Where and why are 10 million children dying every year?

Robert E Black, Saul S Morris, Jennifer Bryce

More than 10 million children die each year, most from preventable causes and almost all in poor countries. Six countries account for 50% of worldwide deaths in children younger than 5 years, and 42 countries for 90%. The causes of death differ substantially from one country to another, highlighting the need to expand understanding of child health epidemiology at a country level rather than in geopolitical regions. Other key issues include the importance of undernutrition as an underlying cause of child deaths associated with infectious diseases, the effects of multiple concurrent illnesses, and recognition that pneumonia and diarrhoea remain the diseases that are most often associated with child deaths. A better understanding of child health epidemiology could contribute to more effective approaches to saving children’s lives.

Substantial reductions in child mortality occurred in low-income and middle-income countries in the late 20th century, but more than 10 million children younger than 5 years still die every year. In 1990–2001, the number of child deaths to achieve such a reduction in the 1990s were not investments in health systems and interventions necessary to reach a global child mortality rate of 100 or more in 1990. In 2000, this gap had increased to 29-fold. In 2000, this gap had increased to 29-fold. In 1990, there were 180 deaths per 1000 livebirths in sub-Saharan Africa and only 9 per 1000 in industrialised countries—a 20-fold difference.

The World Summit for Children in 1990 called for a worldwide reduction in child mortality to below 70 deaths per 1000 livebirths (or a one-third reduction if this yielded a lower mortality rate) by the year 2000. Unfortunately, investments in health systems and interventions necessary to achieve such a reduction in the 1990s were not commensurate with needs. The mortality reduction target was reached for only five of 55 countries with an under-5-year mortality rate of 100 or more in 1990.

In 2002, as part of the millennium development goals for health, nations pledged to ensure a two-thirds reduction in child mortality by 2015, from the base year 1990. In addition to setting such a goal, the global public health community must critically assess how it can be accomplished. A realistic picture of a country’s epidemiological profile and the capabilities of its health system is needed before appropriate public health interventions can be developed and implemented.

Development of these interventions also requires an understanding of the determinants of child mortality. These determinants include, at the most distant level, socioeconomic factors, such as income, social status, and education, which work through an intermediate level of environmental and behavioural risk factors. These risk factors, in turn, lead to the proximal causes of death (nearer in time to the terminal event), such as undernutrition, infectious diseases, and injury. In this paper, we will focus on proximal causes of death and on selected environmental and behavioural risk factors. The fourth article in this series will address the socioeconomic determinants of child mortality.

Where do most child deaths occur?
The estimate for global child deaths in 2000 is 10·8 million. In this series, data from 2000 will be used throughout because they are most complete for this period and little has changed in the past 2 years. About 41% of child deaths occur in sub-Saharan Africa and another 34% in south Asia. Because there is substantial variation in death rates within these regions, planning for health interventions should take place at a national level. The incomplete and unreliable nature of these

Lancet 2003; 361: 2226–34
See Commentary page 2172

Search strategy
The search strategy for the model used to estimate proportionate causes of death has been described. Estimates of the importance of risk factors were taken from published results. For our comorbidity analyses we also contacted researchers and directors of demographic surveillance areas in low-income and middle-income countries.
For personal use. Only reproduce with permission from The Lancet.
Figure 1: Worldwide distribution of child deaths
Each dot represents 5000 deaths."
stipulates one cause of death, which is considered to be
the “disease or injury which initiated the train of morbid
events leading directly to death.” This measure ensures
that the sum of deaths from all possible causes will not
exceed the total number of child deaths. However, such a
classification oversimplifies the situation in low-income
and middle-income countries where serious illnesses
commonly occur sequentially or concurrently before
death.

Measles is often complicated by pneumonia or
diarrhoea. In studies in Bangladesh, the Philippines, and
Uganda it was noted that in children with an illness
serious enough to require admission to hospital, 50–79% of
measles cases were followed by pneumonia or
diarrhoea, which were the reasons for admission. Decreases
in the immune and non-immune host defences as a consequence of measles lead to a high rate of these
subsequent infectious diseases, and also to a higher case
fatality rate when they do occur. Likewise, children with
AIDS have increased susceptibility to diarrhoea,
pneumonia, tuberculosis, and other infections. These
diseases also have a higher case fatality rate in people with
AIDS compared with those without AIDS. In these
examples, measles or AIDS would be judged by ICD rules
to be the underlying cause of death and subsequent
infections would be associated causes of death.

Underweight status (one SD or more below the weight
expected for that age in an international reference
population) and micronutrient deficiencies also cause
decreases in immune and non-immune host defences, and
should be classified as underlying causes of death if
followed by infectious diseases that are the terminal
associated causes. An analysis of ten longitudinal
community-based studies of children younger than 5 years
showed that being underweight conferred an additional
risk of mortality from infectious diseases. The fraction of
disease attributable to being underweight was 61% for
diarrhoea, 57% for malaria, 53% for pneumonia, 45% for
measles, and 53% for other infectious diseases. Fetal
malnutrition, manifested in low birthweight, might
contribute in a similar way to neonatal mortality. Relative
risks for mortality in children younger than 5 years derived
from the ten studies assessed have been used to estimate
that 53% of all child deaths could be attributed to being
underweight (L Caulfield, personal communication). Of
these, 35% of all child deaths are due to the effect of
underweight status on diarrhoea, pneumonia, measles,
and malaria and relative risks of low maternal body-mass
index for fetal growth retardation and its risks for selected
neonatal causes of deaths.

In children with vitamin A deficiency, the risk of dying
from diarrhoea, measles, and malaria is increased by
20–24%. Likewise, zinc deficiency increases the risk of
mortality from diarrhoea, pneumonia, and malaria by
13–21%. The fraction of these infectious-disease deaths
that are attributable to nutritional deficiencies varies with
the prevalence of deficiencies; the highest attributable
fractions are in sub-Saharan Africa, south Asia, and
Andean Latin America. Correct classification of
undernutrition and vitamin A and zinc deficiencies as
underlying causes of death will permit a true estimate of
the importance of these conditions and recognition that
interventions can target both the nutritional condition and
the resulting terminal infectious diseases.

Clinical causes of death
Classification
All countries need sound epidemiological information to
prioritise, plan, and implement public health
interventions. Vital event registration that includes cause-
of-death data is used to establish the cause structure of
mortality in high-income and some middle-income
countries, but these are generally not available for the
countries where 90% of child deaths take place. Of these
countries, only Mexico records more than 95% of causes
death. Where coverage is incomplete, the poorer
segments of the population, which have higher mortality
and might have different causes of death, are often under-
represented. India and China have attempted to
establish sample registration systems, but it is not yet clear
whether they are truly representative and correctly classify
causes of child deaths. Classification of cause of death in
vital registration systems is difficult when large
proportions of child deaths are not medically attended,
and interviews with family members are needed to
establish the cause of death.

Alternatives to the reporting of vital events are use of
data from nationally-representative surveys and special
study populations. With these, ascertainment of death is
usually very complete and post-mortem interviews with
family members are used to establish causes of death.
Although post-mortem interviews have only moderate
sensitivity or specificity for some diagnoses, standard
methods for data collection and analysis can improve
diagnostic accuracy and comparability.

Neonatal disorders
Of the 10.8 million deaths worldwide of children younger
than 5 years, 3–9 million occur in the first 28 days of life—
the neonatal period. The proportion of deaths that
occur in this age interval varies systematically according to
the overall rate of mortality. For example, our analysis of
results from 44 demographic and health surveys showed
that in populations with the highest child mortality rates,
just over 20% of all child deaths occurred in the neonatal
period, but in countries with mortality rates lower than
35 per 1000 livebirths more than 50% of child deaths
were in neonates (figure 2). Regression of the proportion
of deaths in the neonatal period on the proportion of child
deaths due to AIDS in that country showed a strong
association. We used a combination of the natural
logarithm of the rate of deaths in children younger than
5 years and the proportion of such deaths attributable to
AIDS to predict the proportion of deaths in the neonatal
period ($r^2=0.76$). Predicted deaths were deduced from
the neonatal-plus-other category of deaths.

Figure 2: Relation between under-5-year mortality rate and
percentage of these deaths in neonates
Each dot=one survey.
Distribution of global child deaths by cause

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Proportion of deaths due to being underweight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoplastic disorders</td>
<td>*Proportion of deaths due to being underweight</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>1%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>7%</td>
</tr>
<tr>
<td>Malaria</td>
<td>6%</td>
</tr>
<tr>
<td>Other</td>
<td>8%</td>
</tr>
<tr>
<td>AIDS</td>
<td>0%</td>
</tr>
<tr>
<td>Measles</td>
<td>0%</td>
</tr>
<tr>
<td>Unknown</td>
<td>0%</td>
</tr>
</tbody>
</table>

Figure 3: Distribution of global child deaths by cause

Bars=uncertainty bounds. *Work in progress to establish the cause-specific contribution of being underweight to neonatal deaths.

There is a paucity of information about the direct causes of neonatal deaths in low-income communities, but it has been estimated that 24% are caused by severe infections, 29% by birth asphyxia, 24% by complications of prematurity, and 7% by tetanus.\textsuperscript{11}

Distribution of causes of death globally

We used a prediction model to estimate the distribution of deaths in children younger than 5 years by cause for the 42 countries with 90% of all such deaths in 2000.\textsuperscript{14} Estimates and uncertainty bounds were: 22% of deaths attributed to diarrhoea (14–30%), 21% to pneumonia (14–24%), 9% to malaria (6–13%), 1% to measles (1–9%), 3% to AIDS, 33% to neonatal causes (29–36%), 9% to other causes, and fewer than 1% to unknown causes (figure 3). No uncertainty bounds are available for the AIDS estimate because the model did not produce these data (country-level estimates from UNAIDS were used).\textsuperscript{12} Figure 3 also shows the fraction of deaths attributed to various causes in which the underlying cause was being overweight.

Comparison with WHO estimates

Estimates of mortality rates in children younger than 5 years in 2000 by cause are published on the WHO website,\textsuperscript{14} and are being revised (C Mathers, personal communication). Estimates available at the time of writing attribute 13% of deaths to diarrhoea, 19% to pneumonia, 9% to malaria, 5% to measles, 3% to AIDS, 42% to neonatal causes (birth asphyxia, low birthweight, and disorders arising in the perinatal period), and 9% to miscellaneous other causes, including non-communicable diseases and injury. Uncertainty bounds for the WHO estimates are not available.

Our estimates are not comparable with those of WHO, because WHO’s estimates include all WHO member states rather than only 42 countries. Nevertheless, both sets of estimates are generally consistent. WHO and the prediction model identify pneumonia, diarrhoea, and malaria as causing the greatest numbers of deaths in children younger than 5 years. A comparison of proportional mortality by cause derived from the prediction model with the proportions available for Mexico suggests that our model is predicting reasonably well in this context (panel and table 2).

A careful analysis of the differences between the estimates produced by the two approaches, and the reasons for these, will contribute to an understanding of the relative strengths and weaknesses of different sources of child mortality data and different methodological approaches, for all-cause child mortality and for major causes. Methodological work is underway and is expected to lead to updated estimates and reproducible methods that can be applied regularly as new and better data on the causes of child mortality become available.

Distribution of causes of death: comparison of WHO mortality database and cause-of-death model

Uniquely, in the 42 countries where 90% of child deaths take place, Mexico has a vital registration system that is considered complete.\textsuperscript{22} Therefore, the coverage of the system is 95% or more and implies that there is unlikely to be any substantial selection bias in the proportional distribution of mortality by cause in children younger than 5 years in the vital registration data. We are, therefore, able to validate the predictions of the cause-of-death model using vital registration-based data from Mexico, provided by the Department of Evidence and Information for Policy of WHO (table 2).\textsuperscript{23} The following points are of note.

- The model classes all deaths from infectious respiratory illnesses as pneumonia, on the basis that other respiratory illnesses are very rarely fatal, even in young children.
- The model judges undernutrition to be an underlying cause of most infectious illness, and rejects the idea that a few deaths can be singled out as exclusively attributable to nutritional deficiencies. Those deaths ascribed in the WHO mortality database to nutritional deficiencies (3–1%) are therefore reallocated to infectious causes in proportion to their single disease frequencies.
- The model defines neonatal deaths on the basis of a time period (first month of life), which is expected to be roughly equivalent to the sum of deaths from three categories in WHO data—ie, disorders arising during the perinatal period, congenital anomalies, and tetanus. Sepsis deaths in the neonatal period are included in the model but not the WHO estimates, leading to divergence in these values.
- The WHO mortality database does not include a category of deaths due to undetermined causes, because these are reallocated to all causes in proportion to their frequencies. For the model, 0–1% of deaths were in this category.

In the case of Mexico, the WHO mortality database and the cause-of-death prediction model lead to almost identical conclusions about the proportional distribution of deaths by cause in children younger than 5 years. The model results suggest slightly more neonatal deaths (in part because of the difference in definition of this category), and correspondingly fewer deaths from diarrhoea and pneumonia.

### Table 2: Distribution of causes of death in WHO database and cause-of-death model

<table>
<thead>
<tr>
<th>Proportion of deaths</th>
<th>WHO</th>
<th>Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoplastic disorders</td>
<td>47-9%</td>
<td>52-6%</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>17-5%</td>
<td>14-1%</td>
</tr>
<tr>
<td>Respiratory infections</td>
<td>10-4%</td>
<td>8-2%</td>
</tr>
<tr>
<td>AIDS</td>
<td>0-1%</td>
<td>0-3%</td>
</tr>
<tr>
<td>Other</td>
<td>24-1%</td>
<td>24-7%</td>
</tr>
</tbody>
</table>
Figure 4: Cause-of-death profiles for 42 countries with 90% of child deaths
A review of the various models used to estimate under-5-year deaths due to measles is scheduled for later in 2003.

Country typologies by major causes of death
The cause structure of deaths in children younger than 5 years is determined by many environmental and behavioural factors that are often proxied by broad geographical groupings—eg, the countries of sub-Saharan Africa are frequently grouped together. We used the prediction model to estimate that in sub-Saharan Africa the distribution of causes of death would be: neonatal disorders (25%), malaria (22%), pneumonia (21%), diarrhoea (20%), and AIDS (8%). This aggregation is misleading because some countries in sub-Saharan Africa have very little malaria, and others have very few AIDS deaths; whereas others are severely affected by malaria, AIDS, or both.

We propose an alternative way to group countries on the basis of the proportions of death from each major cause. In the 42 countries we considered, the proportions of deaths caused by pneumonia and diarrhoea were fairly consistent, whereas the proportions for malaria, AIDS, and deaths in the neonatal period differed strikingly between countries. The method of grouping is based on causes of death and consists of five profiles.

1. Malaria and AIDS each account for fewer than 10% of deaths and neonatal causes for fewer than 40%.
2. Malaria accounts for at least 10%, but AIDS accounts for fewer than 10%.
3. Malaria and AIDS each account for fewer than 10% and neonatal causes for at least 40%.
4. Both malaria and AIDS account for at least 10%.
5. Malaria accounts for fewer than 10% and AIDS for at least 10% of deaths.

The 42 countries accounting for 90% of all under-5-year deaths are represented in each of the five profiles (figure 4). Countries in profile 1 (average under-5 year mortality rate 109 per 1000) account for most deaths; in these countries, 24% of deaths are attributed to each of diarrhoea and pneumonia and 34% to causes in the neonatal period (figure 5). In profile 2 countries (181 per 1000) 20–26% of deaths are attributed to each of diarrhoea, pneumonia, malaria, and neonatal deaths. In the third largest profile (41 per 1000) diarrhoea and pneumonia account for 23% and 15% of deaths, respectively, but 48% of all deaths are in neonates. Profile 4 (169 per 1000) has 17–19% of deaths attributed to each of diarrhoea and pneumonia and 26% to malaria. In the smallest group, profile 5 (106 per 1000), diarrhoea and pneumonia each account for about 20% of deaths, malaria for 6%, and AIDS for 23%.

Our analysis shows that diarrhoea and pneumonia account for large proportions of deaths in all profiles, even as rates of death fall. Together, they do become somewhat less important at low mortality rates, as in profile 3, in which nearly half of all deaths are in neonates. As mortality rates fall, the proportion of deaths in the neonatal period will increase, which should lead the public health community to increase and improve interventions to prevent deaths in newborns.

Comorbidity in child deaths
Synergy in causes of death
An interaction of two health disorders can have a synergistic effect on mortality—ie, a rate of death that is greater than the sum of the two individual rates of mortality. This has been documented most clearly for the relation between being underweight and infectious diseases.24,35 For example, children who are mildly underweight (–2< z scores<–1) have about a two-fold higher risk of death than those who are better nourished. This risk increases to 5–8 fold in moderately (–3< z scores<–2) to severely (<–3 z scores) underweight children.24

Co-occurrence of infectious diseases
Another form of comorbidity is the co-occurrence of two infectious diseases, which can occur by chance. More commonly, however, two diseases occur together because
they have the same environmental or behavioural risk factors, such as poor sanitation or no breastfeeding in infancy, leading to increased exposure to infections. This comorbidity may also result in synergism, leading to an increased risk of death.

In the past 10 years, it has become more common for studies to include multiple-cause classifications such as diarrhoea plus pneumonia in the causes of death of young children in low-income countries. We did a systematic search for all studies of causes of death of children younger than 5 years in developing countries and identified eight published studies done in Bangladesh, Egypt, the Philippines, and Guinea. Unpublished studies from Bangladesh and Haiti were also found (H Perry, personal communication). In these studies, reported proportions of deaths attributed to diarrhoea—as a sole cause or in combination with another cause—varied from 15% to 44%. Deaths from pneumonia varied from 20% to 42%, and deaths attributed to two causes in combination varied from 4% to 16%. These proportions can be combined with the overall risk of a child from the same population dying before their fifth birthday to obtain risks of dying from diarrhoea, pneumonia, or both diseases in combination.

To show that comorbidity is an important public health problem, it needs to be established whether deaths from causes in combination are greater than would be expected if each cause acted independently. Multiplication of the risk of death from diarrhoea by the risk from pneumonia allows estimation of the risk of death expected from the random co-occurrence of the two causes, assuming no shared risk factors and no synergy. In the ten studies we assessed, co-occurrence was between 2.7 and 34.2 (median 8.7) times greater than that expected if synergy and risk factors were not present. This finding suggests either that there are shared risk factors for severe diarrhoea and severe pneumonia, or that the two disorders together synergistically provoke death in affected children. Most likely, both mechanisms operate, because even the most powerful shared risk factors, such as not breastfeeding, could not account for such a substantial increase in risk of death with both causes present.

Conclusions

Child health epidemiology is developing and increasingly can provide information useful for public health planning, monitoring, and evaluation. Ideally, information on causes and determinants of death would be available for planning at national or subnational levels. Our epidemiological profiles show the extent of variation between major causes of death even within commonly used regional groupings, which highlights the need for disaggregation at regional and global levels to allow public health intervention efforts to be focused appropriately. The availability of valid epidemiological information at country level will be an important determinant of success in meeting and in measuring progress toward the millennium development goal for child survival. Expanded efforts to build capacity and to improve the completeness and accuracy of available data are needed.

Clearly, pneumonia and diarrhoea will continue to be important causes of child deaths until mortality falls to very low rates. Furthermore, nearly two-thirds of deaths in the 42 countries analysed (and 57% of child deaths worldwide) occur in just 19 countries where the predominant causes are pneumonia, diarrhoea, and neonatal disorders—with very little contribution from malaria and AIDS. On the other hand, malaria plays an important part in child mortality in many countries in sub-Saharan Africa. AIDS accounts for more than 10% of deaths in just three of the 42 countries; however, in some smaller countries, such as Botswana and Zimbabwe, AIDS causes more than half of child deaths.

Undernutrition is the underlying cause of a substantial proportion of all child deaths, and better information on its determinants is needed. The identification of risk factors, detection of underlying and associated causes of death, and recognition of comorbidity can lead to selection of effective and affordable interventions that are appropriate for national delivery systems.

Contributors

R Black, S Morris, and J Bryce conceived the idea for this article and wrote the paper.

Conflict of interest statement

None declared.

Acknowledgments

Barbara Ewing provided essential help with the preparation of the figures and references. Colin Mathers reviewed earlier drafts of the manuscript and offered useful suggestions on how it could be improved. Members of the Child Health Epidemiology Reference Group (CHERG) who contributed systematic reviews and analyses that have been partly used include Harry Campbell and Igor Rudan (pneumonia); Cynthia Boschi-Pinto, Claudio Lanata, and Walter Mendoza (diarrhoea); Rick Steketee and Alex Rowe (malaria); and Joy Lawn and Zulfiqar Bhutta (neonatal causes). This work was funded by Bill and Melinda Gates Foundation, WHO Department of Child and Adolescent Health and Development, and Johns Hopkins Family Health and Child Survival Cooperative Agreement with the US Agency for International Development. Substantial work was done during a conference supported by the Rockefeller Foundation at the Bellagio Study and Conference Center. The sponsors had no role in these analyses or the preparation of the manuscript. The views represented in this article are those of the individual authors and do not represent the views of their institutions.

References


