



# WHO estimates of the causes of death in children

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## Summary

**Background** Child survival efforts can be effective only if they are based on accurate information about causes of deaths. Here, we report on a 4-year effort by WHO to improve the accuracy of this information.

**Methods** WHO established the external Child Health Epidemiology Reference Group (CHERG) in 2001 to develop estimates of the proportion of deaths in children younger than age 5 years attributable to pneumonia, diarrhoea, malaria, measles, and the major causes of death in the first 28 days of life. Various methods, including single-cause and multi-cause proportionate mortality models, were used. The role of undernutrition as an underlying cause of death was estimated in collaboration with CHERG.

**Findings** In 2000–03, six causes accounted for 73% of the 10.6 million yearly deaths in children younger than age 5 years: pneumonia (19%), diarrhoea (18%), malaria (8%), neonatal pneumonia or sepsis (10%), preterm delivery (10%), and asphyxia at birth (8%). The four communicable disease categories account for more than half (54%) of all child deaths. The greatest communicable disease killers are similar in all WHO regions with the exception of malaria; 94% of global deaths attributable to this disease occur in the Africa region. Undernutrition is an underlying cause of 53% of all deaths in children younger than age 5 years.

**Interpretation** Achievement of the millennium development goal of reducing child mortality by two-thirds from the 1990 rate will depend on renewed efforts to prevent and control pneumonia, diarrhoea, and undernutrition in all WHO regions, and malaria in the Africa region. In all regions, deaths in the neonatal period, primarily due to preterm delivery, sepsis or pneumonia, and birth asphyxia should also be addressed. These estimates of the causes of child deaths should be used to guide public-health policies and programmes.

## Introduction

Child survival efforts can be effective only if they are based on reasonably accurate information about the causes of deaths. Cause-of-death information is needed to prioritise interventions and plan for their delivery, to ascertain the effectiveness of disease-specific interventions, and to assess trends in disease burden in relation to national and international aims.

Until 2004, global and regional estimates of child deaths attributable to specific causes were available from two major sources. First, technical groups, often collaborating with the United Nations (UN), published estimates of the number of deaths in children younger than age 5 years directly attributable to single diseases such as diarrhoea,<sup>1</sup> measles,<sup>2</sup> and HIV/AIDS.<sup>3</sup> Second, WHO coordinated a yearly process that brought together single-cause estimates from WHO technical units, and reconciled them into a single proportional cause-of-death distribution that represented 100% of deaths in children younger than age 5 years worldwide.<sup>4</sup> These cause-specific proportions were then applied to the total number of deaths in children younger than age 5 years, which we will refer to as the envelope, derived from country-specific mortality rates—ie, probability of dying before age 5 years. WHO,<sup>5</sup> UNICEF,<sup>6</sup> World Bank,<sup>7</sup> and the UN Population Division<sup>8</sup> estimated the mortality envelope in children aged younger than 5 years independently until 2004, producing different figures. WHO and UNICEF have now agreed on and applied standard procedures to

produce a consistent envelope of deaths in this age-group for 2000–03.<sup>9</sup>

Increased attention to evidence-based decision making in public health and the global commitment to the millennium development goals<sup>10</sup> has generated renewed interest in strengthening child-health epidemiology as a foundation for improved efforts to reduce mortality in children younger than age 5 years. Beginning in 1998, WHO sought outside expertise to improve the quality of this area of work. The initial focus was on deaths from pneumonia, but quickly expanded to include other major causes of child mortality as well as morbidity, the role of undernutrition as an underlying cause of death,<sup>11,12</sup> and crosscutting methodological issues.

The Child Health Epidemiology Reference Group (CHERG) was established in 2001 by WHO. Their mandate was to review and improve data collection, methods, and assumptions underlying estimates of the cause-specific proportional distribution of child deaths for the year 2000, beginning with the major causes of child mortality worldwide: pneumonia; diarrhoea; malaria; causes of death in the first 28 days of life, referred to here as neonatal causes; and measles. The CHERG investigators have worked in small disease-specific groups since that time to apply systematic methods and develop new estimates for deaths due to these causes.

In 2004, WHO initiated a consultative process to incorporate CHERG results into the broader WHO mortality estimates for children younger than age 5 years. The final proportional distribution of deaths by cause was

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then applied to the mortality envelope for this age-group. Our aim is to describe the methods and results of these efforts: new estimates for mortality by cause in children younger than age 5 years, worldwide and in the six WHO regions, as the average of yearly estimates for the period from 2000–03.

### Methods

We focus on the WHO process for development of improved estimates of cause-specific mortality in children younger than age 5 years. More detailed information on the methods used by the CHERG working groups for every cause or methodological issue is available elsewhere,<sup>13–17</sup> as are reports on the review and revision of the mortality envelope for children younger than age 5 years,<sup>9</sup> the development of cause-specific estimates of morbidity in this age group due to acute respiratory infections,<sup>18</sup> diarrhoea,<sup>19</sup> malaria,<sup>20</sup> and undernutrition,<sup>11,12</sup> and details of various methodological advances in areas such as accounting for comorbidity at the time of death.<sup>21</sup> After a brief summary of the CHERG methods, therefore, we focus on the consultative process through which WHO and UNICEF incorporated these results into the global estimates of the numbers and proportions of child deaths directly attributable to specific causes.

One CHERG working group developed a model that addresses pneumonia, diarrhoea, malaria, and measles simultaneously by establishing systematic associations between the proportional distribution of deaths by cause and characteristics of study populations and designs.<sup>17</sup> Meetings of investigators at about 6-month intervals provided opportunities for progress reports, peer review, and resolution of methodological issues.

No ethical review committee approval was obtained because the estimation was based on published or otherwise publicly available information.

### Overview of methods used by CHERG working groups

All of the CHERG working groups applied the same general set of procedures to produce their estimates, although these procedures evolved over time and the cause-specific epidemiological models also differed based on the characteristics of the diseases being studied. First, every group of investigators reviewed the methods, assumptions, and results from previous estimates and developed models specifying the key epidemiological variables for every cause or group of causes and their association to one another. These models were reviewed at meetings of the CHERG investigators and then used as the basis for data searches and construction of standardised databases. Vital registration data were used in the estimation process where possible. Investigators also did systematic searches in English without a language filter for publications that included the relevant epidemiological variables. Reference sections of relevant studies were reviewed to identify additional studies. Furthermore,

published or unpublished data were requested from both researchers and institutions.

Databases were constructed for most working groups by the Public Health Interventions Research Unit of the London School of Hygiene and Tropical Medicine, UK, using similar formats and standardisation procedures.<sup>22</sup> Quality control included data abstraction and data entry by two independent workers under close supervision, with differences resolved through reference to the original source material. These databases are being finalised and will be available to all (see weblink).

All studies were screened with a standard set of inclusion criteria: publication date after 1980, a specified minimum of total deaths in the study sample (variable, according to the disease being estimated), a specified maximum of unknown or undetermined causes of death (varying between 20% and 30%), and community-based studies with at least a year of follow-up or exact multiples of a year to reduce seasonal biases when applicable.

All of the CHERG working groups developed comparable procedures to generate estimates from the databases. Three specific challenges faced by multiple groups were: defining and applying appropriate case definitions, applying standard categories for the age of the child at death, and agreeing on how to handle deaths for which no known cause was reported (treated as other rather than reallocating to known causes unless the original investigators could provide additional information). Addressing these and other issues needed considerable follow-up with the original investigators to fill in gaps in the published reports. Another challenge, not yet resolved, was how best to estimate the amount of uncertainty associated with the estimates, especially because the data sets were not drawn from probability samples of national populations. The detailed reports from every working group provide information on how they estimated uncertainty, the range of sensitivity analyses done to assess the effect of various assumptions on the estimated levels of key variables, and efforts to validate the estimates with data from other sources.

### Incorporation of CHERG results into WHO estimates

The CHERG results were incorporated into broader WHO estimates of deaths in children younger than age 5 years by cause with a standard set of procedures (figure 1). Full details are available elsewhere,<sup>9</sup> but the process is described briefly below.

### Estimation of envelope

WHO has updated life tables for its member states every year since 2000, by using mortality rates for children younger than age 5 years jointly produced by WHO and UNICEF.<sup>9</sup> The number of total deaths in this age group was estimated by applying the mortality rates from the WHO abridged life tables to the population estimates obtained from the UN Population Division.<sup>8</sup> The envelope for neonatal deaths was estimated with mortality data

See  
[http://www.who.int/child-adolescent-health/OVERVIEW/CHILDHEALTH/child\\_epidemiology.htm](http://www.who.int/child-adolescent-health/OVERVIEW/CHILDHEALTH/child_epidemiology.htm)

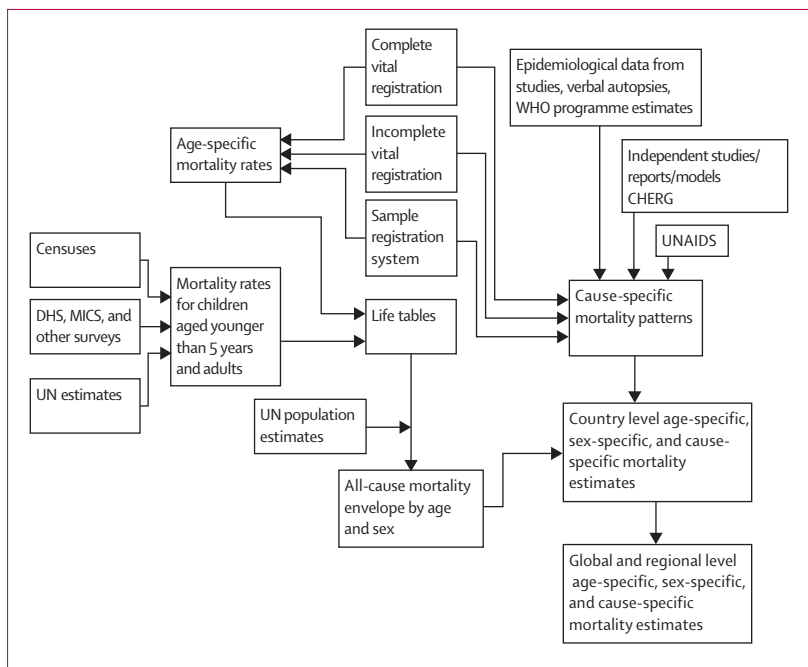
from surveys and vital registration systems in countries where adequate data existed for both neonatal deaths and for those in children aged younger than 5 years. In other countries, a model was used to generate neonatal deaths as a function of deaths in children younger than age 5 years.<sup>23</sup> The global and regional mortality envelopes developed by WHO are the sum of country-specific estimates and indicate average yearly mortality for the period 2000–03.<sup>9</sup> The steps used by WHO to derive the mortality envelope are shown in figure 1.

### Proportional distribution of deaths by cause

WHO uses information on the distribution of child deaths by cause from vital registration systems in the 72 countries where those systems are judged to be sound (based on standard application of coding that follows the rules of the International Statistical Classification of Diseases and Related Health Problems (ICD) for death certificates and reliable diagnostic procedures) and have coverage rates of 85% or above. These data are all from high-income and middle-income countries.

Cause-of-death patterns obtained from registration systems cannot be applied directly to settings without adequate vital registration because the presence of such a system is associated with higher socioeconomic levels and urbanisation rates. The distribution of deaths by cause in settings without adequate vital registration was, therefore, estimated in two steps. First, a statistical model based on historical trends in cause-of-death patterns in high-income and middle-income countries drew on values for all-cause mortality, and income per head and its distribution, as well as information on cause-of-death patterns in neighbouring countries of the same region, to assign deaths to one of three broad categories of causes: communicable diseases, non-communicable diseases, or injuries and external causes.<sup>24</sup> Second, cause-specific mortality estimates for children younger than age 5 years from CHERG, WHO technical programmes, and the Joint UN Programme on HIV/AIDS (UNAIDS)<sup>25</sup> were taken into account in assigning the distribution of deaths to specific causes and undernutrition. CHERG and WHO used various methods, including proportional mortality and natural history models, to develop country-level age-specific, sex-specific, and cause-specific mortality estimates (figure 1).

For estimates of deaths in children younger than age 5 years directly attributable to pneumonia, diarrhoea, and malaria, technical experts from CHERG, WHO, and UNICEF met in Sept, 2004, to compare CHERG estimates derived from single-cause models<sup>13–15</sup> with those generated by the CHERG multicause proportional mortality model,<sup>17</sup> as well as with other estimates from WHO technical programmes or from published work.<sup>1,2,26,27</sup> Important differences in the results were investigated and when possible explained and reconciled by consensus of experts. In general the cause-specific estimates generated by the various sources were roughly consistent.



**Figure 1: Overview of WHO procedures for estimating deaths by cause in children younger than age 5 years**  
DHS=demographic and health survey. MICS=multiple indicator cluster survey.

The one set of estimates with widely divergent methods and numbers from various sources was for measles mortality.<sup>2,17</sup> This discrepancy had been discussed in CHERG meetings, and WHO had therefore convened an expert panel in January, 2004, to review available models and their inputs, assumptions, and results in detail. The panel's recommendations<sup>28</sup> noted the inadequacy of available data and estimation methods for measles mortality and recommended various actions for their improvement. The consultative group convened in September, 2004, lent support to WHO's decision to use an interim number of measles deaths that represented the average of estimates ranging from 2% to 6% of all deaths in children younger than age 5 years. Further work on this estimate is needed.

### Estimation of deaths by cause, 2000–03

The final estimates of the proportional distribution of deaths by cause were applied to the average yearly mortality envelope for all countries without adequate vital registration data for 2000–03. These national estimates were summed to arrive at regional and global deaths by cause in children aged younger than 5 years. A single average yearly estimate was prepared for the period 2000–03 because 2000 was the reference year for all CHERG estimates and only estimates of HIV/AIDS have been updated since then.<sup>9</sup> The contribution of undernutrition to all deaths in children younger than age 5 years and to the subsets of deaths due to pneumonia, diarrhoea, malaria, and measles were estimated by analysis of ten longitudinal datasets as previously described.<sup>11,12</sup>

### 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 all the data in the study and had final responsibility for the decision to submit for publication.

### Results

The new estimates (figure 2) show that worldwide, 73% of deaths in children younger than age 5 years are attributable to six causes: pneumonia (19%), diarrhoea (18%, which includes 17% of deaths in children 1–59 months and 3% of neonatal deaths), malaria (8%), neonatal sepsis or pneumonia (10%), preterm delivery (10%), and asphyxia at birth (8%). The four communicable disease categories account for more than half (54%) of all child deaths. Sepsis or pneumonia in neonates and pneumonia in older children constituted 29% of all deaths. Additionally, undernutrition is an underlying cause of 53% of all deaths in children aged younger than 5 years.<sup>11,12</sup> The estimated proportions of deaths in which undernutrition is an underlying cause are roughly similar for diarrhoea (61%), malaria (57%), pneumonia (52%), and measles (45%).<sup>11,12</sup>

The total numbers and proportional distributions of deaths in children younger than age 5 years by cause are also available for the six WHO-defined regions (figure 3). Although WHO regional groupings of countries are not entirely consistent with epidemiological cause-of-death patterns for children younger than 5,<sup>29</sup> they do represent one of the important organisational frameworks guiding planning of public-health actions and are meaningful in that respect. Among deaths in children younger than age 5 years worldwide, 42% occur in the WHO Africa region, and an additional 29% occur in the southeast Asia region. Cause-of-death profiles vary across the six WHO regions, though the biggest communicable disease killers remain the same with the exception of malaria. Deaths directly attributable to malaria occur almost entirely in the Africa region (94% of global malaria deaths), representing 18% of all deaths in children younger than age 5 years in that region. Though there is also a high prevalence of malaria in a few countries of the eastern Mediterranean region,

87% of the malaria deaths in this region were in two African countries—Sudan and Somalia. Malaria deaths also occurred in other regions, but do not appear in figure 3 because they represent fewer than 1% of all region-specific child deaths. For example, the southeast Asia region had almost 12 000 malaria deaths.

Measles is responsible for 5% of deaths in children younger than age 5 years in the Africa region and fewer in other regions. Most of the mortality burden of HIV/AIDS is in the Africa region. Deaths in the neonatal period represent 43–47% of child deaths in all regions apart from Africa, where the proportion (26%) is depressed by high numbers of post-neonatal deaths, especially those due to malaria. Results of further analyses of deaths in children younger than age 5 years by cause (figure 3) show a burden distribution that is heavily skewed towards the WHO Africa region: ie, 94% of global child deaths attributable to malaria, 89% of child deaths due to HIV/AIDS, 46% of deaths from pneumonia, and 40% of deaths from diarrhoea.

### Discussion

The results presented here provide important information, at new (albeit imperfect) degrees of accuracy, about the causes of child mortality worldwide and in the six WHO regions. What are their implications for policies, public-health priorities, planning, and practice?

The new estimates show that worldwide more than seven in ten of the 10·6 million annual deaths in children younger than age 5 years are attributable to six causes, and that four communicable disease categories account for more than half of all child deaths. These results confirm previous work on geographic variations in cause-of-death.<sup>29</sup> In addition undernutrition is an underlying cause in more than 50% of these deaths.<sup>11,12</sup> These causes can be addressed through existing, available, and affordable interventions.<sup>30,31</sup>

Measles, neonatal tetanus, and HIV/AIDS represent a small proportion of deaths across the six WHO regions, but cannot be ignored. The low number of measles deaths is a success story, but high immunisation coverage rates must be sustained. Neonatal deaths attributable to tetanus have been halved during the 1990s, yet the world seems likely to fail to meet the elimination goal deferred from 1995 to 2005. HIV/AIDS is an important killer of children in a few countries, and all countries need to take action against this growing threat. Neonatal causes of death represent new territory, to some extent uncharted. Reducing deaths in the neonatal period will confront weak health systems with new challenges, especially in low-income countries.<sup>32</sup>

Disease-specific advocacy efforts at global and regional levels should use these WHO estimates, and should contribute to their continued improvement through collaborative work. Every time an inaccurate or misleading estimate of disease-specific burden is published, both the journal and the authors should be questioned about their

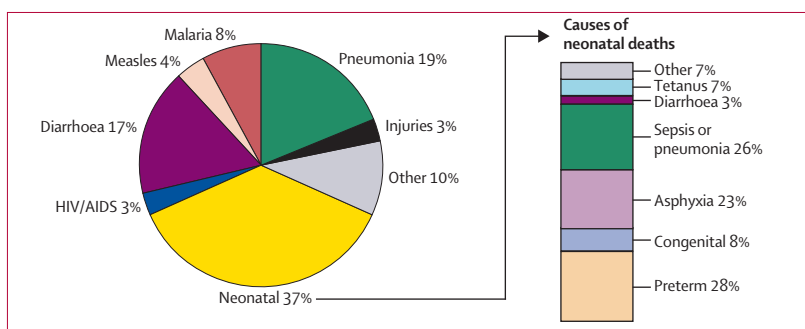
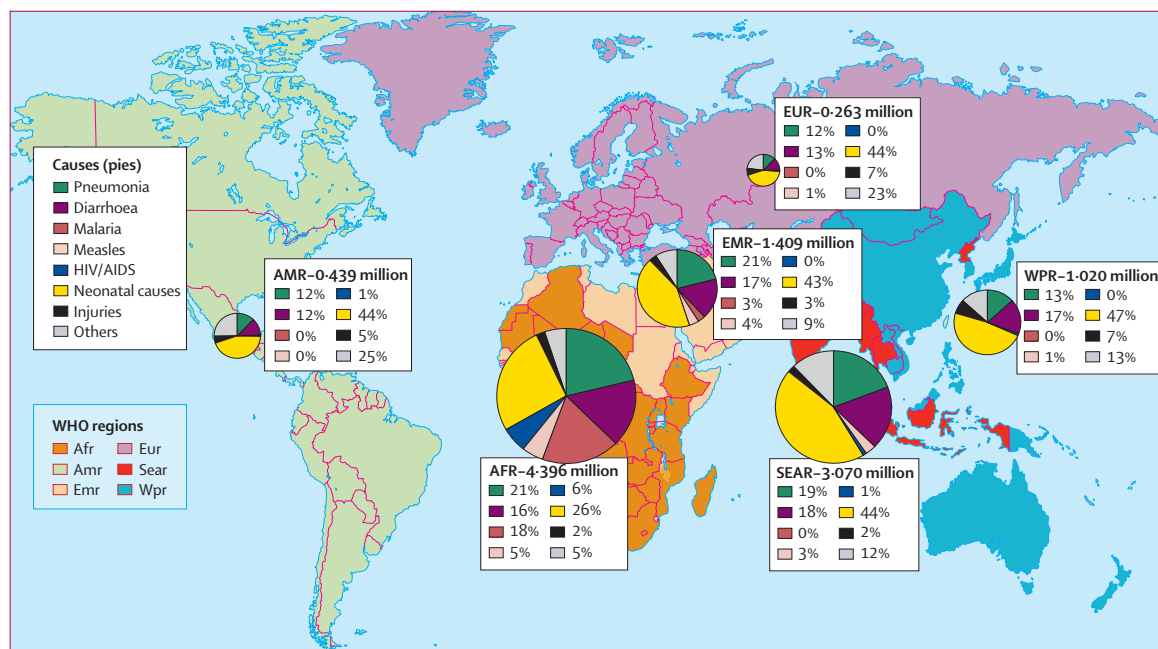


Figure 2: Major causes of death in children younger than age 5 years and in neonates (yearly average for 2000–03)



**Figure 3:** Number of deaths in children younger than age 5 years and their distribution by cause for the six WHO regions (yearly average for 2000–03). Size of circle represents number of deaths in region. Afr=Africa. Amr=Americas. Emr=Eastern Mediterranean. Eur=Europe. Sear=Southeast Asia. Wpr=Western Pacific.

sources to improve validity and plausibility of disease burden estimates for advocacy and planning.<sup>33</sup>

What do these new estimates add to public-health knowledge about child-health priorities and measurement? The results show, using rigorous and transparent methods, that conditions such as pneumonia, diarrhoea, and malaria remain major killers of children younger than age 5 years, and that undernutrition is a major underlying cause in these deaths. The results contribute to a better understanding of the almost 40% of deaths that arise in the first 28 days of life, and quantify the number of deaths due to preterm delivery, sepsis or pneumonia, and birth asphyxia, together accounting for three quarters of these neonatal deaths.<sup>16</sup>

The appropriateness of WHO as a global health monitoring body has been questioned given its simultaneous roles in advocacy, technical support to countries, and assessment, and because the organisation can be subjected to intense political pressure.<sup>34</sup> Estimates produced by WHO must, therefore, be of the highest possible quality, use transparent methods, and be developed or reviewed by an independent expert group.

The major weakness in these estimates is the quality and quantity of data on which they are based. The data points are too few and are not ideally geographically representative to provide optimum global and regional estimates.<sup>35</sup> CHERG continues to work on other factors that limit the estimates, including comparability among cause-specific estimates and development of a standard approach to uncertainty estimation. Despite these weaknesses, however, these estimates have important strengths relative to those previously available. First, we

believe that our comprehensive searches of publications and efforts to contact all investigators involved in major ongoing epidemiological studies have resulted in inclusion of a high proportion of the available data meeting our criteria. Second, the quality control procedures used in all steps of the process, including abstraction of data points from studies, represents a new degree of methodological rigour in the development of epidemiological estimates on mortality. Third, we aimed to introduce a degree of transparency in our assumptions, methods, and calculations that would permit replication, and eventually to provide public access to all databases. We believe that we have largely achieved this aim with the exception of estimates for measles mortality.

The methodological advances engendered through this work, as well as the identification of the limitations of available data,<sup>35,36</sup> are as important as the quantitative results on these causes of death. Together they constitute a mandate for expanded efforts to strengthen child-health epidemiology, and the appropriate use of estimates of disease burden for public-health policy development.

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modelling); Kim Mulholland, Royal Children's Hospital, Australia (technical expert, general methods). Technical staff participating in CHERG work from UN organisations: Edilberto Loaiza, UNICEF; Neff Walker, Joint United Nations Programme on HIV/AIDS and UNICEF; Jennifer Bryce, Cynthia Boschi-Pinto, Lana Tomaskovic (members of CHERG Secretariat), Olivier Fontaine, Eleanor Gouws, Shamim Qazi, Martin Weber, and José Martines, Department of Child and Adolescent Health and Development, Division of Family and Community Health, WHO; Colin Mathers and Kenji Shibuya, Department of Measurement and Health Information Systems, Division of Evidence and Information for Policy, WHO; Bernard Nahlen and Eline Korenromp, Roll Back Malaria Partnership Secretariat, Division of HIV/AIDS, TB and Malaria, WHO; and Jelka Zupan, Department of Reproductive Health and Research, Division of Family and Community Health, WHO.

#### Contributors

J Bryce, R E Black, C Boschi-Pinto, and K Shibuya prepared the first and subsequent drafts of the paper and incorporated work done by CHERG members and their comments on drafts of the paper.

#### Conflict of interest statement

We declare that we have no conflict of interest.

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