Child survival II

How many child deaths can we prevent this year?

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This is the second of five papers in the child survival series. The first focused on continuing high rates of child mortality (over 10 million each year) from preventable causes: diarrhoea, pneumonia, measles, malaria, HIV/AIDS, the underlying cause of undernutrition, and a small group of causes leading to neonatal deaths. We review child survival interventions feasible for delivery at high coverage in low-income settings, and classify these as level 1 (sufficient evidence of effect), level 2 (limited evidence), or level 3 (inadequate evidence). Our results show that at least one level-1 intervention is available for preventing or treating each main cause of death among children younger than 5 years, apart from birth asphyxia, for which a level-2 intervention is available. There is also limited evidence for several other interventions. However, global coverage for most interventions is below 50%. If level 1 or 2 interventions were universally available, 63% of child deaths could be prevented. These findings show that the interventions needed to achieve the millennium development goal of reducing child mortality by two-thirds by 2015 are available, but that they are not being delivered to the mothers and children who need them.

The first paper in this series on child survival presented an unacceptable picture: more than 10 million children dying every year, almost all in low-income countries or poor areas of middle-income countries.[1] 90% of these deaths occurred in just 42 countries,[2] most from one of a short list of causes: diarrhoea, pneumonia, measles, malaria, HIV/AIDS, and the underlying cause of undernutrition for deaths among children younger than 5 years, and asphyxia, preterm delivery, sepsis, and tetanus for deaths among neonates.[1] The assessment of deaths by cause provides a useful starting point for a stocktaking of available child survival interventions.

In this paper we review the state of the evidence for interventions to reduce child mortality for each of the major direct and underlying causes of death in children younger than 5 years (under-5 deaths). The term intervention is used here in a limited sense to refer to a biological agent or action intended to reduce morbidity or mortality. Approaches used to reach children and mothers with the interventions they need are referred to as delivery strategies. We draw on existing research reports and systematic reviews to document the efficacy or effectiveness of each intervention in reducing mortality among children younger than 5 years, to summarise current coverage with these interventions, and to estimate how many child deaths could be prevented if proven interventions were delivered to all the children and mothers who need them. Delivery strategies are addressed in the next paper in the series.[3]

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Our aim, then, is to assess the potential effect of translating current knowledge about child survival interventions into effective action. These questions take on added urgency in view of the millennium development goals, which were set in 2001 and adopted by the member states of the UN.[4] One of these eight goals is to reduce child mortality by two-thirds between 1990 and 2015.[4] We have just passed the halfway mark in this period, and unless there is substantial change, very soon, the target will be out of reach.

Identifying effective child survival interventions

Child mortality is the result of a complex web of determinants at many levels.[5] Although we recognise the important role played by distal determinants such as poverty and characteristics of the physical environment, we focus here on interventions addressing the more proximal determinants of child mortality and those that can be delivered mainly through the health sector. Interventions that addressed more distal determinants, or that would normally be implemented by sectors other than health, were not considered (eg, maternal education, reduction of crowding). Interventions include preventive approaches that may reduce the exposure to the infection or condition[6] or reduce the likelihood of exposure that leads to disease, and both preventive and treatment approaches to reduce the likelihood that the disease or

Search strategy

Estimates of the effectiveness of the interventions were taken either from published articles that summarised previous research results or from systematic reviews by the authors or others in the Bellagio Child Survival Study Group. For the latter, the approach was generally to search for original research reports or reviews using MEDLINE, POPLINE, and other databases. The Cochrane database of randomised controlled trials and WHO Reproductive Health Library were also consulted. Participants in the Bellagio Child Survival Study Group and other experts were asked to contribute based on their extensive knowledge and experience with a wide range of interventions.

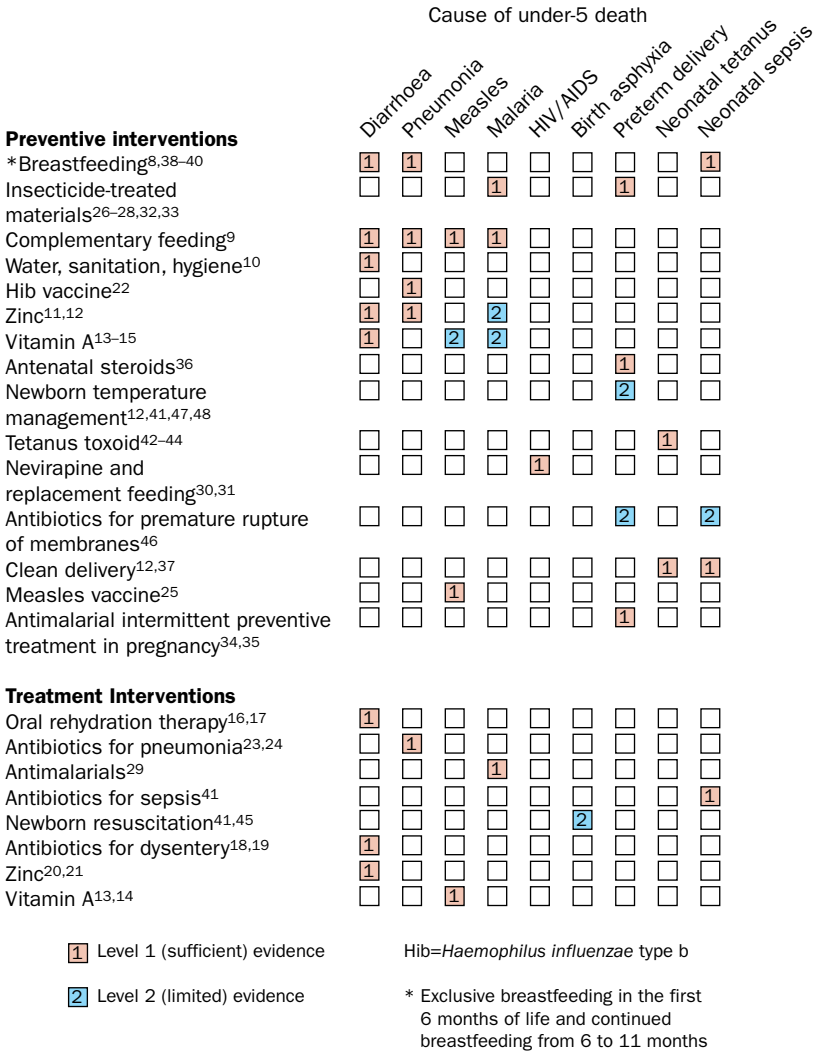

Figure 1: **Child survival interventions with sufficient or limited evidence of effect on reducing mortality from the major causes of under-5 deaths**

condition will lead to death. We focus specifically on interventions that address deaths by cause for the 42 countries with 90% of worldwide under-5 deaths in 2000.[2]

Feasibility for delivery at high levels of population coverage is a central criterion for any intervention intended to reduce child mortality. What is feasible, however, varies widely even among low-income countries. We have therefore focused on an essential set of interventions judged to be feasible for high levels of implementation in low-income countries, assuming that additional interventions can be added and further lives saved in countries with greater levels of resources and health-system capacity.

Each potential intervention was assigned to one of three levels based on the strength of the evidence for its effect on child mortality. Operational definitions for each level were adapted from those used by the International Association for Research on Cancer.[7]

Level 1—sufficient evidence of effect: the working group for this paper believed that a causal relationship had been established between the intervention and reductions in cause-specific mortality among children younger than 5 years in developing countries.

Level 2—limited evidence of effect: the working group believed that an effect was possible, but available data were not sufficient to establish a causal relationship, because, for example: there was conflicting evidence from several studies; low-income countries were not adequately represented in the studies, or there were too few studies to generalise globally; there were unresolved questions about the adequacy of the design, conduct, or interpretation of the studies or the intervention reduced morbidity or risk, but a clear link to mortality had not been established.

Level 3—inadequate evidence of effect: the available data could not be interpreted as showing either the presence or absence of an effect on under-5 mortality because of major qualitative or quantitative limitations.

Information was obtained from published research studies and systematic reviews. 21 interventions supported by level 1 or level 2 evidence are shown in figure 1.[8–48] Zinc and vitamin A are effective both as preventive and therapeutic interventions, leading to a total of 23 measures. The results of the review show that at least one level-1 intervention feasible for implementation at high coverage in low-income countries is available to prevent or treat each of the main causes of under-5 deaths, apart from birth asphyxia, for which a level-2 intervention is available.

Limited evidence of effect was available for three interventions addressing causes of death in the neonatal period—newborn temperature management, antibiotics for premature rupture of the membranes, and newborn resuscitation—showing that neonatal deaths have only recently been identified as a global priority and that there is urgent need for further research in this area. There is sufficient or limited evidence that five of the studied interventions may be effective against more than one of the major causes of death. Further focused research efforts can expand the list of interventions with sufficient evidence of effect to include those with limited evidence of effect at present.

Level-3 interventions, for which current levels of evidence were judged to be inadequate, include those that hold promise of substantial effects on child mortality but have not yet been fully assessed. Several of these interventions are likely to be proven effective for wide scale, affordable use in the near future; these include rotavirus vaccine for diarrhoea prevention,[49] pneumococcal vaccine[50] and reduction of indoor air pollution for prevention of pneumonia;[51] zinc for treatment of pneumonia (Black RE, personal communication); antimalarial intermittent preventive treatment in infants;[52] and advances in low-cost prevention and treatment of HIV in children.

Additionally, several interventions were not considered here because, although they are supported by various levels of evidence, they are not currently feasible for implementation at high coverage in low-income areas (eg, secondary care of newborns).

	Mean estimated coverage of target population (range among countries*)
Preventive interventions	
Breastfeeding (6–11 months)	90% (42–100)
Measles vaccine	68% (39–99)
Vitamin A	55% (11–99)
Clean delivery (skilled attendant at birth)	54% (6–89)
Tetanus toxoid	49% (13–90)
Water, sanitation, hygiene	47% (8–98)
Exclusive breastfeeding (<6 months)	39% (1–84)
Newborn temperature management	20%
Antibiotics for premature rupture of membranes	10%
Antenatal steroids	5%
Nevirapine and replacement feeding	5%
Insecticide-treated materials	2% (0–16)
Hib vaccine	1%
Antimalarial intermittent preventive treatment in pregnancy	1%
Zinc	0%
Complementary feeding	†
Treatment interventions	
Vitamin A	55% (11–99)
Antibiotics for pneumonia	40%
Antibiotics for dysentery	30%
Antimalarials	29% (3–66)
Oral rehydration therapy	20% (4–50)
Antibiotics for sepsis	10%
Newborn resuscitation	3%
Zinc	0%

Data source: State of the World's Children 2003.[2] *Where available. For interventions with no country-level coverage data a single estimate was used for all countries. †The mean weight for age *z* score was used (see text).

Table 1: **Coverage estimates for child survival interventions for the 42 countries with 90% of worldwide child deaths in 2000**

Current coverage with effective child survival interventions

Table 1 shows estimates of global coverage for the preventive and therapeutic interventions with sufficient or limited evidence of effect on child mortality. These estimates were derived from UNICEF child health data sets[2] and other sources (details are available at http://www.childinfo.org/bellagio.htm).[53] Coverage rates are fairly high for a few interventions (breastfeeding, measles vaccine), but for most countries and most interventions coverage is low or very low. *Haemophilus influenzae* type b (Hib) vaccine coverage was universally low and, with few exceptions, insecticide-treated net coverage rates in malarious areas were well below 5%.

These findings show that we have the knowledge and instruments to reduce child mortality, but that children continue to die because the interventions are not reaching them. Poor children are far less likely to receive these interventions than children living in families, communities, and countries with more resources,[54] as shown by the geographical distribution of under-5 deaths.[1] In the next section we examine how many child deaths could be prevented if these inequities were overcome and universal coverage with child survival was achieved.

How many children could we save?

Methods and assumptions

The starting point for this exercise is the 9·7 million children who died in the 42 countries with 90% of the 10·8 million child deaths in 2000.[2] For each of these countries, we first calculated how many deaths from a specific cause could be prevented if present coverage levels were increased to universal coverage. Universal coverage was defined as 99% for all interventions except exclusive breastfeeding among children under 6 months of age, for which the target was set at 90%.

Assumptions about intervention efficacy were based on the review of evidence discussed earlier in this paper. No numerical estimate of effect on mortality was available for complementary feeding among children aged 6 months to 5 years,[9] for which there is sufficient (level 1) evidence of effectiveness against deaths due to diarrhoea, pneumonia, measles, and malaria. This effect is mediated by weight-for-age (underweight) status. A review of controlled trials designed to improve intake of complementary foods[9] showed a mean increase of 0·35 *z* score in weight-for-age. Mean *z* scores were estimated for each country based on current prevalence of underweight, assuming underweight was distributed normally with an SD of 1. This value is typical of what is observed empirically across the whole range of underweight prevalences.[55] Based on the same distribution, the baseline proportion of children in each risk category (severe, <-3 *z* scores; moderate, $-3 \leqslant z$ scores <-2; mild, $-2 \leqslant z$ scores <-1) was calculated. After adding 0·35 *z* score to the mean weight-for-age for each country, these proportions were recalculated. Applying the shift in the weight-for-age distribution with the odds ratio for each category,[56] the reduction in average risk of mortality from each cause (diarrhoea, pneumonia, measles, and malaria) was calculated. The recommended age for the introduction of complementary foods is 6 months,[8] so the potential benefits of complementary feeding were applied only to deaths in children older than 6 months.

For each country, we used the percent increase needed to achieve universal coverage among the target population and the estimates of intervention efficacy to estimate the potential deaths that could be prevented. For example, for

	Estimated under-5 deaths prevented	
	Number of deaths ($\times 10^3$)	Proportion of all deaths
Preventive interventions		
Breastfeeding	1301	13%
Insecticide-treated materials	691	7%
Complementary feeding	587	6%
Zinc	459 (351)*	5% (4%)*
Clean delivery	411	4%
Hib vaccine	403	4%
Water, sanitation, hygiene	326	3%
Antenatal steroids	264	3%
Newborn temperature management	227 (0)*	2% (0%)*
Vitamin A	225 (176)*	2% (2%)*
Tetanus toxoid	161	2%
Nevirapine and replacement feeding	150	2%
Antibiotics for premature rupture of membranes	133 (0)*	1% (0%)*
Measles vaccine	103	1%
Antimalarial intermittent preventive treatment in pregnancy	22	<1%
Treatment interventions		
Oral rehydration therapy	1477	15%
Antibiotics for sepsis	583	6%
Antibiotics for pneumonia	577	6%
Antimalarials	467	5%
Zinc	394	4%
Newborn resuscitation	359 (0)*	4% (0%)*
Antibiotics for dysentery	310	3%
Vitamin A	8	<1%

*Numbers represent effect if both levels 1 (sufficient) and 2 (limited) evidence are included, value number in brackets shows effect if only level-1 evidence is accepted. Interventions for which only one value is cited are all classified as level 1.

Table 2: **Under-5 deaths that could be prevented in the 42 countries with 90% of worldwide child deaths in 2000 through achievement of universal coverage with individual interventions**

insecticide-treated materials (ITMs) we obtained data on current national coverage levels and assumed that this would increase to 99%. We then applied the efficacy of ITMs to reduce malaria deaths, and calculated how many of these deaths would be prevented in each country. For interventions that only apply to a subset of the population, estimates of effect were restricted to these subsets. For example, vitamin A was assumed to have an effect only on children aged 6–59 months who were deficient in this vitamin. Full details of methods and assumptions used in this exercise are available at http://www.childinfo.org/bellagio.htm.[53]

Achievement of universal coverage with individual interventions

Table 2 presents the numbers and proportions of child deaths that could be prevented through application of each intervention alone under two sets of conditions: (1) applying only those interventions for which there is sufficient evidence of effect (level 1); and (2) also applying interventions for which there is limited evidence of effect (levels 1 and 2). Two interventions—oral rehydration therapy and breastfeeding—were each estimated to prevent over 10% of deaths. Six further interventions could each prevent at least 5% of child deaths. These include ITMs, improvement of complementary feeding, antibiotics for neonatal sepsis, antibiotics for pneumonia, antimalarial treatment, and preventive zinc supplementation.

Promotion of breastfeeding in countries with a high prevalence of HIV among women of reproductive age may increase mother-to-child transmission of this virus. This drawback was taken into account in the modelling exercise; otherwise, breastfeeding would have been estimated to prevent 15% instead of 13% of child deaths.

Universal coverage with multiple interventions

We then estimated the number of child deaths, by cause, that could be prevented if the full set of interventions for each cause were delivered at universal coverage levels. To avoid the unrealistic scenario of preventing the same death through more than one intervention, the effect of each additional intervention was applied only to deaths not already prevented by the previously applied interventions. Therefore, the overall effect of applying multiple interventions does not equal the sum of individual intervention effects presented in table 2, which exceeds 100%.

The total proportion of deaths prevented, for any given cause, is independent of the sequencing of the interventions. Although it may make intuitive sense to apply prevention interventions before therapeutic interventions, the summary estimate of effect from our model is independent of this sequence.

Table 3 shows estimates of annual preventable deaths by cause among the 9·7 million child deaths in the 42 countries considered. About 5·5 million deaths (57%) could be prevented by achieving universal coverage with interventions for which there is sufficient evidence (level 1), and 63% if both the sufficient and limited interventions (levels 1 and 2) were universally implemented.

Universal coverage in countries with specific epidemiological profiles

The first paper in the series defined five different country profiles on the basis of proportional distribution of causes of child deaths.[1] All these countries have substantial child mortality due to neonatal causes, diarrhoea, and pneumonia. Countries were categorised as: profile 1 (accounting for 46% of child deaths)—low (less than 10%) AIDS and malaria and low (less than 40%) neonatal; profile 2 (27%)—low AIDS and high malaria; profile 3 (16%)—high neonatal; profile 4 (8%)—high AIDS and malaria; and profile 5 (3%)—high AIDS and low malaria. Figure 2 shows the proportion of under-5 deaths that could be prevented within each of these profiles if the interventions we considered (with either sufficient or limited levels of evidence) were delivered at universal coverage levels. The estimate of preventable deaths ranges from a 54% reduction in child deaths for countries with profile 3 to a 73% reduction in profile-2 countries. The results show that remarkable progress could be made in all countries, regardless of their epidemiological profile, by use of the interventions that are available today and feasible for implementation in low-income countries.

Universal coverage with specific groups of interventions

Thus far we have investigated the potential effects of single interventions, of interventions directed at reducing mortality from specific causes, and at the levels of effect that could be achieved in countries with specific epidemiological profiles. In the real world, however, interventions are often brought together based on the

	Number ($\times 10^3$) of under-5 deaths in 2000* (% of total)	Estimated under-5 deaths prevented	
		Number ($\times 10^3$)	Proportion of total for specified disease
Disease or condition			
Diarrhoea	2135 (22%)	1886	88%
Pneumonia	2055 (21%)	1328	65%
Malaria	915 (9%)	829 (812)†	91% (89%)†
HIV/AIDS	312 (3%)	150	48%
Measles	103 (1%)	103	100%
Neonatal disorders‡	3187 (33%)	1743 (1214)†	55% (38%)†
Birth asphyxia	924 (10%)	359 (0)†	39% (0%)†
Sepsis	797 (8%)	750 (745)†	94% (94%)†
Preterm delivery	765 (8%)	453 (288)†	59% (38%)†
Tetanus	223 (2%)	181	81%
Other	478 (5%)	0	0%
Other	919 (10%)	0	0%
Total	9662 (100%)	6040 (5531)†	63% (57%)†

*Proportional distribution of deaths as produced by the cause-of-death prediction model.[1] †Values represent effect if both levels 1 (sufficient) and 2 (limited) are included, and the number in brackets if only level-1 evidence is accepted. Interventions for which only one value is cited are all classified as level 1. ‡Proportional distribution of deaths in the neonatal period are based on WHO global estimates for 2000 in the State of the World's Newborns report, available at http://www.savethechildren.org/mothers/newborns/thread1.shtml.

Table 3: **Under-5 deaths from specific causes that could be prevented in the 42 countries with 90% of worldwide child deaths in 2000 through child survival interventions addressing that cause**

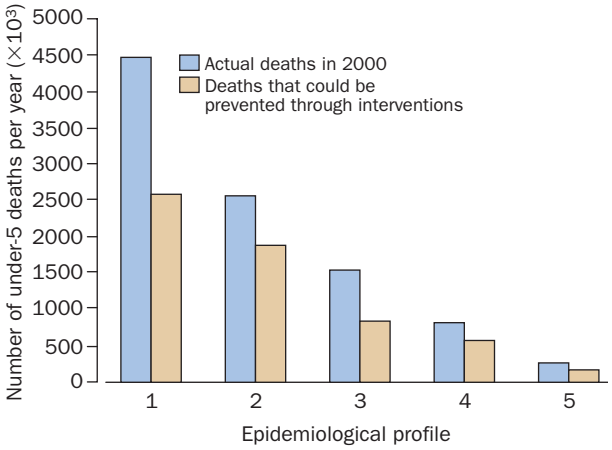

Figure 2: **Actual and preventable under-5 deaths by country profiles for the 42 countries with 90% of under-5 deaths in 2000**

particular age of the child, the specific types of services needed, or as will be suggested in the next paper in the series, based on the potential for combined service delivery. For example, among children living in the 42 countries with 90% of child deaths, a group of effective nutrition interventions including breastfeeding, complementary feeding, vitamin A, and zinc supplementation could save about 2·4 million children each year (25% of total deaths). Effective and integrated case management of childhood infections (diarrhoea and dysentery, pneumonia, malaria, and neonatal sepsis) could save 3·2 million children each year (33% of total deaths). Case-management of interventions is part of Integrated Management of Childhood Illness, a strategy that also includes preventive interventions including breastfeeding promotion and immunisations.[57]

Interventions against deaths in the neonatal period could prevent 55% of these deaths (table 2), or 18% of all child deaths. Although skilled delivery care was not included in the model as a separate intervention, several of its components were considered separately, such as clean delivery, resuscitation, temperature management, and antibiotics for premature rupture of membranes.

It is important to note that some of the most promising interventions may be delivered at the household level, with limited need for external material inputs; these include promotion of breastfeeding, oral rehydration therapy, education on complementary feeding, and insecticide-treated materials. These interventions could jointly prevent more than one-third of all deaths.

Further assessments of the effect that can be expected from groups of interventions—especially those that could be delivered together without further exacerbating inequities—will be useful at country level where local policies, needs, resources, and careseeking patterns can be taken into account.

Further deaths that could be prevented

There are four reasons why this estimate of preventable under-5 deaths is conservative. First and most importantly, only interventions for which cause-specific evidence of effect was available were included in the model. An example of an intervention that was not included is extension of the interval between births to 24 months, which has been estimated to reduce under-5 mortality by 19% in India,[58] and 11% in Nigeria (Rutstein S, personal communication), after controlling for confounding variables including the outcome of the previous birth. Inclusion of birth spacing and other interventions for which cause-specific estimates of effects are not currently available would further increase the proportion of child deaths that could be prevented.

Second, we have included only those interventions that are feasible for implementation at high levels of coverage in low-income countries. This reduction to the least common denominator excluded some interventions for which there is sufficient evidence of effect, but that are only feasible for implementation in countries with higher levels of human, health-system, and financial resources. Emergency obstetric care, for example, would be feasible in most settings in Brazil, Mexico, and other countries where high proportions of the population have access to secondary and tertiary care.

Third, we excluded promising interventions that are currently being assessed, such as pneumococcal and rotavirus vaccines, and several important interventions postulated to reduce deaths in the neonatal period.

Finally, our estimate is limited in scope. Only interventions that address the major causes of child death and selected underlying causes are included. For some conditions that contribute to child mortality, important underlying causes and risk factors are not yet understood. Childhood anaemia provides a good example, especially because there is often little recognition of its important role as a contributor to child mortality.[59] One difficulty is that the causes of anaemia are multifactorial (eg, nutritional deficiencies such as iron and folate, infections such as malaria and HIV, and haemoglobinopathies such as sickle cell and thalassaemia). No single intervention can fully address the problem of childhood anaemia, and available evidence shows that several interventions have some effect.

Conclusions

Our findings show that about two-thirds of child deaths could be prevented by interventions that are available today and are feasible for implementation in low-income countries at high levels of population coverage. Published work on child mortality in low-income and middle-income countries over the past two decades confirms previous evidence of the efficacy and effectiveness of prevention and therapeutic interventions identified before that time, such as measles vaccine and the prevention of dehydration among children with diarrhoea through oral rehydration therapy. Science has moved forward quickly both to document the mortality reduction benefits of additional existing interventions such as micronutrients and other nutritional interventions, and to identify new and highly effective interventions, such as ITMs for the prevention of malaria and Hib vaccine. More than ever before, we have effective interventions and increasing experience in integrated approaches and ways to adapt them to local conditions.[57]

Amid the plethora of new and newly validated interventions, there are signs that the child survival effort has lost its focus. For example, levels of attention and effort directed at preventing the small proportion of child deaths due to AIDS with a new, complex, and expensive intervention seem (although no investment data are available) to be outstripping the efforts to save millions of children every year with a few cents' worth of ITMs, oral rehydration therapy, or efforts to promote breastfeeding. This must change.

These estimates are only a starting point. They can and should be improved through inclusion of further data, through further assessments of intervention effectiveness

in the hands of ministries of health and their partners in low-income and middle-income countries, through expanded sensitivity analyses, and further technical discussion and refinement of the assumptions. Issues related to delivery, feasibility, cost, and sustainability of interventions must be addressed, and much of this work is already under way.[60,61]

Our estimates can only be as valid as the data on which they are based. Although great progress has been made during the past decade in the measurement of coverage levels for child survival interventions through population-based surveys,[62,63] information about the relative efficacy of such interventions has grown more slowly, and some of the assumptions we have used are based on findings from only a few studies. Nevertheless, our overall mortality reduction estimate, based on the combination of several interventions, was very robust. Whenever we changed model parameters so that an intervention was saving fewer lives, other interventions increased the number of deaths they prevented, leading to a fairly stable estimate of overall effect.

Additionally, some interventions were not included in this exercise because sufficient evidence of their efficacy is not yet available, and in due time their inclusion may contribute to saving an even larger proportion of lives. Further efforts to both expand and synthesise the knowledge base for child survival are needed.

Success in achieving high coverage levels with effective interventions leads over time to reductions in deaths, with associated reductions in estimates of preventable deaths. Measles vaccination provides a good example of an effective programme that has achieved high coverage levels and has reduced child mortality, and must continue to be supported within the context of child survival programmes.

This first effort shows that we can achieve large reductions in child mortality and reach the millennium development goal of reducing child mortality by two-thirds with the interventions available today. There is no need to wait for new vaccines, new drugs, or new technology, although all these must remain on the agenda as a basis for improving our efficiency and effectiveness in the future. But they cannot serve as an excuse. The main challenge today is to transfer what we already know into action; deliver the interventions we have in hand to the children, mothers, and families who need them, and thus achieve the millennium development goal of reducing under-5 mortality by two-thirds by 2015.

Contributors

The named authors and the coordinators of the series (J Bryce and C G Victora) constituted a working group that took responsibility for finalising the assumptions underlying the estimation model and the preparation of the manuscript.

The Bellagio Child Survival Study Group

Members include those who participated in a team residency on "Knowledge into action: improving equity in child health" sponsored by the Rockefeller Foundation and held in Bellagio, Italy, in February, 2003. The group contributed to the conceptualisation of the paper, provided technical input, and reviewed and commented on drafts of the manuscript. Members other than the five named authors were: J Armstrong Schellenberg (London School of Hygiene and Tropical Medicine, London, UK), J Bryce (WHO, Geneva, Switzerland), M Claeson (World Bank, Washington, DC, USA), S el Arifeen (ICDDR,B, Bangladesh), T Evans (Rockefeller Foundation, USA), D Gillespie (David and Lucile Packard Foundation, USA), D Gwatkin (World Bank), J-P Habicht (Cornell University, USA), C F Lanata (Instituto de Investigación Nutricional, Lima, Peru), H Mshinda (Ifakara Health Research and Development Center, Ifakara, Tanzania), G Pariyo (Makerere University Institute of Public Health, Kampala, Uganda), H Troedsson (WHO), C G Victora (University of Pelotas, Pelotas, Brazil), A Wagstaff (World Bank).

Conflict of interest statement

None declared.

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The views represented in this article are those of the individual authors and do not represent the views of their institutions.

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