gain in women is one such example. PAL is a dual conditional cash and in-kind transfer programme targeted to poor and remote communities in rural Mexico. An assessment of PAL\(^9\) showed improved household dietary quality, but also increases in total energy consumption in a population that was not energy-deficient and had a high prevalence of overweight and obesity among women at baseline (65%). PAL also increased the already steep annual weight gain in adult women in the control group (425 g, SD 80) by 291 g (111) per year in the food basket group (a 68% increase) and by 222 g (122) per year in the cash group (a 52% increase). The most substantial effect was recorded in adult women who were already obese before the programme started (518g [153] per year in the food basket group and 354 [169] per year in the food basket group; figure 3).\(^7\) The PAL programme’s food basket included several energy-dense staple and basic food products including oil, cookies, and whole milk, and provided an additional 450 kcal per day per adult. To avoid negative effects on populations experiencing the double burden of child stunting and adult obesity, transfer programmes should be designed to respond to the identified needs of target populations, and for food transfers, their specific nutrient gaps.

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**Figure 3:** Estimated effect of Mexico’s Programa de Apoyo Alimentario programme on annual weight gain in women, by initial BMI
BMI=body-mass index. *p<0.05. †p<0.01.
Early child development

Stunting and impaired cognitive development share several of the same risk factors, including deficiencies in protein, energy, and some micronutrients, intrauterine growth retardation, and social and economic conditions, such as maternal depression and poverty.\(^{20}\) Some of the key phases of brain growth and development also encompass the first 1000 days of life, the period of peak susceptibility to nutritional insults. Therefore, some key interventions can protect children from both nutritional and developmental risks; these include core maternal and child nutrition interventions, psychosocial stimulation and responsive parenting, and interventions to alleviate poverty, food insecurity, maternal depression, and gender inequity.\(^{21}\)

Evidence of the effect of early child development interventions, with or without a nutrition component, on child development outcomes has been extensively reviewed in two previous series in The Lancet.\(^{22,23}\) We focus on evidence of how child stimulation and nutrition interventions can have complementary effects on nutrition outcomes (appendix pp 7–9). The most comprehensive, long-term study\(^{20}\) of interventions that provided both child stimulation and food supplementation to stunted children aged 9–24 months in Jamaica showed an additive effect of the two interventions on cognitive development, but not on growth. At adolescence, the additive effects on cognition were not sustained, but the group having received stimulation had long-term benefits, which ranged from improved development outcomes to educational attainment and social behaviour.\(^{111,112}\) In Bangladesh, addition of stimulation and home visits to standard nutrition and health care for severely malnourished children improved development outcomes and weight-for-age Z score (WAZ).\(^{113}\) Another trial in Bangladesh, which added responsive parenting (including feeding) to an informal nutrition and child development education programme, showed benefits on several feeding and parenting behaviours, child self-feeding, and development outcomes; addition of iron-fortified micronutrient powders to the intervention improved weight gain and WAZ but had no additional effect on development outcomes.\(^{114}\) A zinc supplementation and responsive stimulation intervention in underweight children in Jamaica showed synergistic effects on child development between the two interventions: greater benefits on development outcomes were identified in the zinc and stimulation group, compared with little or no effect in the groups receiving either.\(^{115}\) This synergistic effect, however, was not noted for morbidity (reduced only in zinc group) or growth (no effect in either group). A randomised controlled trial of cash transfers to households linked to preschool enrolment in Uganda provides an example of joint benefits on cognition and nutrition; findings showed significant effects of cash transfers on child cognitive development, which were mediated by increased preschool participation, improved diets, and reduced anaemia (Gilligan D, Roy S, International Food Policy Research Institute, personal communication).

Other trials—in India, Pakistan, and Bangladesh\(^{116–118}\)—although successful at improving child development or nutrition outcomes, or both, failed to show additive or synergistic effects between nutrition and stimulation interventions. In India,\(^{116}\) beneficiaries of the Integrated Child Development Services (ICDS) programme were allocated to groups receiving breastfeeding and complementary feeding counselling, or this package plus responsive feeding and psychosocial stimulation skills. Compared with ICDS only, both intervention packages improved child dietary intake and haemoglobin and reduced morbidity, but only the nutrition intervention increased length gain, and only the full package including stimulation benefited development outcomes.\(^{116}\) A factorial design trial in Pakistan\(^{117}\) showed no evidence of additive or synergistic effects of a nutrition (counselling and micronutrient powders) and stimulation intervention (monthly group meetings and home visits for children aged 0–24 months) on child development or nutrition outcomes. Preliminary results show effects of all three intervention packages on developmental scores compared with control, with larger effect sizes among the two stimulation groups. In Bangladesh,\(^{118}\) psychosocial stimulation with or without food supplements among severely underweight children aged 6–24 months on discharge from hospital had an effect on mental development and a small effect on WAZ, but no additive or synergistic effects were noted between the two interventions. One intervention that closely ties feeding practices with child stimulation is responsive feeding. Few studies of this approach, however, have been designed to distinguish messaging on complementary feeding from those on psychosocial care\(^{119}\) and few so far have shown a clear association with nutritional outcomes.\(^{119}\)

Reduction of maternal depression is another way to address risk factors common to both nutrition and child development.\(^{120,121}\) Efforts are being made to link basic health services with a wide range of social support for women. Efficacy trials\(^{122,123}\) show that the benefits might accrue to both mothers and their newborn babies, justifying ongoing efforts to bring these initiatives to scale.

Schooling

Although children are beyond the crucial 1000 days window when they enter school, their schooling experience might be a strong determinant of the nutrition of the next generation. Parental schooling has been consistently associated with child nutritional status, with maternal education often, but not always, having a larger explanatory power than paternal education, controlling for income and schooling choices.\(^{124,125}\) The positive global trends in schooling are, therefore, encouraging for
nutrition. Data from developing countries show an average increase in years of schooling from 2·60 to 7·62 for boys and from 1·50 to 6·64 for girls between 1950 and 2010. The girl to boy ratio shows a substantial improvement over this period, from 37·7% to 83·9%. Enrolment data show parity in girls’ primary schooling in most countries,122 moreover, in many countries more girls than boys are now in secondary school. Still, only about a fifth of adolescent girls in sub-Saharan Africa and two fifths of girls in south Asia are enrolled in secondary education.128

We assessed the level of parental education necessary for a meaningful reduction in child undernutrition by analysing 19 datasets from the Demographic and Health Survey (collected since 1999) and derived estimates of the risk of child stunting associated with maternal and paternal primary and secondary education, controlling for household wealth, rural versus urban residence, and child age and sex. The analysis showed that the risk of stunting is significantly lower among mothers with at least some primary schooling (odds ratio [OR] 0·89, 95% CI 0·85–0·93), and even lower (p<0·001) among mothers with some secondary schooling (0·75, 0·71–0·79). Paternal education at both the primary and secondary levels also reduced the risk of stunting although the respective ORs (0·96, 0·93–1·01; and 0·85, 0·81–0·89) are smaller than for maternal schooling. Despite this overall association, there is appreciable heterogeneity in effect sizes for both maternal and paternal education in individual countries, probably indicative of differences in both quality of education and quality of data.

Schooling directly increases individual earnings and national income and, through these pathways, can affect nutrition in the long term. Thus, programmes to increase schooling via the supply of inputs or through fee waivers or cash transfers can be expected to reduce the risk of undernutrition for the next generation. There is a lack of clarity, however, about which aspects of schooling, beyond the income effect, benefit nutrition. At least five overlapping pathways have been suggested, but not formally tested. Schooling might: 1) transmit information about health and nutrition directly; 2) teach numeracy and literacy, thereby assisting caregivers in acquiring information and possibly nutrition knowledge; 3) expose individuals to new environments, making them receptive to modern medicine; 4) impart self-confidence, which enhances women’s roles in decision making, and their interactions with health-care professionals; and 5) provide women with the opportunity to form social networks, which can be of particular importance in isolated rural areas. The question remains as to whether schooling could do even more to directly affect nutrition, both in the short term for school children and in the long term as they transition into their parental role. Although nutrition modules are available in some school health education programmes,111,112 assessments of the effect of a school health and nutrition curriculum in developing countries on undernutrition or health knowledge, let alone on parenting skills decades later, are absent.

Schools are also suitable venues to introduce programmes to combat obesity. Such programmes can focus on healthy diets and promotion of physical activity. A systematic review123 of 22 studies in low-income and middle-income countries noted that 82% of such programmes had a favourable effect on physical activity, diet, or both.

**Discussion**

In 2008, *The Lancet* Maternal and Child Undernutrition Series included conditional cash transfer programmes and dietary diversification approaches as “general nutrition support strategies”, and noted small positive effects of conditional cash transfers on child anthropometry in three Latin American countries, and an absence of a statistically significant effect of dietary diversification strategies on child nutrition outcomes.124

In the present series, we discuss evidence regarding the nutritional contribution of programmes in four sectors and the potential for enhancing their nutrition-sensitivity. Although the concept of nutrition sensitivity is not new, investments in development and implementation of nutrition-sensitive programmes have intensified in the past few years, prompted by the 2008 series, and spearheaded by the Scaling Up Nutrition movement.9 It is important to recognise, when interpreting the results of our review, that most of the programmes included were retrofitted and tagged as nutrition sensitive without having been originally designed as such.

Targeted agricultural programmes have an important role in supporting livelihoods, improving household food security and healthy diets, and in fostering women’s empowerment. Yet, our review shows inconclusive evidence of effects on child nutritional status, with the possible exception of benefits on vitamin A intake and, to a lesser extent, vitamin A status. These findings are probably the result of a combination of factors, including: weaknesses in programme design and implementation (especially the nutrition, behaviour-change communication, and health components);135 inclusion of households with children outside of the 1000 days window with little potential to benefit in linear growth; and the fact that other pressing constraints to nutrition—such as infectious diseases, helminths, and environmental enteropathy associated with scarcity of access to appropriate water, sanitation, and hygiene—might not be addressed by the programmes. Additionally, the assessments of most of the programmes we reviewed had crucial weaknesses such as an absence of valid comparison and control groups, a possibly too-short duration of intervention, small sample sizes, the inclusion of the wrong age group in effectiveness assessments, and the failure to control for potential confounding factors in the analysis. All these assessment
Panel 6: Research priorities

- Rigorous, theory-based effectiveness and cost-effectiveness assessments of complex and large-scale nutrition-sensitive programmes. These assessments should include:
  - Use of experimental randomised controlled trials, where feasible, to test different methods of delivery and joint packages of interventions.
  - Careful assessment of programme impact pathways and quality of service delivery, use of process evaluation instruments and mixed methods, including assessment of the capacity and efficiency of front-line health workers.
  - Measurement of gender-disaggregated impact indicators; these indicators should be carefully selected on the basis of nutrition goals and interventions included in programmes and could include: anthropometry, micronutrient status biomarkers, child development outcomes, child morbidity.
  - Measurement of intermediary outcomes along the impact pathway (e.g., household consumption; food security and dietary diversity; dimensions of women’s empowerment, maternal physical, and mental health; detailed dietary intake or simpler measures such as dietary diversity for target individuals).
  - Detailed costing for assessment of cost-effectiveness.
  - Development of methods to allow comparison of the social benefits of complex programmes with many objectives and joint outcomes, with the benefits of single-outcome programmes.
  - Formative research and focused ethnographic studies to guide selection, design, and implementation of nutrition interventions to be integrated in nutrition-sensitive programmes, and for overall design of nutrition-sensitive programmes.
  - Qualitative research to understand barriers to participation, adoption, and use of programme inputs and services (e.g., agricultural inputs, compliance with conditions in conditional transfers, recommended feeding or caregiving practices).
  - Research to rigorously test the feasibility and desirability of integration of interventions from several sectors versus co-location. Such research would establish whether programme implementers should develop new instruments and methods for joint planning, implementation, monitoring, and assessment, or whether investments should focus on effective programme co-location and implementation.
  - Research to test and document the scalability of newly released biofortified crops.
  - Assessment of effectiveness large-scale programmes combining early child development and nutrition interventions in different contexts and assessment of synergies both in programming and outcomes.
  - Research to test different delivery platforms for programmes to reduce maternal depression.
  - Research to test different delivery systems for reaching adolescent girls (e.g., school programmes, social safety nets with conditions to keep girls in school, agricultural programmes targeting adolescent girls at home).
  - Assessments of school nutrition programmes and their short-term effect on knowledge of school children and long-term effect on parenting skills.

Estimating the magnitude of effect that could be achieved in poorer settings. Additionally, some aspects of programme design or implementation might have diluted their nutritional effect, including poor timing and short duration of maternal and child exposure, absence of clear nutrition goals, and poor selection or implementation of nutrition interventions in some programmes. Also, the gap between increased use of health and nutrition services and nutrition benefits has been attributed, at least partly, to the poor quality of services provided. Conditional cash transfers are designed to increase health awareness and service demand, but ultimately their nutritional effect rests on the quality of public health services.

Our review of early child development interventions provides little evidence that stimulation alone has a direct effect on nutrition outcomes, but it suggests that combined early child development and nutrition interventions can have additive or synergistic effects on development outcomes, and in some cases on nutrition. The examples of successful joint delivery of these services point to an area in which programmatic synergies, cost savings, and potential benefits for both child development and nutrition might be identified.

Girls’ schooling is increasing in many countries, largely as a result of government interventions to change incentives and reduce barriers to girls’ enrolment and participation. Increases in parental schooling have contributed to reductions in stunting, but larger effects could probably be achieved if effective nutrition education programmes were incorporated into school curricula.
Our review shows the potential of programmes in the four sectors reviewed to improve the lives of poor households and individuals, both in the short-term and the long-term. It also shows, however, that more needs to be done to increase the nutrition sensitivity of programmes so that their potential to deliver on maternal and child nutrition outcomes is unleashed. The nutrition sensitivity of promising programmes can be enhanced in several ways. First, targeting on the basis of nutritional vulnerability (eg, age, physiological status) in addition to geographic targeting on the basis of poverty, food insecurity, or location can help reach households and individuals most likely to benefit from the programme. Alternatively, targeting of nutritionally vulnerable individuals could be used as a second level of targeting for subgroups of programme beneficiaries who meet pre-established criteria. For example, targeting agricultural programmes to households with pregnant or lactating women or children younger than 2 years might be neither logistically feasible nor optimum for community development; however, geographic community-level targeting could be used as a first targeting criteria, with a second level focusing on reaching mothers and young children with a specific package of preventive nutrition and health interventions. Another key target group for nutrition-sensitive programmes is adolescent girls; conditions or other incentives can be used to keep girls in school, help delay first pregnancy, address HIV risk factors, and improve adolescent girls’ nutrition knowledge and micronutrient status to prepare them for motherhood.

Second, evidence shows that nutrition improvements are not automatic even with programmes that are successful at reducing poverty, food insecurity, and sex inequalities. To reach their full potential, programmes such as those reviewed need careful identification of nutrition goals and appropriate design and effective implementation of interventions to achieve them. A third way to enhance the nutrition sensitivity of programmes is to engage women and include interventions to protect and promote their nutritional wellbeing, physical and mental health, social status, decision making, and their overall empowerment and ability to manage their time, resources, and assets. A fourth promising, yet underused approach to enhance the nutrition sensitivity of programmes is to use them as delivery platforms for various nutrition-specific interventions. Nutrition behaviour-change communications, which are incorporated in several agriculture, social safety nets, early child development, and school health programmes are one example of such use. Other opportunities include addition of the distribution of micronutrient-fortified products to nutritionally vulnerable adolescent girls, mothers, and young children, or of preventive health inputs to agriculture, social safety net, early child development, or school programmes.

Finally, a crucial question that remains to be addressed when designing nutrition-sensitive programmes is the degree to which programmes should indeed integrate actions from several sectors, or co-locate programmes managed by different sectors so that they reach and saturate the same communities, households, and individuals. In view of the complexity of integration, especially across many sectors, it is important to carefully assess whether investments should focus on joint planning, implementation, monitoring, and assessment, or on effective programme co-location (panel 6).

Conclusions
Nutrition-sensitive programmes hold great promise for supporting nutrition improvements and boosting the scale, coverage, and benefits of nutrition-specific actions. New incentives are needed to support innovations in nutrition-sensitive programmes and unleash their potential to tackle nutrition while also achieving their own goals. New nutrition-sensitive agriculture and social safety net programme designs, methods, and packages of interventions are being tested and are strengthening links with health services. Rigorous impact evaluations, many of which are based on strong programme-theory and impact pathway analysis, are addressing key weaknesses encountered in previous evaluations and are assessing impacts on a range of nutrition and child development outcomes and several household and gender outcomes along the impact pathway. Evidence generated by these enhanced programmes and assessments in the next 5–10 years will be of crucial importance to inform future investments in agriculture and social safety net programmes to improve nutrition.

The potential benefits of integration of early child development and nutrition programming include cost savings and gains in both child development and nutrition outcomes. Leveraging health, agriculture, or social safety net platforms for joint early child development and nutrition programming during the first 1000 days of life would help focus on the crucial period of peak vulnerability for both nutrition and development. Current work is exploring such approaches. Benefits from psychosocial interventions on cognition, however, extend well beyond the first 2 years, and therefore, continued child development support is required throughout the entire preschool period. Early child development programmes, possibly linked to conditions in transfer programmes or delivered through preschool or community settings, could offer psychosocial stimulation and parenting interventions, while also providing relevant nutrition interventions for children 2 years and older, focusing on micronutrients, healthy diets, and obesity prevention. With improved guidance and curricula for nutrition education in schools, a new emphasis on using schools to improve nutrition knowledge and practices and preparing school children for their future parenting roles should also emerge.

The immense potential of programmes addressing the underlying determinants of undernutrition to complement and enhance the effectiveness of nutrition-specific interventions is real, but is yet to be unleashed.
Investments in nutrition-sensitive programmes can have a pivotal role in prevention of the excess stunting, wasting, and impaired child development that the scale-up of nutrition-specific interventions cannot resolve on its own.

Contributors
MTR and HA conceptualised the report, reviewed the literature, and wrote the all drafts of the report.

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Other contributors
Derek Headly, research fellow at IFPRI, did the analysis and prepared the panel on the relation between income and nutrition. Joe Green, independent consultant, did the analysis of the literature on women’s empowerment, provided background text, and wrote the panel on women’s empowerment and nutrition. Jef Leroy, senior research fellow at IFPRI, reviewed the literature on women’s empowerment, provided background text, and wrote the panel on women’s empowerment and nutrition. Jef Leroy, senior research fellow at IFPRI, did the analysis and wrote the panel on the cash transfer programme in Mexico. Erick Boy, senior research fellow at IFPRI, provided background text and other material for the section on biofortification. Svahn Yosef, programme manager at IFPRI, provided research and editing assistance during all steps of the process.

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. All other authors declare that they have no conflicts of interest. As corresponding author, Marie Ruel states that she has full access to all data and final responsibility for the decision to submit for publication.

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In the past 5 years, political discourse about the challenge of undernutrition has increased substantially at national and international levels and has led to stated commitments from many national governments, international organisations, and donors. The Scaling Up Nutrition movement has both driven, and been driven by, this developing momentum. Harmonisation has increased among stakeholders, with regard to their understanding of the main causes of malnutrition and to the various options for addressing it. The main challenges are to enhance and expand the quality and coverage of nutrition-specific interventions, to maximise the nutrition sensitivity of more distal interventions, such as agriculture, social protection, and water and sanitation. But a crucial third level of action exists, which relates to the environments and processes that underpin and shape political and policy processes. We focus on this neglected level. We address several fundamental questions: how can enabling environments and processes be cultivated, sustained, and ultimately translated into results on the ground? How has high-level political momentum been generated? What needs to happen to turn this momentum into results? How can we ensure that high-quality, well-resourced interventions for nutrition are available to those who need them, and that agriculture, social protection, and water and sanitation systems and programmes are proactively reoriented to support nutrition goals? We use a six-cell framework to discuss the ways in which three domains (knowledge and evidence, politics and governance, and capacity and resources) are pivotal to create and sustain political momentum, and to translate momentum into results in high-burden countries.

**Key messages**

- Emerging country experiences show that rates of undernutrition reduction can be accelerated with deliberate action.
- Politicians and policy makers who want to promote broad-based growth and prevent human suffering should prioritise investment in scale-up of nutrition-specific interventions, and should maximise the nutrition sensitivity of national development processes.
- Findings from studies of nutrition governance and policy processes broadly concur on three factors that shape enabling environments: knowledge and evidence, politics and governance, and capacity and resources.
- Framing of undernutrition reduction as an apolitical issue is short sighted and self-defeating. Political calculations are at the basis of effective coordination between sectors, national and subnational levels, private sector engagement, resource mobilisation, and state accountability to its citizens.
- Political commitment can be developed in a short time, but commitment must not be squandered—conversion to results needs a different set of strategies and skills.
- Leadership for nutrition, at all levels, and from various perspectives, is fundamentally important for creating and sustaining momentum and for conversion of that momentum into results on the ground.
- Acceleration and sustaining of progress in nutrition will not be possible without national and global support to a long-term process of strengthening systemic and organisational capacities.
- The private sector has substantial potential to contribute to improvements in nutrition, but efforts to realise this have to date been hindered by a scarcity of credible evidence and trust. Both these issues need substantial attention if the positive potential is to be realised.
- Operational research of delivery, implementation, and scale-up of interventions, and contextual analyses about how to shape and sustain enabling environments, is essential as the focus shifts toward action.

**Introduction**

The nutrition landscape has shifted fundamentally since the first *Lancet* Series on Maternal and Child Undernutrition was published in January, 2008. Since then, almost every major development agency has published a policy document about undernutrition. In a very difficult fiscal climate, official development assistance to the basic nutrition category has increased from US$529 million in 2008, to $418 million in 2011—a rise of more than 60% (although it was $541 million in 2009). Furthermore, the G8 countries reported increases of almost 50% in bilateral spending on nutrition-specific and nutrition-sensitive interventions between 2009 and 2011. According to Google Trends, “malnutrition”, now matches “HIV/AIDS” in terms of internet interest, whereas 5 years ago, HIV/AIDS received twice as much interest as malnutrition. This shift is attributable to several factors: the food price spikes of 2007–08 sparked renewed media and policy interest in undernutrition, The *Lancet* 2008 Series provided policy makers with a set of tangible interventions that were effective in various locations, and the 2008 Copenhagen Consensus concluded that nutrition interventions were among the most cost effective in development. The Scaling Up Nutrition (SUN) movement, which started in September 2010, is the most important symbol of the increased interest in nutrition. By the middle of May, 2013, the movement had grown to include 35 countries that are committed to the scale-up of direct nutrition interventions and the advancement of nutrition-sensitive development, including 21 of the...
34 highest burden countries where 41% of the global burden of child stunting is located (or 56% if India is omitted). As SUN nears its 1000th day, several countries have made advances in terms of building multistakeholder platforms, aligning nutrition-relevant programmes within a common results framework, and mobilising national resources, but it is too soon to evaluate the effect of SUN on rates of undernutrition reduction.

As interest in nutrition has changed, so too has our thinking. The large economic returns to nutrition-specific interventions (paper two in this Series), are clear and we recognise the potential of nutrition-sensitive interventions (paper three) and the importance of an enabling environment for reduction of undernutrition—the focus of this report. Most of the concepts and ideas that we develop about enabling environments apply to both undernutrition and the growing problems of overweight and obesity as documented in the first paper in this Series. We focus mainly on undernutrition because as the 2010 Global Burden of Disease estimates show, undernutrition remains the number one risk factor in sub-Saharan Africa, and the fourth in south Asia. We use evidence generated within academic and scientific institutions and that generated in more real-world, action oriented, transdisciplinary ways that embed nutrition within wider social and political contexts.

We used this mixture of evidence types partly because of the paucity of the first type of evidence and partly in recognition that the second type is often more appropriate because it is more practical, politically feasible, and therefore actionable. However, the second type of evidence is not as easy to independently verify or systematise with standard systematic review protocols.

Beyond the nutrition-sensitive programmes and interventions discussed in paper three, other macro-level drivers exist that lie at the end of long causal pathways. Seemingly quite remote from the nutritional wellbeing of children, many such drivers are nonetheless crucially important to shape both national and global political landscapes for nutrition, and basic-level determinants of nutrition status. These aspects are particularly important because each of the various determinants of nutritional outcomes can be vulnerable to sudden changes within, or caused by, these drivers. Examples include climate change, trade, the rate and pattern of economic growth, food and energy prices and volatility, and land-use policies. Previous empirical work at the country level has shown that household income growth is a necessary, but not sufficient driver, of nutrition status. In a cross-country study of the drivers of nutritional change over time, four factors emerged as the most robust predictors of reductions in undernutrition worldwide: secondary education for girls, reductions in fertility, accumulation of household assets, and increased access to health services. In view of the scarce evidence for these drivers we do not discuss the related scientific literature. Rather, we reiterate that through the approaches for shaping enabling environments for nutrition, described here, we might be better able to advocate for attention to nutrition within these broad development debates.

Characterisation of enabling environments
What does an enabling environment for undernutrition reduction look like? In recognition of the general consensus that income growth is necessary but not sufficient for undernutrition reduction, we undertook a systematic review of the nutrition-relevant policy process and governance literature (panel 1). After a surge of activity in the late 1970s to early 1980s, a two decade gap ensued in research of nutrition policy processes, punctuated by one book in 1993, until interest re-emerged in 2003. In the past decade, several multicity and single-country studies of such processes have been undertaken, in which conceptual and analytical frameworks have been applied. These studies sought to uncover key structures, pathways, and dynamics of policy processes for nutrition, with an emphasis on challenges and constraints. In doing so, research from other specialties (eg, political science and health systems) was drawn on to adopt and adapt analytical frameworks and research methods to study nutrition policy.

We define an enabling environment as political and policy processes that build and sustain momentum for the effective implementation of actions that reduce undernutrition. Rather than wait for political will to emerge by chance, our review clearly shows that a political momentum can be developed and sustained.
Panel 2: Framework for creation of an enabling environment for accelerated undernutrition reduction

Framing, generation, and communication of knowledge and evidence

Issues and challenges to creation and sustaining of momentum
- Framing and narratives
- Evidence of outcomes and benefits
- What works and how well do nutrition interventions work relative to others?
- Advocacy to increase priority (civil society)
- Evidence of coverage, scale, and quality

Issues and challenges to conversion of momentum into results
- Implementation research (what works, why, and how?)
- Programme evaluation (impact pathways)
- Generation of demand for evidence of effectiveness

Political economy of stakeholders, ideas, and interests

Issues and challenges to creation and sustaining of momentum
- Incentivising and delivering of horizontal coherence (multisectoral coordination)
- Development of accountability to citizens
- Enabling and incentivising of positive contributions from the private sector

Issues and challenges to conversion of momentum into results
- Delivery of vertical coherence
- The role of civil society and the private sector in delivery

Capacity (individual, organisational, systemic) and financial resources

Issues and challenges to creation and sustaining of momentum
- Leadership and championing
- Systemic and strategic capacity
- Making the case for additional resource mobilisation

Issues and challenges to conversion of momentum into results
- Delivery and operational capacity
- New forms of resource mobilisation
- Prioritisation and sequencing of nutrition action
- Implementation and scale-up

Creation and sustaining of momentum

Narratives, knowledge, and evidence

The 2008 Lancet Nutrition Series showed how effective marshalling of evidence can create momentum by identifying a set of interventions that were effective at reducing undernutrition in various contexts, identifying a window of opportunity—1000 days—as a focal point, and imparting a sense of priority and feasibility by showing how undernutrition is concentrated in a small set of high-burden countries. The 2008 Series also emphasised the fragmented nature of the international nutrition community with regard to messaging, priorities, and funding, and contributed to birth of the SUN movement (panel 3). Undernutrition has unique features that guide the kinds of knowledge and evidence needed for progress (panel 2).

The importance of framing

Reduction of undernutrition is a multisectoral activity, thus choices exist for how it is framed. In Guatemala and Bolivia, framing has been focused on hunger elimination, strongly determined by Brazil’s own Zero Hunger campaign. In Peru, civil society developed undernutrition reduction as an electoral issue.
Panel 3: Main points from an online electronic consultation among stakeholders from six Scaling Up Nutrition (SUN) countries

SUN represents an unprecedented opportunity for coordination, collaboration, cross learning, and advocacy to catalyse sustainable nutrition gains at national and global levels. Membership implies a national commitment to address undernutrition. SUN’s own monitoring system is centred on four key indicators (appendix). However, to track and compare progress between so many countries, monitoring systems will tend to default to quantitative data of what does or does not exist. Quality and process is not so easily measured. For this reason, and to help us to uncover local perceptions about key issues, challenges, and constraints related to translation of SUN ambitions on the ground, online discussions—organised by the Institute of Development Studies and the International Food Policy Research Institute—were undertaken (appendix). 75 key stakeholders from different sectors in Bangladesh, Nepal, Indonesia, Ethiopia, Nigeria, and Kenya were actively involved over the 8 days of consultation, from Nov 27, 2012, to Dec 4, 2012.

In brief, perceived expectations of joining SUN are that it provides a framework and platform for improved coordination and cooperation in nutrition. SUN encourages advocacy, which has increased the number of stakeholders across sectors who are working to address undernutrition. In turn, this increase is hoped to increase leveraging of resources, knowledge sharing, and institutional capacity. The SUN movement is also considered to hold stakeholders (especially the government) accountable, and secure further commitment to improve resource mobilisation and allocation. Areas of perceived progress include increased awareness and advocacy across sectors. Ambassadors and champions for nutrition at various levels, from the prime minister to the community, have pushed nutrition onto the agenda. Policy makers are increasingly aware of nutrition as a development issue, and some countries have increased nutrition-relevant budgets.

The main perceived challenges and constraints to SUN within countries include little coordination and collaboration between (and within) different ministries, related scarcity of clarity and consensus vision on what scaling up means, undefined roles and responsibilities, and few or ineffective policies and political commitment. Decentralisation of SUN is a major challenge in some countries. Translation of SUN from national to community levels is restricted. The issue of weak capacity (all types and at all levels) was raised several times with particular challenges, including inadequately qualified personnel (eg, doctors and nurses) and community and extension workers (eg, front-line workers and health volunteers) in remote areas, and high employee turnover. Financial resources are often unsustainable and unpredictable with funding for nutrition interventions largely donor driven. Funding for scale-up is insufficient and issues exist about budgetary allocation (emphasis on treatment over prevention) and coordination. Poor quality of monitoring and evaluation data affects assessment of the effect of interventions, weakens advocacy strategies, and jeopardises funding. Finally, views about engagement with the private sector were mixed and suspicion around motivations was reported. Private sector involvement needs close regulation and a framework within which to engage.

(appendix). In India, nutrition has risen on the agenda through a combination of advocacy around the finding that economic growth has not generated nutritional benefits, a strong rights-based movement led by the Right to Food initiative, and a growing stakeholder consensus of the need for multisectoral action. In Ghana, which has achieved the fastest decline in child stunting in sub-Saharan Africa in the past 5 years (from 35% in 2003, to 28% in 2008, a rate of 1.5 percentage points per year), the agenda was one of investment in agriculture as a driver of economic growth and poverty reduction, together with feeding initiatives for infants and young children, all in the context of a stable political environment.

The multisectoral nature of undernutrition reduction adds some complexity to the implementation of effective programmes. Even breastfeeding promotion, for example, needs action on various fronts: behavioural change from breastfeeding mothers, workplace opportunities to breastfeed, responsible advertising about breast-milk substitutes, and effective legislation to define and monitor unacceptable behaviour or to challenge countervailing narratives. The returns to high-quality impact evaluation in the face of such complexity are likely to be large. The inclusion of nutrition objectives and targets within nutrition-sensitive programmes is thought to be important to leverage resources for nutrition within those programmes; however, this hypothesis needs to be tested.

The timeliness, credibility, and persuasiveness of data

The irreversibility of undernutrition early in life makes quick and effective action crucial. The availability of timely and credible data presented in accessible ways can help governments and other stakeholders to be responsive to changing circumstances, and help civil society organisations to hold them accountable for the effectiveness of their interventions. Data from the Demographic and Health Survey and the Multiple Indicator Cluster Survey are essential for evaluation of national trends, but are only collected every 3–5 years and are less useful for immediate programmatic decision making. Surveillance mechanisms, for tracking of nutrition trends and to inform timely decision making, only exist in a few countries. Advances in health management information systems and the growing availability of new technologies could facilitate the real-time monitoring of nutrition outcomes and programme coverage and quality.
When, where, how, and why these new technologies are practical and will lead to responsive and effective action for nutrition are important research issues."^{36,46}

**Communication of the benefits to improved nutrition**

The benefits of undernutrition reduction are lifelong, and yet their temporal distribution reduces their political appeal. The studies in Guatemala of the long-term benefits of undernutrition prevention"^{6,46} have been extremely influential worldwide, and the Consortium on Health Oriented Research in Transitional Societies (COHORTS) group is starting to yield multicountry evidence about the long-term implications of early childhood nutrition."^{46,46} The challenge is to generate contemporary political payoffs to these nutritionally driven long-term labour-market benefits. The demographic transition that many developing countries are experiencing and debating at the highest policy circles presents an example of one such opportunity to communicate the importance of nutrition in ways that resonate. The so-called demographic dividend"^{6,46} due to the declining ratio of adults of non-working age to those of working age will be greatly enhanced if those of working age can secure market employment. Investments in maternal and early childhood nutrition that build human capital can be framed as one way to secure this dividend.

**Panel 4: Nutrition post-2015**

Despite the negligible presence of nutrition in the Millennium Development Goals (one indicator of one goal), inclusion of the underweight indicator has probably helped donors and development agencies justify increased attention to nutrition. This increased attention needs to be shown more fully in the next set of development goals to maintain the high levels of commitment and to guide action. We recommend the following approach:

1. Find a location for nutrition as an equal partner within a likely goal, such as hunger reduction or poverty or health. This location in a vertical goal will raise the profile of nutrition
2. Make sure that nutrition indicators—nutrition-specific and nutrition-sensitive—are located within an additional number of vertical goals, such as gender equity, education, and employment. All these indicators should be linked across the different goals with the framework developed in paper one of this Series to generate a horizontal nutrition goal
3. Endorse the six global targets for nutrition-specific indicators (including replacing of underweight with stunting) proposed by the World Health Assembly in 2012

Why not advocate for a separate nutrition goal? A stand-alone nutrition goal has many desirable features: it makes ignoring of malnutrition harder and is likely to galvanise stakeholders in the nutrition (and possibly development) community and in the general public. However, extensive reading of the post-2015 scientific literature"^{46} suggests that support for a separate goal is insufficient. Building of support might still be possible, but nutrition lags behind other more high-profile disease burdens; stiff competition might come from other constituencies who think they should have a separate goal (eg, water, sanitation, population); and the case has to be made as to why nutrition would not fit better into closely related goals, such as food or health. There are risks to having a separate nutrition goal: constitutencies of the other goals might find it easier to ignore nutrition, and we know that reductions in malnutrition require their engagement. We judge our recommendation as more feasible politically and if done strategically it could well leverage more resources for nutrition, especially from nutrition-sensitive programmes and interventions.

**Political economy and governance**

The politics of undernutrition reduction have long been neglected. The multitude of involved stakeholders at many levels, the invisibility of undernutrition, and the imbalance of power between governments and multinational organisations, generate little accountability for commitment and delivery, and fuel the political economy of undernutrition reduction.

**Global governance**

National governments, civil society (global and national), international and regional organisations (including UN agencies, development banks, and the African Union), bilateral donors, charitable foundations, international research organisations (eg, the Consultative Group on International Agricultural Research), academia, and private-sector companies all have a role in the global institutional architecture for nutrition. 5 years ago, the stewardship or governance of this system was fragmented and dysfunctional."^{46} Since then, a process to reform UN institutional architecture has started and the SUN movement has emerged (panel 3), engaging more than 100 bodies within these organisations. SUN is governed by a lead group of heads of state and other key stakeholders, but is focused mainly on galvanising national and country-led action (panel 3).

Despite SUN’s substantial convening power, some external and country-level confusion exists about the role of the SUN movement, the UN Standing Committee on Nutrition, and the UN REACH programme (the latter two focus on UN level technical support and governance coordination, respectively). Most individuals recognise the continued value of the UN Standing Committee, but it remains in a fragile position and in need of further internal reform (unpublished). Other important global initiatives include the multinational 1000 days partnership, the partnership of G8 countries, and the New Alliance for Food Security and Nutrition (consisting of several African countries and private companies). Meanwhile, the UN Secretary-General’s High Level Task Force on the Global Food Security Crisis and a revitalised Committee on Food Security have emerged as important bodies, coordinating UN and global responses to food insecurity and complementing the role of existing UN food and agriculture bodies. The World Health Assembly’s agreement on six new global undernutrition targets to be achieved by 2025 has also become an important part of the global nutrition focus; however, questions remain about the achievability of these targets"^{46} and their incorporation within the framework of the Millennium Development Goals (panel 4).

The true potential of the SUN movement will be realised through its application in each SUN country. Success of the movement will need maintenance of support and consensus amongst all SUN stakeholders, and development of a strong sense of country-level ownership, the absence of which was a major reason for
the failure of the multisectoral nutrition planning experiments of the 1970s. As SUN’s global scope increases, so will demands for effective information and knowledge management. Presentation of results that correlate SUN activities with measurable reductions in nutrition indicators will become a key focus.

The need for horizontal coordination

Different agencies, each with different and frequently competing agendas, need to work together if undernutrition is to be reduced. Associations are horizontal (at the same level of government) and vertical (at central, state, and district levels) and the potential for conflicting agendas in all directions is substantial. A political analysis of the horizontal and vertical associations in Brazil, Peru, Ethiopia, Zambia, India, and Bangladesh reached several conclusions regarding the roles of the executive branch of government and well-resourced coordination bodies, the importance of narratives that link nutrition with development, and civil society pressure mechanisms. Another study of multisectoral (horizontal) coordination in Senegal and Colombia emphasised the importance of inclusiveness of institutions and stakeholders, incentives, and lateral (as opposed to top-down) leadership. SUN has sought to promote horizontal coherence through establishment of multisectoral platforms to catalyse and enable coherence through establishment of multisectoral platforms. SUN has sought to promote horizontal coherence through establishment of multisectoral platforms to catalyse and enable coherence through establishment of multisectoral platforms.

The need to strengthen accountability

Providers, governments, donors, and the private sector need strong mechanisms to incentivise and hold them accountable for the quality and effectiveness of any nutrition investment. Although the evidence base for nutrition lags behind the positive evidence base for a range of other sectors, investments to increase commitment and accountability for nutrition services and measure their effects could be one of the most rewarding applications of research to macro (commitment) and micro (accountability) levels. Increases in nutrition commitment and accountability could be achieved through trialing and identification of various innovative new methods and mechanisms (figure), including information and communication technology monitoring systems, commitment indices, and social accountability mechanisms. One such method is the PolicyMaker software for analysis of the political economy of nutrition.

Indices of a country’s progress towards particular goals, such as the UN Human Development Index and the International Food Policy Research Institute’s Global Hunger Index, are increasingly common in development and, if methodologically sound, can be a useful focal point for civil society advocacy. The pros and cons of such indices have been evaluated with the conclusion that a separate index that measures political will and commitment to fighting hunger and malnutrition is needed. For governments and donors, the Institute of Development Studies has developed a Nutrition Commitment Index for cross-country and country-specific comparisons over time (panel 5). For food and beverage manufacturers, a new index has been launched by the Global Alliance for Improved Nutrition to evaluate their policies, practices, and performance in contribution to the reduction of undernutrition and overweight and obesity. The potential of mechanisms, such as social audits and community monitoring, to promote accountability and improve the provision of direct public services is clear and has been positively appraised, but has not yet been empirically tested for the provision of frontline nutrition services. Empirical evidence about the effect of such accountability mechanisms on the quality of care and health facilities is weak, but encouraging. A trial of community-based monitoring of health service provision in Uganda showed a 33% reduction in mortality in children younger than 5 years and a significant 0.14 increase in weight-for-age Z score.

Civil society engagement

Most of the roughly 100 organisations who have signed up to the SUN movement are civil society organisations. Their role in combating undernutrition is as multi-faceted and multi-functional as the sector itself, but the effect of citizen engagement is difficult to evaluate. Of the many roles of these organisations, four stand out: (1) global and national advocacy to call attention to nutritional deprivation and galvanise commitment to act, (2) ensuring of accountability for nutrition-relevant service coverage and quality, (3) generation of context-specific knowledge about

Figure: Examples of methods to improve the commitment, accountability, and responsiveness to undernutrition reduction

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Panel 5: The Nutrition Commitment Index

Nutrition outcomes are the result of many factors that governments do and do not have control of. Climate change and associated droughts and floods, and cross-border issues such as arms and drugs trading, mass migration, and capital flight can have enormous effects on nutrition outcomes. Conversely, the commitment to nutrition can be generated and shaped by governments, and should, if informed by evidence, be a positive force for future undernutrition reduction. If commitment can be measured, can it be used to strengthen accountability?

The Nutrition Commitment Index (NCI) is the first attempt to measure government commitment to reducing rates of undernutrition. The index combines secondary data for 12 indicators across three domains (spending, policies, and legislation) at three levels (direct [nutrition-specific] interventions, indirect [nutrition-sensitive] interventions, and the fundamental drivers) to construct an overall index. The 2012 NCI results, in order, Guatemala (most commitment to undernutrition reduction), the Gambia, Nepal, Mozambique, Bangladesh, Malawi, Brazil, Indonesia, Madagascar, Tanzania, Peru, and the Philippines as the top 12 of 45 countries for which recent data are available. India, the country which has a third of the undernutrition burden, is in the bottom half of the 45 countries on commitment to reduce undernutrition. The appendix shows case studies for Peru and Malawi. When the NCI ranks are set against a country’s nutrition outcome indicators, we can see how the index might be used to guide resources. In countries where commitment is low and undernutrition rates are high, some resources need to be allocated towards strengthening of commitment. Where both commitment and undernutrition rates are high, most resources can be allocated to the scale-up of and capacity to deliver nutrition programmes.

Although the countries that do well on the NCI do have high levels of stunting, they have some of the fastest declines in stunting rates over the past 20 years. The top 12 countries show a decline in stunting rates between the 1990s and 2000s that is twice as high as the remaining countries. Additionally, the ranks show that the commitment to hunger reduction and the commitment to malnutrition reduction are only weakly correlated: a commitment to hunger reduction does not automatically equate to a commitment to malnutrition reduction. Future econometric work will rigorously explore the associations between nutrition outcomes and nutrition commitment, with attention on other independent variables, which could explain stunting and the time lags between changes in commitment and changes in stunting. Future qualitative work will focus on whether and how the NCI helps mobilise commitment for undernutrition reduction.

key drivers of undernutrition and relevant remedial options, and (4) implementation of nutrition programmes and provision of delivery platforms to maximise scale-up and ensure equity by reaching the un-reached. Organisations should also be held accountable for their commitment and performance in reducing malnutrition. The table outlines key roles and principles of civil society and private sector engagement in nutrition.

Private sector engagement: maximising potential and managing risks

The scale, know-how, reach, financial resources, and existing involvement of the private sector in actions that determine nutrition status is well known. The share of food and health care purchased through the market is increasing steadily, at all levels of income. This increase has partly taken place because malnutrition exists at all income quintiles and because companies are looking to the base of the pyramid—ie, to the poorest socioeconomic groups—to expand market share if the initial market size is large enough. Private sector involvement in food and health-care choices goes well beyond the large multinational food and pharmaceutical companies. Agri-food businesses, medium-scale and small-scale processors of staple foods, and private health networks now have an active involvement in the production, marketing, and consumer choice in the purchase of food and other nutrition-relevant goods and services. Other developments increase the opportunity for the private sector to contribute to acceleration of malnutrition reduction. For example, new private philanthropic support for development has expanded, logistics and information and computer technology businesses have emerged, and m-health (health services using mobile technologies) initiatives have flourished, with benefits to service delivery and care management. New forms of public–private partnerships have emerged in the health sector from which lessons can be learned about how to identify a balance of interests and incentives among partners. As a result of these many public and private-sector intersections, the interest of the public sector towards business involvement in undernutrition efforts has increased substantially. The SUN Business Network is one indication of this change in interest.

The fourth paper in the 2008 Lancet Series acknowledged the “inextricable” role of the private sector and its importance, but also called for additional evaluation of effectiveness and documentation of best practices. However, although the private sector is now even more important in the national nutrition system, too few independent and rigorous evaluations have been done of the effectiveness of involvement of the commercial sector in nutrition. In the absence of such evaluations, distrust of the private sector, especially the food industry, remains high and is somewhat linked to the decades-long tension related to the marketing of breast-milk...
substitutes in developing countries and sugar-sweetened beverages and fast foods worldwide. Much of the private-sector dialogue centres around the International Code of Marketing of Breast-milk Substitutes (ie, how to enforce it and the extent of its domain) and around whether the Codex Alimentarius food and nutrient standards give businesses too much freedom to downscale nutrition concerns. Some commentators have argued that particular interpretations of the code have almost completely driven the private sector out of activities to reduce undernutrition. The public sector (elected governments) should set a regulatory framework and policy direction; national nutrition plans are needed to positively shape the substantial and existing effect of the private sector, to harness innovation (eg, mobile health and other information and communication technologies in nutrition), and to explore any comparative advantage in goods and service delivery.

A troubled history combined with continued violations makes it increasingly difficult for the private sector to be a major contributor to the collective creation and sustenance of momentum for malnutrition reduction. This sector has yet to earn the trust of some groups of the nutrition community. In view of the needs and the considerable resources, effect, and convening power of the private sector, this opportunity might be missed. Additionally, opportunities exist for collaboration around advocacy, monitoring, value chains, technical and scientific collaboration, and fortification of staple foods that are uncontentious and deserve further exploration.

When the interests of different participants are not perfectly aligned and when substantial information and power asymmetries exist, such as between large corporations and under-resourced governments, the search for win–win solutions for undernutrition and overweight and obesity is a matter of governance arrangements: how rules are set, monitored, and enforced. Lessons need to be learned from the long experience of the regulation and legislation of fortified foods and from the experiences of public–private partnerships in international health, which suggest that such solutions can be identified on the basis of sufficient trust and verification. Such experiences suggest that some urgency exists towards building of trust, especially around infant feeding. Recommendations for building of trust in companies manufacturing infant formula feeds include establishment of a public register of meetings between companies and governments about the International Code of Marketing of Breast-milk Substitutes, strengthening of whistleblowing procedures within companies, and implementation of prevention of code violations into the job descriptions of companies’ senior representatives in each country.

Governments need to play their part by enshrining the code and subsequent resolutions into national law, and putting independent, transparent, and effective monitoring mechanisms in place.

Capacity and resources

Leadership in nutrition

All the nutrition success stories—eg, in Brazil, Peru, Vietnam, and Thailand—have strong and effective networks of national nutrition leaders at their core. For undernutrition reduction to be sustained, nutrition leaders at all levels should be able to forge strong alliances (across and between government, civil society, and the private sector), take timely and decisive action, and create and be subject to strong accountability. Enhancement of effective leadership needs investment and yet only a handful of courses in nutrition leadership are offered worldwide. Every year, the African Nutrition Leadership Programme, an African-led initiative, enrols 30 participants for 10 days—a less than one professional per African country per year. No nutrition leadership programme exists in south Asia; however, UNICEF India’s engagement with young political leaders through the Citizens’ Alliance Against
Malnutrition seeks to strengthen political leadership. Panel 6 summarises research done to identify what makes a champion in nutrition.

Leaders and champions in nutrition need systemic and organisational capacity to create and sustain nutrition policy and institutional change. Again, civil society can play a strong part in this aspect as shown, for example, in Peru where civil society champions were linked with political and financial decision makers (appendix).

Understanding of the financial resources available to build commitment for nutrition

A focus on three areas is needed to make the case for additional resources to build and sustain momentum for undernutrition reduction: the cost, an understanding of present resource flows to nutrition, and more and better estimates than presently exist of benefit to cost ratios for nutrition investments at the country level. Answers to these questions could help convince financial analysts in the public and private sectors to invest. Estimations for the SUN movement clearly show the costs of addressing undernutrition via nutrition-specific interventions.9 More work is needed to contextualise and specify these costs for different countries and this work is ongoing. Unfortunately, investments in nutrition are hard to track because of the weak designation of donor and government spending. For example, analyses of data from the Creditor Reporting System, which is maintained by the Development Assistance Committee of the Organisation for Economic Cooperation and Development, show that a substantial proportion of spending designated as nutritional, is actually being spent on non-nutrition projects. Similarly, much nutrition spending is in categories that are not nutritional.93,94 Data for donor spending on nutrition often do not match those of governments (unpublished).

However, cost–benefit estimates are quite favourable. With assumptions about the 11% uplift in income attributable to prevention of a third of stunting by age 3 years, and about the 5% discount rate of future benefit streams, average cost–benefit estimates have been generated for 20 countries,4 with a median ratio of 18 (Bangladesh). These ratios compare extremely favourably with other investments for which public funds compete.95 Findings from the COHORTS study96 reinforce the consensus that the first 1000 days is the key window of opportunity for investments. With data from five countries, the COHORTS investigators reported that the growth effects on human capital are largest at age 2 years. The most powerful way of building commitment to increased resource allocation to nutrition could be shown in the example set by countries that have achieved scale-up. The three case studies identified in the appendix provide examples of

Panel 6: What makes a nutrition champion?

In seeking to achieve large-scale, systemic changes to address undernutrition, several initiatives have recognised the important role of key individuals—leaders, champions, catalysts, and policy entrepreneurs—in the development of beneficial policy changes.21,23,30,31 Because level of change does not necessarily correspond to levels of formal power, visibility, ambition, or technical knowledge, research is being done to identify and better understand the capacities and attributes of the individuals who have substantially contributed to policy advances for nutrition. This research is based on principles and concepts from complexity science and adult development. Through network and power mapping and consultations with key informants, relevant stakeholders were identified in Kenya and Bangladesh (about 75 stakeholders per country) and semi-structured interviews were done with a purposive sample of these stakeholders (30 in Kenya and 24 in Bangladesh). These interviews provided information to assess the attributes of the interviewee and other influential stakeholders (ie, self-reporting and peer-reporting) and provided further insights into network and power dynamics and case studies. In Kenya and Bangladesh, this research shows that a handful of catalytic individuals, well-connected and trusted in their formal and informal social networks,34,36 have played a crucial part in transfer of information, changing of perceptions, and resolving of conflicts; achievements that have proven essential to advance the nutrition agenda in the context of fragmentation and competing interests between and within various groups of stakeholders.37,38,39,40

Preliminary findings show that these individuals have, in addition to extensive knowledge and experience in nutrition, relatively strongly developed stakeholder awareness and perspective awareness. They show an understanding of the stakeholders relevant to nutrition policy processes and the associations among them, and tend to view the properties of their own and others’ perspectives as perspectives with complex contributory causes. Patterns of sense making generally shape one’s goals and activities,40–42 and the catalytic individuals identified in this study tended to identify ways in which shifts in stakeholder views and associations can lead to positive outcomes; genuinely adapt behaviour, language, and framing of issues to different stakeholders; and focus on establishment of associations of mutual trust, rather than unidirectional forms of influence. This research, led by the Transform Nutrition consortium, is ongoing and will continue in Ethiopia and India. Future research will focus on the ways to move beyond identification and assessment of champions to evaluating ways of supporting them, including through training and capacity building, curricula development, public recognition and support for identified champions (eg, through awards and scholarships); and the development of competency frameworks and institutional and workplace incentives.43

For more on the Transform Nutrition consortium see http://www.transformnutrition.org
what can be done to improve nutrition. A few SUN countries should show that increased commitment can be turned into real results—such examples will act as a spur for many others.

Conversion of momentum into results
Knowledge and evidence
Building of momentum for undernutrition reduction is not an easy task, nor is it sufficient; such momentum needs to be translated into ground-level results. Again the three dimensions of an enabling environment come into play: knowledge and evidence about how to scale up interventions in an effective way, the political economy behind the interplay between national and subnational levels of government, and the capacity and resources needed to scale and expand coverage of programmes while retaining cost-effectiveness.

Implementation research: what works, why, and how?
Despite calls to action,91,92 and by stark contrast with the Countdown to 2015 report on maternal, newborn, and child survival,93 no systematic process is in place for collation of the implementation-related evidence base about how to scale up the vast array of nutrition-specific and nutrition-sensitive interventions with quality and equity. Development of this scientific literature needs careful attention to several factors, but perhaps most importantly, needs a relentless focus on unpacking of programme impact pathways to effects107,108 and documenting of contextual factors that affect implementation. Comprehensive frameworks already exist to provide insights into the types of process-related and contextual factors that need to be further studied through implementation research. A process convened by the New York Academy of Sciences and WHO for setting of research agendas in nutrition emphasises crucial gaps and a framework to undertake implementation research in nutrition.102 Examples of such research have been emerging in the form of feasibility studies since the first Lancet Series was published—partly because of persisting ethical concerns and conceptual and practical difficulties posed by research in such situations.103,104 This scientific literature about implementation provides insights into the types of process-related and contextual factors that need to be further studied through implementation research.

Monitoring of programme coverage
Inherent in the SUN process is the acknowledgment that programme coverage of nutritionally vulnerable populations has to increase from very low levels; however, routine mechanisms to monitor nutrition-related intervention coverage worldwide are poorly designed. Research of child survival105 has shown the large gap in scale-up of evidence-based interventions for maternal, newborn, and child survival, many of which have substantial benefits for nutrition, but several nutrition indicators are not yet embedded in these monitoring processes. WHO’s Nutrition Landscape Information System117 needs to be strengthened by generation of a consensus on, and expansion of the range of, interventions to be tracked.

Programme evaluations to learn and improve
Programme evaluations play a crucial part in informing the scale-up, reconfiguration, or cessation of programmes. Solid guidance now exists to bring rigour to evaluations of nutrition programmes.118,119–121 This guidance is needed to create solid ground for evaluation of the progress, and pathways to progress, of nutrition interventions.106,107,112 with theory-driven and qualitative evaluations exploring the whys and hows of progress and the extent.108,120 Analyses of effectiveness and operational evaluations of innovations that are introduced into scaled-up programmes, or of the process of scale up of innovative programmes from small-scale pilots to a large scale, are essential, but challenging.

Learning during crisis
Increases in the frequency of natural disasters122 and the persistence and repeated cycles of conflict123 raise government needs and stifle progress in reduction of undernutrition in fragile contexts. The need for effective surveillance; early warning; mitigation; and timely, appropriate, and effective responses to nutrition-related crises is greater than ever. Yet little new evidence has been generated of the effectiveness of emergency interventions since the first Lancet Series was published—partly because of persisting ethical concerns and conceptual and practical difficulties posed by research in such situations.124 The time has come for increasing recognition of government accountability to lead in the provision of services that are needed to meet short-term emergency-related spikes in demand.125 This situation creates a growing tension between stakeholders who are driven by the humanitarian imperative to deliver timely and effective assistance, and those who seek to strengthen government systemic capacity to lead general efforts to scale up nutrition-related interventions and services. A pertinent example is the community-level treatment of wasting, which in the past decade has moved from being a programme led by non-governmental organisations, to a service integrated within national health systems, which is intended to be accessible to children in need throughout
the year.126 How to enable such systems to protect and reinforce the resilience of populations in fragile contexts, and to create a surge in response to increases in acute needs, is still a major challenge.

Political economy and governance

Subnational governance

Just as building and sustaining of commitment is a political process, so too is conversion of momentum into results. Political scientists often conclude that most policy is formulated at the front line, and the situation should be no different for efforts to reduce undernutrition. Findings from the six country nutrition governance study40 suggest that in addition to the key ingredients for building of momentum, a further five are crucial to generate change: (1) local government capacity to deliver effective nutrition services, (2) local politicians who care about nutrition and are empowered via decentralised budgets and knowledge that nutrition can be a vote winner, (3) timely data for undernutrition, (4) nutrition funding channelled through one funding mechanism rather than fragmented funding streams, and (5) earmarked and protected nutrition funding commitments and exploration of new revenue streams.

The findings for local government incentives and capacity are highly relevant because many countries in Asia and sub-Saharan Africa are rapidly moving to decentralised political, administrative, and financial systems. Decentralisation necessitates building of commitment and capacity at various political and bureaucratic levels at which decisions are made and resources allocated. Although scientific literature is emerging for decentralisation of health systems,7,111 the research base is limited to a handful of studies.9,27,11,117 In Vietnam for instance, the role of provincial planning for nutrition has been identified as an important bottleneck. The findings of local government incentives and capacity are highly relevant because many countries in Asia and sub-Saharan Africa are rapidly moving to decentralised political, administrative, and financial systems. Decentralisation necessitates building of commitment and capacity at various political and bureaucratic levels at which decisions are made and resources allocated. Although scientific literature is emerging for decentralisation of health systems,7,111 the research base is limited to a handful of studies.9,27,11,117 In Vietnam for instance, the role of provincial planning for nutrition has been identified as an important bottleneck.

Intersectoral action

The wide recognition that action from several sectors is needed to address nutrition has gained momentum, and several country governments are implementing multisectoral and intersectoral plans. However, few examples exist of the factors and processes that should align to enable intersectoral action to generate scaled up nutrition-specific interventions and a nutrition-sensitive household and community environment in which provisions for water, sanitation, social protection, health care, and food security are ensured. Research so far has been of intersectoral planning and action at a policy level,5,138 whereas several questions remain about how best to achieve such outcomes at subnational and local levels. Even integration of nutrition actions within the health sector (which is arguably the most ready to absorb nutrition actions) often raises many challenges.114 Although such integration has been the focus of several large-scale nutrition initiatives in the past (eg, LINKAGES) and of some health-sector initiatives (eg, Integrated Management of Childhood Illness), published works of what is needed, and how to achieve integration, are scarce. Integration of nutrition into other sectors, which are less oriented to nutrition, is hampered by issues related to motivations, capacities, and clear guidance.114 Therefore, building of experiential learning and systematic evidence about processes related to intersectoral and multisectoral integration of actions is urgently needed to reduce undernutrition.

Private sector engagement

Several promising areas for private sector engagement in nutrition value chains have been summarised in the past few years.66,140 Similarly, many promising non-peer reviewed case studies exist about how food fortification not only generates sales and reputational gains for businesses, but also nutritional benefits via increased consumption of fortified foods.146,149 The potential of other types of private sector companies to contribute to nutrition scale-up is also considered important (eg, via mobile technology providers). A major constraint in realisation of this potential is the dearth of independent peer-reviewed studies of such activities and the complete absence of any review of the available evidence, although a review is underway by the Transform Nutrition consortium.

Of peer-reviewed studies relating to the first 1000 days of life, one noted that marketing and selling of multi-nutrient powders in China to the caregivers of children aged 6–24 months reduced the risk of anaemia by 87%.150 Another reported decreases in iron and vitamin A deficiency in children aged 6–35 months in western Kenya from the sale of multinutrient powders via community vendors.151 The private sector has a part to play in the provision of fortified foods that could assist in addressing undernutrition. Attention should be paid to, and guidance be given to, the appropriate marketing of complementary foods for young children older than 6 months, that both protects breastfeeding and allows for caregivers to make informed choices from available fortified complementary foods.

Beyond direct private-sector support through core business operations and investments, many individuals have argued that the sector has a much broader responsibility to ensure the health, nutrition, and welfare of their workforces and the larger communities that are dependent upon them. The creation of shared value approach is intended to be achieved through creation of economic value via company’s policies and operating practices, with simultaneous advancement of the economic and social conditions in the communities in which it operates.66 Results of this approach should be carefully monitored, and best practices underscored, through initiatives such as the Ethical Trading Initiative, which none of the leading food and beverage companies on the Access to Nutrition Index have signed up to.146
On the basis of the suggested guidelines in the table, and of insights from other sectors, several factors are key to maximising the private sector's potential contribution to nutrition status with minimisation of the risks to vulnerable populations: (1) understand the bottlenecks that the private sector could help overcome; (2) incentivise positive roles and the development of business models that support them; (3) regulate ongoing activities for potential risks to nutrition, with strong monitoring processes; (4) be transparent about the role of the private sector in the policy process and any potential conflicts of interest; and (5) independently evaluate public–private partnership activities and make the data and analyses publicly available.

Capacity and resources

Sequencing and prioritisation of nutrition actions

Ideally, all the links in the nutrition chain would be addressed at the same time; if this is not possible for resource, capacity, or political reasons, priorities need to be set. A frequently heard complaint from ministries of finance in high-burden countries is what to do first when it comes to stimulation of economic growth? In response to this question, a group of researchers at Harvard University and elsewhere have developed an economic growth diagnostics process. The process combines evidence about the technical (what works here?), capacity (can we scale-up?) and, importantly, the political (are there any windows of opportunity for change?) aspects. The rationale is that sequencing matters and some issues can be highly rate-limiting. With nutrition, specific factors need to be in place for specific processes to take place. Similar nutrition diagnostic methods need to be developed to help prioritise nutrition plans of action.

Capacity for scale up

Several types of capacity are needed for effective scale up of priority nutrition interventions (panel 7). Insights can also be gained from the wider scientific literature of human resources in health systems research, including the need to agree on exactly what should be scaled up, consider lessons on scale-up from related areas, honestly document experiences, and understand that scaling up of interventions requires a scaling down of certainties, and inclusiveness and building of relations to sustain momentum. Finally, we suggest that the existence of poor quality training programmes and academic curricula in nutrition in regions of poor quality service delivery is not a coincidence. Many of these studies are from high-burden regions and they find the training and curricula to be outdated, impractical, and misaligned with local nutrition priorities. We reiterate the conclusion of the 2008 Series that much more needs to be done to strengthen strategic and operational capacity. Governments and donors should allocate more resources to establish a more sustainable foundation for nutrition implementation by training the next generation of implementers who in turn will be mentors for the generation after that.

Financial resources to support scale up

The second paper in this Series estimates that at least Int$9·6 billion per year will be needed to scale up the 11 proven nutrition-specific interventions for the 34 countries that account for 90% of the burden of stunting. If this scale-up could be achieved, at least a quarter of present stunting cases could be addressed. Paper two suggests that roughly $3 billion to $4 billion of this total could come from external donors and, as SUN requires, would work together with established guidelines for aid effectiveness, including the importance of country ownership and the avoidance of aid dependency. Scaling up of nutrition programmes continues to be the place to start to reduce malnutrition; however, we need estimates of what it would take to make agriculture, social protection, education, and women's empowerment policies and programmes, for example, sufficiently nutrition-sensitive to have a further substantial effect on malnutrition rates. Paper three provides some suggestions about how to reallocate nutrition-sensitive programme resources to achieve win–win solutions. The extra resources needed to

Panel 7: Key issues and core elements of nutrition-relevant capacity

Individual capacity: methods and skills

- Performance capacity: are the methods, money, and equipment, for example, available to do the job?
- Personal capacity: are staff sufficiently knowledgeable, skilled, and confident to perform properly? Do they need training, experience, or motivation? Are they deficient in technical, managerial, interpersonal, or specific role-related skills?

Organisational capacity: staff and infrastructure

- Workload capacity: do enough staff have broad enough skills to cope with the workload? Are job descriptions practicable? Is skill mix appropriate?
- Supervisory capacity: are reporting and monitoring systems in place? Are lines of accountability clear? Can supervisors physically monitor all staff? Are effective incentives and sanctions available?
- Facility capacity: are training centres, offices, and workshops big enough, with the right staff in sufficient numbers, to support the workload?
- Support service capacity: are there training institutions, supply organisations, building services, administrative staff, research facilities, quality control services?

Systemic capacity: structure, systems, and roles

- Structural capacity: are there decision-making forums or multistakeholder platforms at which intersectoral discussion of nutrition could take place, consensus is generated, collective decisions are made and recorded, and individuals called to account for non-performance?
- Systems capacity: do flows of information, money, and managerial decisions happen in a timely and effective manner? Are proper filing and information systems in use? Can private sector services be contracted as needed? Is there good communication with the community? Are links with non-governmental organisations sufficient?
- Role capacity: have individuals, teams, and committees been empowered to make decisions to ensure effective performance—eg, regarding schedules, money, and staff appointments?
incentivise such reallocations might well be modest, but more experience and evidence are needed to identify the surplus requirement. The allocation of scarce public resources between nutrition and other activities (and indeed among nutrition activities) will be guided by political and technical considerations. Nutrition tends to have no institutional champion, hence the emphasis within SUN on institutional mechanisms to address this issue, both formally (via multisector platforms) and informally via the framing around movements. Other mechanisms for promotion and protection of nutrition spending exist, such as the example in Peru of embedding of nutrition within electoral commitments (appendix), and more analysis is needed about the variety and effectiveness of these mechanisms.

We previously discussed private sector possibilities for additional resources. For public sources, high-burden countries together with donors and multilateral organisations have a responsibility to increase allocations to nutrition-specific and nutrition-sensitive programmes. To do this within an official development assistance budget that has peaked, albeit with increasing tax revenues from high-burden countries,\textsuperscript{10} will be politically challenging, hence the need to build leadership, commitment, and accountability at national and international levels.

### Panel 8: Research priorities to build commitment and accelerate progress

#### Framing, generation, and communication of knowledge and evidence

**Creation and sustaining of momentum for undernutrition reduction**
- What types of issue framing approaches and narratives yield attention to nutrition in different contexts?
- What advocacy and policy engagement strategies are most effective at galvanising political attention to nutrition?
- What types of evidence are most powerful for creation versus sustaining of national and subnational attention to nutrition?
- Can real-time monitoring of nutrition outcomes and coverage lead to more responsive nutrition actions and improved nutrition outcomes?

**Conversion of momentum to effect on nutrition status**
- How can nutrition interventions be mainstreamed and integrated into other sectors
- What types of programme evaluations and operations research are crucial to enabling programmatic actions at different stages in the life of nutrition investments?
- What types of learning mechanisms best enable inclusive stakeholder engagement with evidence?
- What types of stakeholder engagement approaches can enhance the demand for evidence of effect?

#### Political economy and governance of stakeholders, ideas, and interests

**Creation and sustaining of momentum for undernutrition reduction**
- What strategies are most effective at enabling multisectoral coordination and strategic coherence for nutrition?
- Which accountability strategies are most effective at mobilising commitment at different levels of government and society (eg, indices, scorecards, social audits, community monitoring)?
- In what ways can the private sector be regulated to protect and support exclusive breastfeeding?

**Conversion of momentum to effect on nutrition status**
- What aspects of decentralisation are most crucial for enabling vertical translation of national guidance to programmatic action?
- What types of roles can (and should) the private sector and civil society have in supporting service delivery and scaling up?

#### Capacity (individual, organisational, systemic) and financial resources

**Creation and sustaining of momentum for undernutrition reduction**
- What are the characteristics of nutrition policy champions? What effect do university curricula and leadership training investments have in creation of nutrition leaders?
- What types of institutional investments and capacity building activities yield the best systemic and strategic capacity for nutrition within national and subnational organisations?
- How should the resources allocated to nutrition-sensitive programmes be assigned to nutrition improvement?
- To what extent can research on the costing of interventions and the tracing of financial flows mobilise additional resources for nutrition and improve the effectiveness of resource allocation?
- What methods are effective in helping to prioritise and sequence nutrition actions?

**Conversion of momentum to effect on nutrition status**
- What institutional and front line capacities are most important to enable scale-up of different types of direct nutrition interventions through community-based programmes and the health sector?
- How can nutrition-sensitive sectors operationalise their interventions to achieve nutrition results for women and children?
- Which new forms of resource mobilisation show the greatest promise for improvement of nutrition status?
- Does prioritising and sequencing of simple nutrition actions (eg, vitamin A supplementation, micronutrients, treatment of severe acute malnutrition) create enabling conditions for closing gaps on more complex interventions (behaviour change interventions for infant and young-child feeding?).
However, the gap is unlikely to be closed from these sources. Innovation is needed across all sectors to leverage private-sector and public-sector resources and to generate additional public funding. The nutrition sector can draw on several innovative ideas from other sectors, including advance market contracts to promote investment, market levies, and taxes, on either unhealthy externalities or external sectors, as in the airline ticket levy by UNITAID or the mining levy funding health in Zambia. Nutritional impact bonds are another option, entailing the creation of a social impact partnership fund by private investors, which receives public funds if key service delivery targets are met. In this way, public funds catalyse and leverage private investment for which the service providers bear the risk, but also stand to generate additional revenue. Key to the success of these schemes is the collection of credible metrics. More research and experimentation is desperately needed in this area.

Looking ahead
In the past 5 years, the nutrition community has made major progress, but it should be judged against the effect emerging in the next 5 years and beyond. Momentum needs to be sustained and converted into lasting effects. SUN will reach its 1000th day when this Lancet Series is launched in June, 2013. Since SUN’s own launch in September 2010, the movement has substantially elevated and energised the discourse on nutrition and has changed institutional arrangements. In some countries, the movement is beginning to catalyse resource mobilisation and programme alignment. Emphasis should now escalate to action, translating commitment into results on the ground. SUN needs to build on its commitment to be country led and results driven. To enable this development, SUN should harness and catalyse national leadership, capacity and resources, politics, and knowledge generation. Documented SUN proof-of-concept success stories are also needed to galvanise further action.

One clear overarching priority is the need to strengthen strategic and operational capacity to scale up nutrition interventions and embed nutrition considerations in other sectoral actions. This point was emphasised in the 2008 Lancet series and remains the case today. National and global resources need to be invested in the long term to support capacity development, at individual, organisational, and systemic levels. Leadership is needed to galvanise and spearhead action, and this again will need to be seeded, funded, and nurtured. For too long the issue of capacity has been recognised but overlooked—a convenient excuse for failed plans. It is easy to neglect such issues when constructing business plans to support nutrition strategies and yet without sufficient capacity of the right type at the right level, plans become hollow wish lists.

Fairly silent to date, the nutrition community needs to be a lot more engaged in the post-2015 process to ensure that interest in nutrition is locked into the post-2015 development settlement (panel 4). If nutrition is to be embedded into broader development processes, the nutrition community needs to actively forge alliances with those for whom malnutrition reduction is not a top priority and to do this in a politically aware manner. We have drawn on a range of evidence in this report, both academic and from the field. The academic evidence we used is valuable, but much of it is from areas outside of nutrition. We call for more research of what defines enabling environments for nutrition. We also call for more systematic ways to capture and share the learning from policy and programme operations. Panel 8 shows priority areas for research.

Finally, the core problem itself is changing as the burden of disease caused by poor nutrition continues to shift from undernutrition to a double burden of undernutrition and overweight and obesity. Future Lancet series on nutrition will have to pay much greater attention to this double burden than we have. But the disease burden attributable to child underweight remains substantial in many countries, in other words, there is an enormous unfinished agenda.

Contributors
All authors contributed to the conceptualisation and structuring of the paper, and reviewed all drafts. SG led overall development and finalisation of the paper and appendix, and coordinated inputs of coauthors and contributors. He led on the enabling environments section, Scaling Up Nutrition (SUN) electronic consultation, and case studies; prepared the first draft of the conceptual framework; wrote the sections about capacity, civil society, the abstract, and introductory and closing sections; contributed to other sections of the paper; and prepared and submitted the final draft. LH first proposed to focus the paper on the politics of nutrition and led on drafting the sections about the wider context, financial resources, horizontal and vertical coordination, the private sector, the nutrition commitment index, and the post-2015 discussions; and had responsibility for construction of the first complete draft of the paper. VM prepared background sections on private sector, SUN, civil society, and financing, which were used in the development of those sections, and made contributions to each draft. PM wrote sections about implementation research and translation of commitment to action, and provided written inputs to the private sector and enabling environment sections. NN prepared the accountability and global governments sections and the Peru case study, contributed to the enabling environments section and coedited one of the first full drafts. Four of the authors are researchers and one (VM) is a practitioner. The researchers combine expertise in nutrition, economics, politics, sociology, and anthropology. All authors are embedded in the global policy community and all are very familiar with one or more country policy communities. All authors operate at the interface between policy, practice, and research and three have done so since the 1980s. This is the basis for their collective knowledge.

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Conflicts of interest
REB serves on the Boards of the Micronutrient Initiative, Vitamin Angels, the Child Health and Nutrition Research Initiative, and the Nestlé Creating Shared Value Advisory Committee. VM serves on the Nestlé Creating Shared Value Advisory Committee. The other authors declare that they have no conflicts of interest. As corresponding author, Stuart Gillespie states that he had full access to all data and final responsibility for the decision to submit for publication.

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Mortality risk in preterm and small-for-gestational-age infants in low-income and middle-income countries: a pooled country analysis


Summary

Background Babies with low birthweight (<2500 g) are at increased risk of early mortality. However, low birthweight includes babies born preterm and with fetal growth restriction, and not all these infants have a birthweight less than 2500 g. We estimated the neonatal and infant mortality associated with these two characteristics in low-income and middle-income countries.

Methods For this pooled analysis, we searched all available studies and identified 20 cohorts (providing data for 2015–2019 livebirths) from Asia, Africa, and Latin America that recorded data for birthweight, gestational age, and vital statistics through 28 days of life. Study dates ranged from 1982 through to 2010. We calculated relative risks (RR) and risk differences (RD) for mortality associated with preterm birth (<32 weeks, 32 weeks to <34 weeks, 34 weeks to <37 weeks), small-for-gestational-age (SGA; babies with birthweight in the lowest third percentile and between the third and tenth percentile of a US reference population), and preterm and SGA combinations.

Findings Pooled overall RRs for preterm were 6.82 (95% CI 3.56–13.07) for neonatal mortality and 2.50 (1.48–4.22) for post-neonatal mortality. Pooled RRs for babies who were SGA (with birthweight in the lowest tenth percentile of the reference population) were 1.83 (95% CI 1.34–2.50) for neonatal mortality and 1.90 (1.32–2.73) for post-neonatal mortality. The neonatal mortality risk of babies who were both preterm and SGA was higher than that of babies with either characteristic alone (15.42; 9.11–26.12).

Interpretation Many babies in low-income and middle-income countries are SGA. Preterm birth affects a smaller number of neonates than does SGA, but is associated with a higher mortality risk. The mortality risks associated with both characteristics extend beyond the neonatal period. Differentiation of the burden and risk of babies born preterm and SGA rather than with low birthweight could guide prevention and management strategies to speed progress towards Millennium Development Goal 4—the reduction of child mortality.

Funding Bill & Melinda Gates Foundation.

Introduction

An estimated 20 million infants every year are born with low birthweight (LBW; <2500 g), and these infants have an increased risk mortality in the first year of life. The primary causes of LBW are preterm birth, intrauterine growth restriction (IUGR), or a combination of the two. Of 135 million children born in low-income and middle-income countries (LMICs) in 2010, an estimated 29.7 million were born both term and small-for-gestational-age (SGA), 10.9 million were born preterm and appropriate-for-gestational-age (SGA), and 2.8 million were born preterm and SGA. Risk factors and interventions to reduce the number of babies born SGA might differ from those to reduce the number of babies born preterm. The survival and growth patterns of preterm or growth-restricted newborn babies are not well described in LMICs and the contribution to mortality of non-LBW babies (≥2500 g) who are preterm or those with IUGR in such settings is unknown.

Few studies in LMICs have investigated differences in mortality by extent of prematurity, IUGR, or the two in combination, or mortality risk in infants who are SGA stratified by gestational age. Examination of the mortality risk by degree of prematurity and SGA as a proxy for IUGR might be crucial in understanding the attributable disease burden, especially because regions such as south Asia have a reported SGA prevalence of about 40%. Such mortality risk estimates and attributable burden could enable the specific targeting of these disorders with appropriate interventions to more effectively save lives.

The Child Health Epidemiology Reference Group (CHERG) previously examined the risk of infant mortality associated with term-LBW as a proxy for IUGR. However, term-LBW excludes growth-restricted infants weighing more than 2500 g and high risk infants born both preterm and SGA, and such
associations between mortality and SGA-non-LBW or SGA-preterm have not been well described in LMICs. With more population-based studies in LMICs now collecting data for gestational age in addition to birthweight, the CHERG identified an opportunity to assess the mortality risk of SGA and preterm on early neonatal, late neonatal, post-neonatal, and infant mortality.

Methods
Dataset identification
We searched Medline, WHO regional databases (African Index Medicus, LILAS, EMRO), bibliographies of sentinel articles and reviews, and grey literature to identify potential datasets from low-income and middle-income countries that recorded data for gestational age and birthweight, and systematically recorded vital status from delivery through at least 28 days of life. The most recent search was done on Feb 22, 2010. We applied no no date or language restrictions. Search terms included “preterm or SGA”, “neonatal or infant mortality”, and “developing country” (see appendix for detailed search terms). CHERG investigators also identified additional datasets that were not retrieved in our search. We excluded datasets for the following reasons: greater than 25% missing data for birthweight or gestational age, or loss to follow-up; measured weight only after the first week of life; did not have systematic follow-up of vital status in the first month of life; determined gestational age in months or by fundal height; or when we deemed gestational age determination inaccurate or poorly linked to birthweight (appendix). We aimed to include only datasets that were population-based, representing all deliveries arising from specific geographical or catchment areas, whether home-based or facility-based. We excluded stillbirths from the analyses of these cohorts. We approached principal investigators to do a set of standard analyses themselves, or to share their data with the CHERG working group to do the analyses. Datasets that were shared with the working group did not contain personal identifiers and were therefore deemed exempt by the Johns Hopkins Bloomberg School of Public Health institutional review board. Datasets analysed by the original study investigators were covered under existing institutional review board approvals.

Exposure definitions
If more than one gestational age measurement was available we used estimates in the following order of preference: ultrasound, best obstetric estimate (combination of ultrasound, date of last menstrual period, and neonatal clinical exam), last menstrual period, or clinical examination of the infant within 72 h of birth. Prematurity was defined as a gestational age of less than 37 completed weeks. We categorised prematurity into less than 32 weeks (early preterm), 32 weeks to less than 34 weeks (moderate preterm), and 34 weeks to less than 37 weeks (late preterm). Weight was analysed if measured within 72 h. SGA was defined as birthweight below the tenth percentile of a standard optimal reference population for a given gestational age and sex. Appropriate-for-gestational-age (AGA) was defined as above the tenth percentile. WHO previously recommended data in a study by Williams and colleagues (collected in California from 1972 to 1976) as the reference. We chose the more recent and commonly cited Alexander reference, which includes 3134879 nationally representative, multi-ethnic births in the USA in 1991. Because that dataset provided data at only the tenth percentile, we identified another dataset (Oken and colleagues) based on US data from 1999–2000 (6690717 births) that provided Z scores. We created two categories of SGA using a combination of these two reference populations: the tenth percentile of Alexander to the third percentile of Oken and colleagues, and the lowest third percentile of Oken and colleagues. AGA included large-for-gestational-age (LGA) infants (≥90% birthweight for gestational age). However, in these datasets, the prevalence of LGA was very small and their inclusion in the reference population likely had very little effect on mortality risk.

We created four mutually exclusive exposures to capture interaction between preterm (<37 weeks) and SGA (<10%): term and appropriate-for-gestational-age (as reference), term-SGA, preterm and appropriate-for-gestational-age, and preterm and SGA. We defined mortality as early neonatal (birth to 7 days), late neonatal (8–28 days), neonatal (birth to 28 days), post-neonatal (29–365 days), and infant (birth to 365 days) mortality. For late neonatal and post-neonatal infant mortality, the denominators were infants alive at the start of the interval of interest with vital status available through the end of the interval.

Analysis of individual datasets
The same analysis was done on each dataset. We used an algorithm developed by Alexander and colleagues to exclude infants with incompatible birthweight-gestational age combinations. Gestational ages of less than 24 weeks and more than 48 weeks were also excluded. We calculated the prevalence of LBW, preterm, SGA, and the overlap of these disorders for each dataset. We calculated relative risks (RRs) and risk differences (RDs) for early, late, neonatal, post-neonatal, and infant mortality associated with preterm and SGA categories.

RRs were adjusted for all confounders available in each dataset (including occupation of head of household, land ownership, years of maternal and paternal education or literacy, and maternal age and parity). We did adjusted analyses on 13 of the 20 datasets. Regression coefficients for the primary associations of interest were attenuated at less than 10% in all datasets except for one, for which the parameters were not statistically significant.
**Missing exposure data**

All studies had few missing gestational age data (<10%). Analyses of mortality risk by preterm categories used all available gestational age data, irrespective of missing birthweight (full gestational age cohort). There were two main reasons for missing birthweight data (most of which were from home deliveries): some infants who died soon after delivery were not weighed, and infants who were weighed were measured at different times after delivery. For risk estimates associated with SGA, we included infants with weights taken within 72 h of birth (weighed cohort). For four Asian and two African studies with missing data for birthweight or that measured some weights after 72 h, we used multiple imputation\(^4\) to impute birthweights (appendix). The imputed datasets were used to estimate the RRs and RDs.

**Pooled analysis**

Because multivariate adjustment did not substantially modify estimates of associations, we used the crude RRs and 95% CIs, and pooled data for the major UN Millennium Development Goal regions (Asia, Africa, and Latin America). We estimated overall and regional RRs of mortality for each exposure variable (preterm, SGA, and combinations). We used Stata (version 11) for all statistical analyses. Random effects models used the DerSimonian-Laird pooled RRs and 95% CIs, given between-study heterogeneity.\(^5\)

**Role of the funding source**

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to most of the datasets, had access to all summary estimates from each dataset for meta-analysis, and had final responsibility for the decision to submit for publication.

**Results**

We included 20 datasets with 2015019 livebirths from sub-Saharan Africa, Latin America, and south and southeast Asia, with gestational age available for 2008675 babies and both gestational age and birthweight available for 1996763 babies (table and appendix).\(^6\) Study dates ranged from 1982 through to 2010. The Chilean national birth registry\(^7\) provided much of these data. The prevalence of preterm birth (<37 weeks) in the study datasets ranged from 2.7% to 28%, with varying methods of gestational age determination (see appendix for specific study

<table>
<thead>
<tr>
<th>Country</th>
<th>Setting</th>
<th>Primary study design</th>
<th>Study population</th>
<th>N (original cohort)</th>
<th>N (analysed cohort for preterm/SGA)</th>
<th>NMR (deaths per 1000 livebirths)</th>
<th>IMR (deaths per 1000 livebirths)</th>
<th>Systematic follow-up period</th>
<th>% LBW</th>
<th>% preterm</th>
<th>% SGA</th>
<th>% facility delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bangladesh (2005)(^1)</td>
<td>Rural Sylhet</td>
<td>Cluster RCT of community sepsis treatment</td>
<td>Population-based recruitment of all pregnant women in study area</td>
<td>10585</td>
<td>10585/10350*</td>
<td>31</td>
<td>--</td>
<td>1 month</td>
<td>30%</td>
<td>19%</td>
<td>50%</td>
<td>6%</td>
</tr>
<tr>
<td>India (2000)(^2)</td>
<td>Rural Tamil Nadu</td>
<td>RCT of newborn vitamin A supplementation</td>
<td>Population-based recruitment of all pregnant women in study area</td>
<td>13294</td>
<td>12693/12693*</td>
<td>38</td>
<td>--</td>
<td>6 months</td>
<td>33%</td>
<td>14%</td>
<td>62%</td>
<td>63%</td>
</tr>
<tr>
<td>Nepal (1999)(^3)</td>
<td>Rural Sarlahi</td>
<td>Cluster RCT of multiple micronutrient supplementation</td>
<td>Recruitment of all pregnant women in study area</td>
<td>4130</td>
<td>4122/4094*</td>
<td>42</td>
<td>67</td>
<td>1 year</td>
<td>39%</td>
<td>22%</td>
<td>56%</td>
<td>6%</td>
</tr>
<tr>
<td>Nepal (2003)(^4)</td>
<td>Peri-urban/rural Dhanusha</td>
<td>RCT of antenatal micronutrient supplementation</td>
<td>Antenatal clinic-based recruitment of pregnant women in study area</td>
<td>1106</td>
<td>1106/1052</td>
<td>25</td>
<td>--</td>
<td>1 month</td>
<td>22%</td>
<td>7%</td>
<td>53%</td>
<td>53%</td>
</tr>
<tr>
<td>Nepal (2004)(^5)</td>
<td>Rural Sarlahi</td>
<td>Cluster RCT of newborn skin-umbilical cord cleansing with chlorhexidine</td>
<td>Population-based recruitment of all pregnant women in study area</td>
<td>23662</td>
<td>23650/22723*</td>
<td>32</td>
<td>--</td>
<td>6 months</td>
<td>30%</td>
<td>18%</td>
<td>52%</td>
<td>10%</td>
</tr>
<tr>
<td>Pakistan (2003)(^6)</td>
<td>Rural Sindh</td>
<td>Cluster RCT of maternal micronutrient supplementation</td>
<td>Population-based recruitment of all pregnant women in study villages</td>
<td>1548</td>
<td>1464/1434</td>
<td>18</td>
<td>--</td>
<td>1 month</td>
<td>19%</td>
<td>28%</td>
<td>28%</td>
<td>100%</td>
</tr>
<tr>
<td>Philippines (1983)(^7)</td>
<td>Urban Cebu</td>
<td>Longitudinal health-nutritional survey of infant feeding patterns</td>
<td>Population-based, random cluster sample of census</td>
<td>3080</td>
<td>3050/2785</td>
<td>14</td>
<td>36</td>
<td>2 years</td>
<td>11%</td>
<td>18%</td>
<td>25%</td>
<td>34%</td>
</tr>
<tr>
<td>Thailand (2001)(^8)</td>
<td>Urban Bangkok</td>
<td>Prospective follow-up of birth cohort</td>
<td>Longitudinal birth cohort of all births in four districts</td>
<td>4245</td>
<td>4032/3860</td>
<td>5</td>
<td>6</td>
<td>1 year</td>
<td>8%</td>
<td>9%</td>
<td>22%</td>
<td>99%</td>
</tr>
</tbody>
</table>

(Continues on next page)
The proportions of preterm births before 32 weeks of gestation ranged from 0% to 4% (appendix). Comparison of preterm prevalence by method of assessment was not possible because few studies used more than one method. The prevalence of SGA was generally higher than that of preterm births, ranging from 7% in the Chile national registry to 62% in a community-based trial in south India (appendix). The proportion of LBW infants who were SGA or preterm varied by region (figure 1). In the Asian cohorts, 83% of LBW infants were SGA and 33% were preterm (67% of LBW were term and SGA). In the African cohorts, 79% of LBW infants were SGA and 38% were preterm (62% of LBW were term and SGA). In the Latin American cohorts, 53% of LBW infants were SGA and 71% were preterm (29% of LBW were term and SGA). South Asia had the highest prevalence of preterm births and number of LBW and SGA infants. A substantial proportion of SGA infants did not have LBW in Asia (54%), Africa (65%), and Latin America (59%).

### Table: Study characteristics of 20 included datasets

<table>
<thead>
<tr>
<th>Setting</th>
<th>Primary study design</th>
<th>Study population</th>
<th>N (original cohort)</th>
<th>N (analysed cohort for preterm/for SGA)</th>
<th>NMR (deaths per 1000 livebirths)</th>
<th>IMR (deaths per 1000 livebirths)</th>
<th>Systematic follow-up period</th>
<th>% LBW</th>
<th>% preterm</th>
<th>% SGA</th>
<th>% facility delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sub-Saharan Africa</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burkina Faso (2004)³⁴</td>
<td>Rural Hounde RCT of multiple micronutrient supplementation</td>
<td>Prospective, community-based cohort</td>
<td>1373</td>
<td>1311/1212*</td>
<td>21</td>
<td>6/7</td>
<td>1 year</td>
<td>17%</td>
<td>16%</td>
<td>35%</td>
<td>77%</td>
</tr>
<tr>
<td>Burkina Faso (2006)³⁴</td>
<td>Rural Hounde RCT of maternal fortified food supplementation</td>
<td>Prospective, community-based cohort</td>
<td>1316</td>
<td>1261/1067</td>
<td>20</td>
<td>-</td>
<td>1 month</td>
<td>16%</td>
<td>18%</td>
<td>29%</td>
<td>84%</td>
</tr>
<tr>
<td>South Africa (2004)³⁵</td>
<td>Urban Soweto RCT of birth canal and newborn skin cleansing with chlorhexidine</td>
<td>Facility-based delivery, tertiary care hospital</td>
<td>8113</td>
<td>8113/8098</td>
<td>7</td>
<td>-</td>
<td>1 month</td>
<td>8%</td>
<td>4%</td>
<td>16%</td>
<td>100%</td>
</tr>
<tr>
<td>Tanzania (1998)³⁶</td>
<td>Rural Mwanza Maternal syphilis treatment, observational cohort</td>
<td>Facility-based recruitment, urban, antenatal clinics</td>
<td>1406</td>
<td>1425/1172</td>
<td>16</td>
<td>-</td>
<td>3 months</td>
<td>10%</td>
<td>3%</td>
<td>25%</td>
<td>98%</td>
</tr>
<tr>
<td>Tanzania (2001)³⁷</td>
<td>Urban Dar es Salaam RCT of multivitamin supplementation</td>
<td>Facility-based, antenatal clinics</td>
<td>7752</td>
<td>7740/7557</td>
<td>28</td>
<td>-</td>
<td>6 weeks</td>
<td>8%</td>
<td>17%</td>
<td>20%</td>
<td>97%</td>
</tr>
<tr>
<td>Tanzania (2008)³⁸</td>
<td>Rural Korogwe Observational malaria study</td>
<td>Facility-based recruitment, antenatal clinics, community follow-up.</td>
<td>915</td>
<td>820/731</td>
<td>33</td>
<td>-</td>
<td>28 days</td>
<td>11%</td>
<td>5%</td>
<td>22%</td>
<td>88%</td>
</tr>
<tr>
<td>Uganda (2005)³⁹</td>
<td>Rural Kabale district RCT intermittent preventive malaria therapy and insecticide-treated nets</td>
<td>Facility-based recruitment ANC, clinics; only include facility births</td>
<td>1561</td>
<td>1553/1477</td>
<td>17</td>
<td>-</td>
<td>1 month</td>
<td>7%</td>
<td>6%</td>
<td>10%</td>
<td>100%</td>
</tr>
<tr>
<td>Zimbabwe (1997)³⁰</td>
<td>Urban Harare RCT of maternal-neonatal vitamin A supplementation</td>
<td>Facility-based recruitment, 14 maternity clinics and hospitals</td>
<td>14110</td>
<td>13960/13914</td>
<td>127</td>
<td>93</td>
<td>1 year</td>
<td>14%</td>
<td>8%</td>
<td>33%</td>
<td>100%</td>
</tr>
<tr>
<td><strong>Latin America</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brazil (1982)³¹</td>
<td>Urban Pelotas city, Rio Grande do Sul, southern Brazil Longitudinal birth cohort survey</td>
<td>Population-based, all births in Pelotas hospitals (100% facility delivery)</td>
<td>5914</td>
<td>465/4570</td>
<td>11</td>
<td>28</td>
<td>1 year</td>
<td>7%</td>
<td>6%</td>
<td>17%</td>
<td>100%</td>
</tr>
<tr>
<td>Brazil (1993)³²</td>
<td>Urban Pelotas city, Rio Grande do Sul, southern Brazil Longitudinal birth cohort survey</td>
<td>Population-based, all births in Pelotas hospitals (100% facility delivery)</td>
<td>5279</td>
<td>4707/4632</td>
<td>7</td>
<td>14</td>
<td>1 year</td>
<td>9%</td>
<td>11%</td>
<td>19%</td>
<td>100%</td>
</tr>
<tr>
<td>Brazil (2004)³³</td>
<td>Urban Pelotas city, Rio Grande do Sul, southern Brazil Longitudinal birth cohort survey</td>
<td>Population-based, all births in Pelotas hospitals (100% facility delivery)</td>
<td>4287</td>
<td>3993/3837</td>
<td>10</td>
<td>17</td>
<td>1 year</td>
<td>11%</td>
<td>16%</td>
<td>15%</td>
<td>100%</td>
</tr>
<tr>
<td>Chile (2000)³⁴</td>
<td>Chilean national birth registry Birth registry</td>
<td>Population-based registration</td>
<td>1901611</td>
<td>1898250/1898250</td>
<td>5</td>
<td>-</td>
<td>1 month</td>
<td>6%</td>
<td>7%</td>
<td>7%</td>
<td>98%</td>
</tr>
</tbody>
</table>

RCT=randomised controlled trial. SGA=small for gestational age. NMR=neonatal mortality rate. IMR=infant mortality rate. LBW=low birthweight. *Weights imputed for datasets that met criteria described in appendix. †Enrolment of newborn babies occurred up to 96 h after birth, and the study might have missed neonatal deaths that happened before enrolment.
proportion of children who were both SGA and preterm was small in these datasets (4% in Asia, 1% in Africa, and 2% in Latin America). In Africa and Asia, term infants were more often SGA than were preterm infants, but the opposite was true in Latin America (figure 1).

Neonatal mortality rates and relative risks increased with decreasing gestational age across studies and regions (figure 2). Although the highest relative risks (RRs) were seen in Latin America (mainly due to the very low mortality in the reference group), the risk differences were similar across regions. The overall pooled RRs across all regions were 6.82 (3.56–13.07) for neonatal mortality and 2.50 (1.48–4.22) for post-neonatal mortality. The overall pooled RRs across all regions for late preterm (34 weeks to <37 weeks), when most preterm births occur, were 3.05 (2.02–4.60; figure 2 and appendix). The RDs per 1000 livebirths for late preterm ranged from nine (95% CI 0–18) in Africa to 18 (9–28) in Asia, with an overall RD per 1000 livebirths of 13 (9–18; appendix). The overall pooled RRs for early preterm (<32 weeks) were 28·82 (15·51–53·56; figure 2 and appendix), although the RDs per 1000 livebirths ranged from 196 (95–297) in Asia to 350 (189–511) in Latin America, with an overall RD of 245 per 1000 livebirths (192–297; appendix). Early and late neonatal and post-neonatal infant mortality followed similar patterns, but the RRs were more attenuated the longer the follow-up period extended (appendix), except for early preterm in Latin America, when mortality risk decreased substantially across the early-post-neonatal to late-post-neonatal periods. However, a statistically significantly increased mortality risk persisted into the post-neonatal infant period in all regions for preterm compared to term.

Imputation of missing birthweights did not alter the prevalence of SGA, which was already high, although it did increase the risk of mortality associated with SGA (figure 3 and appendix). Neonatal mortality rates increased with severity of SGA (figure 3). The overall pooled RRs for SGA across all regions were 1·83 (1·34–2·50) for neonatal mortality and 1·90 (1·32–2·73) for post-neonatal mortality. The highest RR for SGA in neonates below the third percentile was in Latin America, compared with 1·91 (1·40–2·60) in Asia, although the CIs overlapped. The overall RR was 2·41 (1·66–3·50). The RRs associated with SGA were of similar magnitude in the early-neonatal, late-neonatal, and post-neonatal periods across regions (appendix). The RRs associated with SGA were overall of smaller magnitude than preterm, and the association with increased mortality did not attenuate beyond the neonatal period and persisted through the first year of life.

Relative to term and AGA, the increased risk of neonatal mortality was lowest in those born term-SGA (overall RR 2·44, 1·34–2·50) for neonatal mortality and 1·90 (1·32–2·73) for post-neonatal mortality. For Asian cohorts (A), percentages are for 78,048 infants. For African cohorts (B), percentages are for 38,248 infants. For Latin American cohorts (C), percentages are for 1,910,734 infants.

Figure 1: The relation between birthweight and gestational age in Asia (A), Africa (B), and Latin America (C)
higher RRs in Latin America were probably driven by the low mortality rate (2.4 per 1000) in the reference group. Pooled RDs were similar across regions (appendix). The RRs for term-SGA babies did not vary by timing of mortality (figure 5). For preterm-AGA and preterm-SGA babies, RRs were highest in the early neonatal period and lowest in the post-neonatal period, although the CIs largely overlapped (ie, no statistically significant between-group differences; figure 5 and appendix). This pattern of attenuated risk by length of follow-up was probably driven by prematurity and not SGA.

Discussion
We identified a large percentage of infants who were SGA but not LBW or preterm (21% in Asia, 16% in Africa, and 4% in Latin America), although their mortality rates were lower than preterm infants or SGA-LBW infants. Although most LBW was in term and SGA babies in Asia and Africa, the majority of babies with LBW in Latin America were preterm. Preterm mortality risk associations were generally higher at all gestational age categories (late, moderate, and early preterm) than SGA (3% to <10% or <3%). However, the attributable mortality risk for SGA infants is substantial, because many infants in LMICs are born SGA, especially in south Asia. The predominant increased mortality risk associated with preterm birth occurred in the first week of life, with statistically significant but attenuated risk remaining in the late-neonatal and post-neonatal periods. Although CIs overlapped, mortality risks associated with SGA were slightly higher in the late than early neonatal period, with persistent risk in the post-neonatal period.

The highest neonatal and infant mortality rates were detected in the Asian and African studies. The highest RRs for all exposures were seen in Latin America, although absolute risk differences were more comparable across regions. This higher RR in Latin America is due to very low mortality in the reference group in Latin America compared with Africa and Asia. In particular, the Latin America analysis was dominated by national registry data from Chile in which term neonatal mortality was 1.7 per 1000 livebirths. By comparison with these data, the average term neonatal mortality was 11 per 1000 livebirths in the African datasets and 19 per 1000 livebirths in the Asian ones. Alternately, preterm infants might be more severely preterm and survive delivery in Latin America but have delayed mortality.

Preterm birth was associated with an increased mortality risk compared with term birth. The proportion of infants born within 32 weeks of gestation was low but these infants had substantially higher mortality risks than did term infants in the first week of life. Late preterm birth comprised 50–96% of preterm births, and was associated with a smaller but statistically significant neonatal mortality risk ranging from 2·52 in Asia to 5·58 in Latin America (risk differences per thousand livebirths were nine in Africa, 11 in Latin America, and 18 in Asia).

Evidence-based, low-cost interventions are feasible for LMICs and could reduce mortality related to preterm birth complications, such as antenatal corticosteroids for preterm labour, Kangaroo mother care, and treatment of neonatal infections. Our findings suggest that simple interventions to target the improved care of late and moderate preterm infants could have a large effect on the reduction of mortality burden in preterm infants. In areas with a large proportion of facility deliveries and much post-delivery care, clinical interventions such as surfactant administration and continuous positive airway pressure might also improve survival.
Using a common US birthweight reference population, the prevalence of SGA and term-SGA babies was very high (higher than 50%) in many of the community-based South Asian cohorts. In statistical modelling to estimate national and regional prevalences of SGA, we estimated that 42% of babies were term-SGA and that 3% of babies were preterm-SGA. These findings contrast with a much lower prevalence of SGA in Africa, despite the high prevalence of risk factors such as malaria and HIV infection in pregnancy. SGA neonates had roughly double the mortality risk of appropriate-for-gestational-age infants, with slightly higher risk in those with more severe SGA. A large proportion of SGA infants weighed 2500 g or more, although their mortality risk was similar to that of term-AGA babies. The very high rates of SGA in South Asia might be explained by higher rates of adolescent pregnancy, chronic maternal malnutrition, low pre-pregnancy body-mass index, low weight gain in pregnancy, and low maternal height.

The mortality risk associated with being preterm-SGA was substantially higher than for either alone. An estimated 2-8 million infants are born both preterm and SGA in LMICs annually and these infants are at a 10-40 times increased risk of dying in the first month of life compared with term and appropriate-for-gestational-age infants. These children are key targets for public health interventions.

A strength of this analysis was the large number of representative livebirths analysed from a wide range of studies and geographical regions, producing internal validity and reduced variance of estimates. We adjusted for several covariates but noted that they did not alter the risk estimates. Although the cohort sizes varied substantially, with the Chilean national registry data dominating in absolute numbers, the use of random effects models to do meta-analyses downweights the effect of such large datasets. Although it constitutes 92% of the data, its contribution to the Latin American mortality risk estimate is about 50% and its contribution to the global estimate is 9-7%. While Chile is probably a good representation of a middle-income country in Latin America, it does not represent other low-income countries in the region. The earliest Brazilian cohort might be more representative of such countries because it was done in a low-income setting.

We re-analysed individual data to estimate SGA prevalence and risk, applying a common SGA reference population. This reduced the variation associated with the use of different SGA reference populations commonly seen across studies. Although the use of a common reference population is a controversial issue, with arguments made about whether it is appropriate to apply one standard to all populations, we selected one reference population to be able to better compare our analyses across populations. Our use of a birthweight rather than fetal growth standard might have systematically under-represented SGA in preterm infants because preterm infants might have more pathological IUGR than fetuses that remain in the womb for longer. The Intergrowth Study is collecting data for a common fetal growth reference using healthy populations from many countries. The use of this standard will help resolve this limitation in the future.

The large sample size allowed us to stratify preterm and SGA into severity categories and to pool mortality risk associated with each category by re-analysing primary data. Available covariates varied by study and residual confounding could have occurred. However, these findings might not be generalisable to countries or regions as a whole because they are derived from cohorts or randomised trials in which the geographical

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**Figure 4:** Relative risk of neonatal mortality associated with preterm and size for gestational age

<table>
<thead>
<tr>
<th>Region</th>
<th>Term and appropriate for gestational age</th>
<th>Preterm and appropriate for gestational age</th>
<th>Preterm and small for gestational age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td>7.9</td>
<td>15.97</td>
<td>58.4</td>
</tr>
<tr>
<td>Africa</td>
<td>8.4</td>
<td>17.85</td>
<td>116.2</td>
</tr>
<tr>
<td>Latin America</td>
<td>2.4</td>
<td>2.85</td>
<td>10.05</td>
</tr>
</tbody>
</table>

Median neonatal mortality rate (per 1000 livebirths): 7.9, 8.4, 2.4

**Figure 5:** Relative risk of early-neonatal, late-neonatal, and post-neonatal infant mortality associated with preterm and size for gestational age

Using a common US birthweight reference population, the prevalence of SGA and term-SGA babies was very high (higher than 50%) in many of the community-based South Asian cohorts. In statistical modelling to estimate national and regional prevalences of SGA, we estimated that 42% of babies were term-SGA and that 3% of babies were preterm-SGA. These findings contrast with a much lower prevalence of SGA in Africa, despite the high prevalence of risk factors such as malaria and HIV infection in pregnancy. SGA neonates had roughly double the mortality risk of appropriate-for-gestational-age infants, with slightly higher risk in those with more severe SGA. A large proportion of SGA infants weighed 2500 g or more, although their mortality risk was similar to that of term-AGA babies. The very high rates of SGA in South Asia might be explained by higher rates of adolescent pregnancy, chronic maternal malnutrition, low pre-pregnancy body-mass index, low weight gain in pregnancy, and low maternal height.

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The large sample size allowed us to stratify preterm and SGA into severity categories and to pool mortality risk associated with each category by re-analysing primary data. Available covariates varied by study and residual confounding could have occurred. However, these findings might not be generalisable to countries or regions as a whole because they are derived from cohorts or randomised trials in which the geographical

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Interventions to prevent preterm exist, several interventions beyond the neonatal period. Although few effective than in Asia. In both these regions, these risks extend to a greater contributor to attributable risk in Latin America associated with a higher mortality risk and seems to be a birth affects a smaller number of neonates but is more recently (during the past decade) maternal micronutrient supplementation. As measurement of gestational age improves in LMICs, targeting interventions and tracking outcomes that reduce the incidence and improve the survival of babies born preterm and SGA rather than with a LBW might more clearly guide progress towards the reduction of child mortality.

Contributors
JK, ACL, and NK did the literature review, collected the data, analysed the data, and drafted the paper. JEL, SC, HB, ME, ZAB, and REB helped draft the analysis plan and reviewed the paper. JKN, AS, MFS, and AV did analyses of their individual studies, contributed data, and reviewed the paper. TM, BAW, LA, FB, AHB, PC, WF, RG, JH, LH, PK, AM, LCM, RN, DO, DR, CS, JT, SCV, CGV, and DWJ contributed data and reviewed the paper.

Conflicts of interest
We declare that we have no conflict of interest.

Acknowledgments
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References


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

Linda S Adair, Caroline H D Fall, Clive Osmond, Aryeh D Stein, Reynaldo Martorell, Manuel Ramirez-Zea, Harshpal Singh Sachdev, Darren L Dahly, Isabelita Bas, Shane A Norris, Lisa Micklesfield, Pedro Hallal, Cesar G Victora, for the COHORTS group

Summary

Background Fast weight gain and linear growth in children in low-income and middle-income countries are associated with enhanced survival and improved cognitive development, but might increase risk of obesity and related adult cardiometabolic diseases. We investigated how linear growth and relative weight gain during infancy and childhood are related to health and human capital outcomes in young adults.

Methods We used data from five prospective birth cohort studies from Brazil, Guatemala, India, the Philippines, and South Africa. We investigated body-mass index, systolic and diastolic blood pressure, plasma glucose concentration, height, years of attained schooling, and related categorical indicators of adverse outcomes in young adults. With linear and logistic regression models, we assessed how these outcomes relate to birthweight and to statistically independent measures representing linear growth and weight gain independent of linear growth (relative weight gain) in three age periods: 0–2 years, 2 years to mid-childhood, and mid-childhood to adulthood.

Findings We obtained data for 8362 participants who had at least one adult outcome of interest. A higher birthweight was consistently associated with an adult body-mass index of greater than 25 kg/m² (odds ratio 1·28, 95% CI 1·21–1·35) and a reduced likelihood of short adult stature (0·49, 0·44–0·54) and of not completing secondary school (0·74, 0·70–0·80). Faster linear growth was strongly associated with a reduced risk of short adult stature (age 2 years: 0·23, 0·20–0·26; mid-childhood: 0·39, 0·36–0·43) and of not completing secondary school (age 2 years: 0·74, 0·67–0·81; mid-childhood: 0·87, 0·83–0·92), but did raise the likelihood of overweight (age 2 years: 1·24, 1·17–1·31; mid-childhood: 1·12, 1·06–1·18) and elevated blood pressure (age 2 years: 1·12, 1·06–1·19; mid-childhood: 1·07, 1·01–1·13). Faster relative weight gain was associated with an increased risk of adult overweight (age 2 years: 1·51, 1·43–1·60; mid-childhood: 1·76, 1·69–1·91) and elevated blood pressure (age 2 years: 1·07, 1·01–1·13; mid-childhood: 1·22, 1·15–1·30). Linear growth and relative weight gain were not associated with dysglycaemia, but a higher birthweight was associated with decreased risk of the disorder (0·89, 0·81–0·98).

Interpretation Interventions in countries of low and middle income to increase birthweight and linear growth during the first 2 years of life are likely to result in substantial gains in height and schooling and give some protection from adult chronic disease risk factors, with few adverse trade-offs.

Funding Wellcome Trust and Bill & Melinda Gates Foundation.

Introduction

Promotion of faster weight gain in children with growth failure is an important goal of paediatric care in countries of low and middle income, in view of the well known associations between poor growth and impaired cognitive development and increased morbidity and mortality. However, some studies suggest that rapid weight gain in the first 2 years of life is related to an increased risk of obesity and insulin resistance later in life. Reports about this so-called catch-up dilemma draw attention to the potential risks and benefits of faster early growth. Much of the concern is based on studies of weight gain in children in high-income countries, without a concomitant consideration of how linear growth and weight gain relative to linear growth affect outcomes later in life. Separation of their effects is important because, although early linear growth strongly predicts adult height, lean body mass, attained schooling, employment, and earnings, excess adiposity is a well recognised risk factor for cardiometabolic diseases. The key questions for paediatricians and policy makers are: what is the optimum age for promotion of growth for enhanced survival and human capital, and will this promotion necessarily lead to an increase in cardiometabolic disease? We explored how birthweight, linear growth, and weight gain relative to linear growth in childhood and adulthood are related to body size and composition, cardiometabolic risk factors (blood pressure and plasma glucose concentrations), and human capital outcomes (height and attained schooling) in young adults. We
compared results across these diverse outcomes to explore possible trade-offs. We focused on birth and the period from 0 to 2 years to provide additional insights into the long-term importance of the first 1000 days—widely recognised as a particularly sensitive period for child health and development.

**Methods**

**Study design and participants**

We used data from five prospective birth cohort studies included in the Consortium for Health Orientated Research in Transitional Societies (COHORTS): the 1982 Pelotas Birth Cohort (Brazil); the Institute of Nutrition of Central America and Panama Nutrition Trial Cohort (Guatemala); the New Delhi Birth Cohort (India); the Cebu Longitudinal Health and Nutrition Survey (Philippines); and the Birth to Twenty Cohort (South Africa). All studies of these cohorts were reviewed and approved by appropriate ethics review boards.

**Procedures**

We identified common ages of childhood measurements across the five sites, and focused on birthweight, birthlength (available for Guatemala, India, and the Philippines), weight and length at age 2 years, and weight and height mid-childhood (aged 4 years for Brazil, Guatemala, India, and South Africa; 8 years for the Philippines). Birthweight was measured in hospitals at delivery in South Africa and Brazil, in the community by research staff within 72 h of birth in India, in hospitals or at home by birth attendants provided with project scales in the Philippines, and by a project nurse at home or in a health-care centre in Guatemala. Gestational age estimates were based on the mother’s report of the date of her last menstrual period. Birthlength was measured by trained research staff within 72 h of birth in India, within 6 days in the Philippines, and by a project nurse at home or in a health-care centre in Guatemala. Gestational age estimates were based on the mother’s report of the date of her last menstrual period. Birthlength was measured by trained research staff within 72 h of birth in India, within 6 days in the Philippines, and 15 days after birth in Guatemala.

Statistical methods are needed to separate the effects of linear growth and weight gain because they are strongly correlated, as are repeat measurements taken in the same individual. We derived standardised residuals by regressing current size (represented as Fisher-Yates transformed weight-for-age and length-for-age Z scores) on all previous size measures to produce conditional size measures. Conditional height is present length or height accounting for previous length or height, and weight (but not present weight). Conditional relative weight is present weight accounting for present height and all previous weight and height measures. For example, adult conditional relative weight is derived from a regression of adult weight on adult height, weight and height at mid-childhood, weight and length when aged 2 years, and birthweight.

Conditional variables represent children’s deviation from the expected size on the basis of their own previous measures and the growth of the other children in each cohort, and can be interpreted as representing faster or slower relative weight gain or linear growth. For example, a child with a positive value for mid-childhood conditional height is taller than expected in view of previous size and thus had a faster rate of linear growth than would be expected from age 2 years to mid-childhood. Our exposure variables represent birthweight and conditional height and conditional relative weight when aged 2 years, during mid-childhood, and during adulthood. Equivalents of the conditional variables (g or kg, and cm) are shown in the appendix (p 20).

We calculated conditional variables separately for each site and sex from the largest sample with complete non-pregnant anthropometric data at all selected ages to avoid bias as a result of including only individuals with adult outcomes. Because birthlength was not available for Brazil and South Africa, we included only birthweight in the regression models for all sites. In separate analyses of the three sites for which data for birthlength were available, we compared results with and without the inclusion of birthlength. Associations of the resulting conditional relative weight and conditional height variables with later outcomes were similar with each method.

Height, weight, and waist circumference were measured with standard techniques. Binary variables represent overweight and obesity (body-mass index [BMI] ≥25 kg/m² or the International Obesity Task Force equivalent for individuals aged <18 years) and short stature (height-for-age Z score <−2 when aged <19 years; or <150·1 cm for women and <161·9 cm for men if aged ≥19 years). Fat mass, fat-free mass, and percentage body fat were calculated with site-specific methods (bioelectrical impedance in Brazil; validated equations including weight, height, and abdominal circumference in Guatemala, or skinfold thickness in India and the Philippines; and dual x-ray absorptiometry [Delphi, Hologic] in South Africa). Within each site and sex, we used a Fisher-Yates transformation to express fat mass and fat-free mass in SD units to enable comparisons within and between sites.

Blood pressure was measured by aneroid sphygmomanometer in Brazil, mercury sphygmomanometer in the Philippines, and digital devices elsewhere ([UA-767 [A and D Medical] in Guatemala; Omron M6 [Omron] in South Africa; and Omron 711 [Omron] in India). Participants were measured seated after 5–10 min of rest, with appropriate cuff sizes. We used the mean of three measurements (Philippines), two measurements (Brazil and India), or the second and third of three measurements (Guatemala and South Africa). In accordance with international recommendations, elevated blood pressure was defined as a systolic blood pressure of 130 mm Hg or more or a diastolic blood pressure of 85 mm Hg or more in view of the young ages and low prevalence of hypertension in several cohorts.

Fasting blood glucose concentration was measured in all cohorts except in Brazil, where a random finger-prick capillary whole-blood sample was obtained and adjusted for time since previous meal. Adjustments were made for more on the first 1000 days see http://www.thousanddays.org

For details of each cohort study see http://www.cohortgroup.org
for differences in plasma, whole venous blood, and capillary values. Participants with glucose concentrations of 6.1 mmol/L or more, or those taking drugs for diabetes were considered to have dysglycaemia (ie, impaired fasting glucose or diabetes).

The number of completed years of schooling was recorded in all sites. As an adverse outcome, a binary variable indicates failure to complete secondary school. Socioeconomic status at birth was represented by gestational age (weeks) affected the coefficients of the conditional variables.

Statistical analysis
We used linear regression for continuous outcomes and logistic regression for categorical outcomes to estimate associations with conditional height and conditional relative weight at different ages. Models for each outcome included the largest sample with complete data. We excluded women who were pregnant at the time of measurement from all analyses. We compared our main analysis sample with samples with adult data but incomplete anthropometric, and with those with birth measures but without adult outcome data by use of Bonferroni-adjusted ANOVA to account for multiple comparisons. To

### Table 1: Characteristics of participants in the five cohorts

<table>
<thead>
<tr>
<th>Brazil</th>
<th>Guatemala</th>
<th>India</th>
<th>Philippines</th>
<th>South Africa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (n=1889)</td>
<td>Women (n=1122)</td>
<td>Men (n=170)</td>
<td>Women (n=1122)</td>
<td>Men (n=584)</td>
</tr>
<tr>
<td>Birthweight (kg)</td>
<td>3.29 (0.52)</td>
<td>3.77 (0.51)</td>
<td>2.85 (0.44)</td>
<td>2.98 (0.41)</td>
</tr>
<tr>
<td>Birthlength (cm)</td>
<td>NA</td>
<td>NA</td>
<td>49.8 (2.4)</td>
<td>48.8 (2.1)</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>39.3 (1.9)</td>
<td>39.3 (1.9)</td>
<td>39.1 (2.5)</td>
<td>39.2 (2.2)</td>
</tr>
<tr>
<td>Adult age (years)</td>
<td>22.7 (0.4)</td>
<td>22.7 (0.4)</td>
<td>31.4 (1.4)</td>
<td>31.1 (1.3)</td>
</tr>
<tr>
<td>Adult height (cm)</td>
<td>173.8 (6.9)</td>
<td>160.9 (6.2)</td>
<td>163.0 (6.1)</td>
<td>151.1 (5.2)</td>
</tr>
<tr>
<td>Adult weight (kg)</td>
<td>72.1 (14.0)</td>
<td>60.6 (12.6)</td>
<td>64.3 (10.1)</td>
<td>61.3 (11.5)</td>
</tr>
<tr>
<td>Adult body-mass index (kg/m²)</td>
<td>23.8 (4.1)</td>
<td>23.4 (4.7)</td>
<td>24.1 (3.3)</td>
<td>26.8 (4.6)</td>
</tr>
<tr>
<td>Adult waist circumference (cm)</td>
<td>80.9 (10.2)</td>
<td>74.8 (10.5)</td>
<td>85.3 (8.3)</td>
<td>92.6 (8.3)</td>
</tr>
<tr>
<td>Adult body fat (%)</td>
<td>16.3 (3.8)</td>
<td>NA</td>
<td>19.4 (5.9)</td>
<td>34.9 (6.9)</td>
</tr>
<tr>
<td>Adult body fat mass (kg)</td>
<td>12.2 (5.0)</td>
<td>NA</td>
<td>13.0 (5.9)</td>
<td>22.1 (8.5)</td>
</tr>
<tr>
<td>Adult fat-free mass (kg)</td>
<td>60.4 (9.6)</td>
<td>NA</td>
<td>51.3 (5.2)</td>
<td>39.1 (3.3)</td>
</tr>
<tr>
<td>Adult diastolic blood pressure (mm Hg)</td>
<td>123.5 (14.4)</td>
<td>111.2 (6.2)</td>
<td>117.0 (10.4)</td>
<td>107.7 (12.2)</td>
</tr>
<tr>
<td>Adult plasma glucose concentration (mmol/L)</td>
<td>5.1 (0.7)</td>
<td>4.9 (0.7)</td>
<td>5.2 (0.6)</td>
<td>5.1 (1.1)</td>
</tr>
<tr>
<td>Number of completed years of schooling</td>
<td>8.9 (3.2)</td>
<td>9.9 (3.1)</td>
<td>5.0 (0.5)</td>
<td>4.8 (0.5)</td>
</tr>
<tr>
<td>Mother’s height (cm)</td>
<td>156.7 (6.1)</td>
<td>156.3 (5.8)</td>
<td>148.5 (4.8)</td>
<td>148.5 (5.3)</td>
</tr>
<tr>
<td>Number of years mother spent in school</td>
<td>6.5 (4.1)</td>
<td>6.6 (4.3)</td>
<td>1.3 (1.6)</td>
<td>1.2 (1.5)</td>
</tr>
<tr>
<td>Body-mass index &gt;25 kg/m²</td>
<td>58.4 (1828) (31.0%)</td>
<td>43.7 (1701) (25.7%)</td>
<td>54.1 (357) (34.4%)</td>
<td>86.1 (641) (61.0%)</td>
</tr>
<tr>
<td>Elevated blood pressure†</td>
<td>66.1 (1828) (35.4%)</td>
<td>24.6 (1701) (12.3%)</td>
<td>29.6 (357) (32.0%)</td>
<td>10.1 (641) (6.6%)</td>
</tr>
<tr>
<td>Dysglycaemia§</td>
<td>148.7 (1828) (9.3%)</td>
<td>98.1 (1701) (5.6%)</td>
<td>4.1 (357) (3.5%)</td>
<td>5.7 (641) (3.7%)</td>
</tr>
<tr>
<td>Short stature§</td>
<td>74.1 (1828) (3.9%)</td>
<td>57.7 (1701) (3.4%)</td>
<td>69.5 (357) (43.5%)</td>
<td>59.1 (641) (41.8%)</td>
</tr>
<tr>
<td>Did not complete secondary school</td>
<td>952 (2770) (43.8%)</td>
<td>651 (1619) (40.2%)</td>
<td>154 (1619) (9.1%)</td>
<td>144 (154) (33.5%)</td>
</tr>
</tbody>
</table>

Data are mean (SD) or n/N (%). Participants had at least one adult outcome of interest and complete anthropometric data. NA=not available. †Female body composition not measured in Brazil because examination occurred at an army recruitment centre. §Systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg. ‡Plasma glucose concentration >6.1 mmol/L or taking drugs for diabetes. ††Height-for-age Z score <-2 when aged <19 years, or <150.1 cm for women or <161.9 cm for men aged ≥19 years.

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assess potential bias related to attrition and missing data, we compared results estimated by Heckman selection models with standard regression models.

We assessed site and sex heterogeneity with $F$ tests, allowing other predictors (eg, age and socioeconomic status) to vary across sites. To measure the variation of effect sizes between combinations of sex and site, we used restricted maximum likelihood to estimate the SD of the effect size for each site and sex around their pooled value. This SD value is close to the SD of estimates specific to each site and sex for each growth variable with each outcome. When it is zero, the effect sizes for each sex and site are compatible with a fixed-effects model.

Glucose and blood-pressure models included birthweight, and conditional height and conditional relative weight when aged 2 years, at mid-childhood, and during adulthood. Because attained schooling cannot be affected by subsequent growth in people who dropped out as children or adolescents, schooling models exclude adult conditional relative weight and conditional height. Adult size outcomes (height, BMI, and body composition measures) also exclude adult conditional height and conditional relative weight. Because conditional height and conditional relative weight variables are not correlated, they can be included together in models without concerns about collinearity.

Because we noted heterogeneity by site and sex for at least one conditional relative weight or conditional height variable in most models, we present results stratified by sex and site; stratified by sex and adjusted for site; and pooled, adjusted for site and sex. Because of the large number of outcomes, we created detailed tables (appendix) that include all estimated coefficients, but summarised results graphically to present site and sex-specific coefficients, with sex-stratified pooled results. We adjusted all models for adult age. Adjustment for gestational age or socioeconomic status at birth did not meaningfully alter coefficients or p values in the models for body composition or cardiometabolic outcomes, so for these models we present results unadjusted for these factors. We adjusted height and schooling models for socioeconomic status at birth, and additionally adjusted height for maternal height to account for differences in genetic growth potential. Information about paternal height was not available. We used Stata (version 12) for analyses.

**Role of the funding source**

The sponsors of the study provided financial support for data management and data analysis, but had no other role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and all authors made the decision to submit for publication.

**Results**

We obtained data for 8362 participants who had provided information about at least one adult outcome of interest.
Participants who were lost to follow-up or excluded because of missing data rarely differed significantly from those who were included (appendix p 2).

Mean adult age at which measurements were taken ranged from about 18 years in South Africa to more than 31 years in Guatemala (table 1). The prevalence of adverse outcomes generally reflects the age and relative economic development of the five samples. Adult height and fat-free mass were highest in Brazilian men (table 1). Dysglycaemia was too rare to analyse in sex-stratified models in the South African cohort (table 1).

Higher birthweight and conditional relative weight at age 2 years and mid-childhood were consistently associated with higher adult BMI in men and women (figure 1, appendix p 5). The association between conditional relative weight and BMI strengthened with age at measurement: overall, BMI increased by 0·5 kg/m² per SD increase in birthweight, by 1·0 kg/m² at 2 years, and 1·3 kg/m² in mid-childhood. Higher conditional height at 2 years and mid-childhood was also associated with higher adult BMI, but coefficients were smaller than those for conditional relative weight and diminished with age (figure 1). The findings were similar for the binary outcome of obesity (table 2, appendix p 6). Heterogeneity between sexes and sites was primarily a result of size rather than direction of coefficients.

All conditional relative weight and conditional height variables were associated with higher adult fat mass and fat-free mass (figure 1, appendix pp 7–8). Coefficients for birthweight and relative weight increased with the age at which size was measured, while conditional height coefficients decreased (figure 1). Birthweight and conditional relative weight at age 2 years were more strongly associated with fat-free mass than with fat mass, contrasting with stronger associations of conditional relative weight in mid-childhood with fat mass than with fat-free mass (appendix pp 7–8). Conditional height at age 2 years and mid-childhood were more strongly associated with fat-free mass than with fat mass, and both associations were stronger at 2 years than at mid-childhood. The findings for percentage body fat and waist circumference (appendix pp 9–10, 21–22) were similar to those for fat mass and BMI. Heterogeneity between sexes and sites was greater for fat mass than for fat-free mass.

Birthweight was unrelated to systolic blood pressure (figure 2, appendix p 11). Higher conditional relative weight at all ages was associated with higher systolic blood pressure, and the associations strengthened with increasing age at measurement (figure 2). Conditional height at age 2 years and mid-childhood was also positively related to systolic blood pressure (figure 2).

The association between birthweight and systolic blood pressure was not the same in Guatemala as in other sites (figure 2, appendix p 11). The β coefficients for associations between conditional relative weight at mid-childhood and adulthood and conditional height at 2 years were larger in men than in women (appendix p 11). The findings were similar for diastolic blood pressure and elevated blood pressure (table 2, appendix pp 12–13, 23), except that higher birthweight was associated with a reduced likelihood of elevated blood pressure in adulthood (table 2).

Conditional relative weight in adulthood and, in women only, in mid-childhood were associated with higher plasma glucose concentration in adulthood (figure 2, appendix p 14). Conditional relative weight at age 2 years was unrelated to glucose, and birthweight was inversely associated with plasma glucose concentration in women (figure 2, appendix p 14). Conditional height at any age was unrelated to adult plasma glucose concentration (figure 2, appendix p 14). The findings were similar for dysglycaemia (table 2, appendix p 15). Heterogeneity between sexes and sites was significant only for conditional height at age 2 years (appendix).

Each SD of birthweight predicted 1·5 cm higher adult height in the pooled sample (figure 3). Conditional relative weight at age 2 years was unrelated to adult height, but conditional relative weight at mid-childhood was inversely related (figure 3, appendix p 16). By contrast, increased conditional height at age 2 years and mid-childhood strongly predicted an increase in adult height in all sites (3·2 cm per SD increase in conditional height at age 2 years and 1·9 cm per SD mid-childhood; figure 3,

See Online for appendix

<table>
<thead>
<tr>
<th>Body-mass index &gt;25 kg/m²</th>
<th>Elevated blood pressure*</th>
<th>Dysglycaemia†</th>
<th>Short stature‡</th>
<th>Did not complete secondary school</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall number affected</td>
<td>2170/8297 (26·2%)</td>
<td>1571/8233 (19·1%)</td>
<td>511/6947 (7·4%)</td>
<td>1235/8302 (16·0%)</td>
</tr>
<tr>
<td>Birthweight</td>
<td>1·28 (1·21–1·35)</td>
<td>0·93 (0·88–0·99)</td>
<td>0·89 (0·81–0·98)</td>
<td>0·49 (0·44–0·54)</td>
</tr>
<tr>
<td>Conditional relative weight at age 2 years</td>
<td>1·51 (1·43–1·59)</td>
<td>1·07 (1·01–1·13)</td>
<td>0·95 (0·86–1·04)</td>
<td>0·94 (0·86–1·03)</td>
</tr>
<tr>
<td>Conditional relative weight mid-childhood</td>
<td>1·76 (1·66–1·86)</td>
<td>1·22 (1·15–1·30)</td>
<td>1·08 (0·98–1·18)</td>
<td>1·13 (1·04–1·23)</td>
</tr>
<tr>
<td>Conditional height at age 2 years</td>
<td>1·24 (1·17–1·31)</td>
<td>1·12 (1·06–1·19)</td>
<td>0·98 (0·89–1·18)</td>
<td>0·23 (0·20–0·25)</td>
</tr>
<tr>
<td>Conditional height mid-childhood</td>
<td>1·12 (1·06–1·18)</td>
<td>1·07 (1·01–1·13)</td>
<td>0·94 (0·86–1·03)</td>
<td>0·39 (0·36–0·43)</td>
</tr>
</tbody>
</table>

Data are n/N (%) or odds ratio (95% CI). Odds ratios calculated with logistic regression models of the pooled sample and indicate how a difference of 1 SD in each measure affects the likelihood of the adverse outcome. All models were adjusted for adult age. The models for short stature and completion of secondary school were further adjusted for mother’s education and household wealth at birth; the model for short stature was also adjusted for mother’s height. *Systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg. †Plasma glucose concentration ≥6·1 mmol/L or taking drugs for diabetes. ‡Height z score <–2 when aged <19 years; <150·1 cm for women or <161·9 cm for men when aged ≥19 years.
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Heterogeneity was a result of site and sex differences in the size rather than direction of coefficients (coefficients in men more than coefficients in women). Birthweight and conditional height at age 2 years and mid-childhood were strongly inversely related to the chance of short adult stature (table 2, appendix p 17).

One SD higher birthweight predicted about 0·2 years more schooling (figure 3, appendix p 18). One SD higher conditional relative weight at 2 years was associated with 0·14 years more schooling in men, but there was no association in women. Conditional relative weight at mid-childhood was unrelated to attained schooling (figure 3).

In Guatemala, conditional relative weight at 2 years was inversely related to attained schooling in both sexes (appendix p 19); by contrast, higher conditional height at 2 years was strongly related to higher attained schooling (except in South Africa), with one SD in conditional height at 2 years relating to a half year increase in the pooled sample (figure 3). Lower birthweight and conditional height at age 2 years were associated with increased odds of failing to complete high school (table 2, appendix p 19).

Overall, heterogeneity reflected differences between sites rather than between sexes.

Estimations produced by Heckman selection models did not produce coefficients that were substantially different from those estimated with standard linear and logistic regression models.

Discussion

We have shown that higher birthweight is related to increased likelihood of adult overweight in five populations in countries of low and middle income, but to lower likelihood of other adverse outcomes. Although higher conditional relative weight at age 2 years was associated with higher risk of adult overweight and a slightly increased risk of elevated blood pressure, it was unrelated to dysglycaemia, adult stature, or educational attainment. By contrast, conditional relative weight in mid-childhood was associated with higher likelihood of adult overweight and elevated blood pressure, but was unrelated to schooling. Although associated with slightly increased likelihood of adult overweight (mostly related to lean mass) and elevated blood pressure, higher conditional heights at age 2 years and at mid-childhood were related to lower risk of short stature and poor educational attainment.

Few studies from low-income and middle-income settings have followed up cohorts to adulthood. Individuals in the cohorts that we studied were born when poor early life nutrition was more common than it is now, which is shown by the high prevalence of stunting during infancy.30 However, the individuals grew up in rapidly changing environments that fostered development of obesity and chronic disease risk. Countries that are challenged by the dual burden of persistent undernutrition and emerging obesity need information about the many effects of early child growth, particularly during the important first 1000 days. Although the studies included in our analysis cannot be fully representative of the countries in which they were done, the many similarities of results across settings suggest that results may be generalised to other low-income and middle-income settings.

Another strength of our study is that we were able to separate linear growth from relative weight gain. Weight gain is a result of linear growth and soft tissue gain (fat mass and fat-free mass); our conditional relative weight variables represent weight change that is separated from change in height. Conditional relative weight and conditional height variables are uncorrelated, and we expressed them in SD units to allow direct comparison of coefficients within regression models. Our variables

Figure 2: Association of birthweight, conditional relative weight, and conditional height with (A) systolic blood pressure and (B) log plasma glucose concentrations

Site-specific datapoints represent β coefficients from linear regression models done separately for each site and sex. *Significant heterogeneity between sexes and sites.
therefore have advantages when compared with other representations of growth, and give more nuanced results than do those that are based on weight gain alone. In our study, one SD in conditional relative weight at 2 years corresponds to change in weight-for-age Z score from birth to 2 years that is slightly less than the 0.67 units typically used to define rapid weight gain. In a previous COHORTS report, one SD of conditional weight at age 2 years related to 0.4 years more schooling. Here, we showed that attained schooling was predominantly associated with conditional height in the first 2 years, and an increase in conditional relative weight in this period contributed to a rise of only 0.09 years of schooling. These findings are important, because an extra half year of schooling is associated with a 5% annual return to income.

Each estimate for conditional relative weight or conditional height represents an independent age-specific association. We noted that associations of conditional relative weight with adult adiposity and cardiometabolic risk factors strengthened substantially with age. Thus, the most important period for adverse associations of higher relative weight gain with adult cardiometabolic risk was after the age of 2 years. This finding is consistent with the ALSPAC study in the UK, which also showed that associations of conditional weight for length after infancy with systolic blood pressure and BMI were strongest at age 10 years, and with previous studies that showed increased risks related to fast weight gain after infancy. By contrast, for cardiometabolic risk factors, conditional height coefficients were smaller than conditional relative weight coefficients and decreased with age, which is consistent with a Brazilian study.

In view of the nature of conditional growth variables, we could assess independent associations of birthweight with subsequent outcomes, without concern about statistical issues such as the reversal paradox. Furthermore, in our analysis, gestational age was not a confounder of the relation between conditional variables and adult outcomes. A separate analysis of COHORTS data (unpublished) established that a premature birth or being small for gestational age were related to persistent deficits in adult height and schooling, but did not affect blood pressure or plasma glucose concentrations.

We addressed potential trade-offs of different early growth patterns by comparing human capital outcomes known to be associated with impaired child growth and development with cardiometabolic disease risk factors. Birthweight and faster conditional relative weight in the first 2 years of life had little relation with adult cardiometabolic risk factors, but were important for fat-free mass. Indeed, early weight gain was more strongly associated with adult fat-free mass than with adult fat mass. This finding could explain the negative associations of birthweight and the small or non-significant associations of early relative weight gain with elevated blood pressure and dysglycaemia. Faster mid-childhood relative weight gain was more strongly associated with fat mass than fat-free mass, and increased risk of elevated blood pressure and dysglycaemia. The positive associations of all growth variables at all ages with adult BMI and risk of overweight and obesity are probably a result of their joint effect on fat mass and fat-free mass, and the fact that overweight adults have highly variable amounts of body fat.

Despite being restricted to participants with complete data, the sample that we analysed differed little from individuals who were excluded, and estimates produced with Heckman selection models were not different from models estimated with conventional methods. Therefore, our estimated coefficients do not seem to have been biased by attrition or missing data. Some
Panel: Research in context

Systematic review
A 2008 systematic review examined how birthweight and weight-for-age and length-for-age Z scores at age 2 years related to adult human capital and chronic disease risk. Therefore, we searched PubMed for reports published in any language since Jan 1, 2009, which related birthweight and childhood growth rates to these same adult outcomes. We focused on studies that attempted to assess both weight gain and linear growth at different ages, and that involved appropriate statistical methods to differentiate their effects on subsequent outcomes. Our search terms were “weight gain”, “linear growth”, “rapid weight gain”, “birth cohorts”, and “prospective studies”. Few identified studies were done in low-income and middle-income countries, and few used the statistical methods needed to model correlated life course data. Although many reports associate rapid weight gain with obesity and related outcomes, we identified only two that directly compared how linear growth and relative weight gain related to adult blood pressure, glucose metabolism, body composition, height, or schooling. No report directly compared several outcomes representing health and human capital to enable assessment of risks and benefits of early growth patterns.

Interpretation
We have studied life course determinants of young adult human capital and disease risk factors in five countries of low and middle income, by using appropriate statistical methods to directly compare how faster relative weight gain and faster linear growth relate to these outcomes. We have shown that effects on the different outcomes are age specific. Fast linear growth in the first 2 years of life is associated with increased adult height and amount of schooling. Adverse associations with fast relative weight gain are largely confined to mid-childhood and adulthood. Our data support the current focus on promotion of nutrition and linear growth in the first 1000 days of life (from conception to age 2 years), and also reinforce the importance of prevention of rapid relative weight gain after age 2 years. These findings have implications for present practices in low-income and middle-income countries, particularly emphasising the need to monitor linear growth as well as weight, and to avoid promotion of excess weight gain in children older than 2 years. Optimum growth patterns in early life are likely to lead to less undernutrition, increased human capital, and reduced risks of obesity and non-communicable diseases, thus addressing both components of the double burden of nutrition.

differences between our cohorts were unavoidable, such as methods for measurement of birthweight, plasma glucose concentration, blood pressure, and adult body composition, and also age at mid-childhood and adulthood. Our choice of age intervals was determined by the availability of measurements in each cohort rather than what we might have chosen for the greatest biological signal, such as within the first 2 years. Heterogeneity, as represented by significant site or sex interactions, or both, with key exposures, could be a result of the differences between cohorts or true effect modification. Although data for 48 months were not available in the Philippines, mid-childhood estimates did not differ systematically from other sites. Although our cohorts differed in childhood size and adult cardiometabolic risk profile, significant site and sex heterogeneity mostly reflected differences in size of associations, not direction. Therefore, use of pooled analyses to draw conclusions seems to be justified. Outliers were usually from Guatemala (which provided the smallest sample) or South Africa (the youngest). For example, the unique absence of an association between early height gain and schooling in South Africa is probably because participants aged 18 years had no opportunity for education after secondary school. Additionally, the absence of significant predictors of glucose concentration in South Africa is probably a result of the cohort’s young age and little variation in glucose concentration (few concentrations were >6 mmol/L).

Our findings suggest that interventions to increase birthweight and linear growth during the first 2 years of life are likely to result in substantial gains in height and schooling (key aspects of human capital), and give some protection from development of adult chronic disease risk factors, with no or negligible adverse trade-offs. Consistent with a growing body of research, our results indicate that faster relative weight gain after the age of 2 years has little benefit for human capital, and weight gain after mid-childhood could lead to large adverse effects on later cardiovascular risk factors. Notably, this finding is particularly true for weight gain that is not accompanied by height gain. Our data support the present focus on promotion of improved nutrition and linear growth in the first 1000 days of life, and also reinforce the importance of prevention of rapid relative weight gain after age 2 years.

Although the associations we describe do not prove causation, our results challenge several programmes in countries of low and middle income (panel). Rapid weight gain should not be promoted after the age of 2–3 years in children who are underweight but not wasted. Growth monitoring programmes should incorporate length and height measures, not just weight measures. New interventions that specifically promote linear growth instead of weight gain should be developed, tested, and promoted; exclusive breastfeeding, high-quality protein (eg, animal), and micronutrients could be further investigated. Traditional school feeding programmes that increase BMI with little effect on height might be doing more harm than good in terms of future health.

Mortality and undernutrition are falling substantially in most parts of the world, except for Sub-Saharan Africa, and new targets are being formulated to replace the present set of 2015 Millennium Development Goals.
analyses provide strong justification for the proposal of a new goal for optimum linear growth that is expressed as a reduction in stunting. This goal should replace the present target of a reduction in underweight alone, which is one of the indicators for the first Millennium Development Goals towards the eradication of extreme poverty. Whereas promotion of linear growth in early life could build human capital in adults without increasing the burden of non-communicable diseases, the present focus on underweight might have detrimental repercussions, particularly if interventions take place after 1000 days.

Contributors
LSA, CHDF, and CO led the writing team. LSA and CO did data analysis. LSA and CHDF wrote the report and had final responsibility for the content. All authors contributed to data collection, and reviewed analyses. LSA and CHDF wrote the report and had final responsibility.

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References