Nutritional status as a predictor of child survival: summarizing the association and quantifying its global impact

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By pooling the results from five previously published prospective studies, we have obtained estimates of the relative risks of mortality among young children 6–24 months after they had been identified as having mild-to-moderate or severe malnutrition. These risk estimates, along with global malnutrition prevalence data, were then used to calculate the total number of young-childhood deaths "attributable" to malnutrition in developing countries.

Young children (6–60 months of age) with mild-to-moderate malnutrition (60–80% of the median weight-for-age of the reference population) had 2.2 times the risk of dying during the follow-up period than their better nourished counterparts (>80% of the median reference weight-for-age). Severely malnourished young children (<60% of the reference median weight-for-age) had 6.8 times the risk of dying during the follow-up period than better nourished children. Each year approximately 2.3 million deaths of young children in developing countries (41% of the total for this age group) are associated with malnutrition.

The comparability of studies, methods used to derive pooled values, potentially confounding factors that may influence risk estimates, and the validity of the results are discussed. Child survival programmes should assign greater priority to the control of childhood malnutrition.

Introduction

Attempts to reduce child mortality in developing countries through selective primary health care have focused primarily on the prevention and control of specific infectious diseases, with less effort being directed to improving children's underlying nutritional status (1). This situation may have resulted for one or both of the following reasons: a lack of information on the relative magnitude of the relationship between malnutrition and risk of mortality; and a general perception that nutrition intervention programmes are too complicated or costly compared with alternative disease control programmes.

To summarize available information on the relationship between pre-existing nutritional status, as assessed by anthropometric indices, and subsequent mortality, we reanalysed published information and developed pooled estimates of the relative risk of different degrees of malnutrition. These data were then combined with estimated prevalences of malnutrition to calculate the numbers of childhood deaths in developing countries that can be "attributed" to malnutrition. The magnitude of the attributable risk of malnutrition was then compared with that of other diseases that currently receive greater attention in global child survival programmes.

Methods

Identification of published studies

We identified published studies on the relationship between nutritional status (defined by anthropometry) and childhood mortality through MEDLINE, references in published papers, and personal communications. Only prospective, longitudinal field studies in developing countries were considered. A total of 10 relevant studies were identified from the follow-
ing countries: Bangladesh (2–6), India (7), Zaire (8), Papua New Guinea (9), Guinea-Bissau (10), and United Republic of Tanzania (11) (Table 1).

Selection of studies for inclusion in the analyses

The 10 studies identified were reviewed with regard to the following factors: ages of children, nutritional status indicators, length of follow-up, presentation of data, and analytical methods. Because the greatest number of studies included children aged 6–60 months and used weight-for-age to assess nutritional status, these criteria were used for inclusion of individual studies in the final pooled analysis. Weight-for-age nutritional indices were of particular value because global prevalences of low weight-for-age are available (12), thus permitting an estimate of the total number of child deaths that might be attributable to undernutrition defined by this indicator.

Of the studies identified, five (2, 4, 5, 8, 10) could not be included in the pooled analysis. These studies were eliminated for the following reasons: two (2, 5), because they did not contain information on the children’s weight-for-age; one (8), because the 100-day follow-up period was substantially shorter than the other studies; one (10), because the anthropometric cut-off points were substantially different from the other studies; and one (4), because the data were not reported in sufficient detail to permit calculation of relative risks.

The remaining five studies used methods that were sufficiently similar and detailed to permit their results to be combined in a single analysis (3, 6, 7, 9, 11). These studies are summarized in Table 2.

Analyses

For each of the five studies selected, estimates of the relative risks and their 95% confidence limits were calculated using established methods (13). For mild-to-moderate malnutrition, children who were 60–80% (6, 7, 9) or 60–75% (3, 11) of the reference median weight-for-age were compared with their “well-nourished” counterparts, who were defined as having either >80% (6, 7, 9) or >75% (3, 11) of the reference median weight-for-age. For severe malnutrition, mortality rates of children <60% of the ref-

Table 1: Details of the studies reviewed

<table>
<thead>
<tr>
<th>Author (location, year) (ref.)</th>
<th>Subjects</th>
<th>Duration of follow-up</th>
<th>Relative risk</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Age (months)</td>
<td>(months)</td>
<td></td>
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<tr>
<td>Sommer &amp; Loewenstein (Bangladesh, 1975) (2)</td>
<td>3 757&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12–48</td>
<td>18</td>
<td>4.5&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Kasongo (Zaire, 1983) (8)</td>
<td>8 680</td>
<td>6–59</td>
<td>3</td>
<td>3.3&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Bairagi et al. (Bangladesh, 1985) (5)</td>
<td>1 000</td>
<td>12–48</td>
<td>12</td>
<td>—</td>
</tr>
<tr>
<td>Fried et al. (Bangladesh, 1986) (5)</td>
<td>922</td>
<td>12–48</td>
<td>6</td>
<td>6.8&lt;sup&gt;g&lt;/sup&gt;</td>
</tr>
<tr>
<td>Smedman et al. (Guinea-Bissau, 1987) (10)</td>
<td>2 228</td>
<td>6–59</td>
<td>8–12</td>
<td>—</td>
</tr>
<tr>
<td>Kielmann &amp; McCord (India, 1978) (7)</td>
<td>2 804&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6–36</td>
<td>12</td>
<td>14.3&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
<tr>
<td>Chen et al. (Bangladesh, 1980) (3)</td>
<td>2 019</td>
<td>13–23</td>
<td>24</td>
<td>3.1&lt;sup&gt;i&lt;/sup&gt;</td>
</tr>
<tr>
<td>Heywood (Papua New Guinea, 1982) (9)</td>
<td>740</td>
<td>6–30</td>
<td>18</td>
<td>10.0&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
<tr>
<td>Alam et al. (Bangladesh, 1989) (6)</td>
<td>2 449&lt;sup&gt;c&lt;/sup&gt;</td>
<td>12–59</td>
<td>6</td>
<td>19.2&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
<tr>
<td>Yambi et al. (United Republic of Tanzania, 1991) (11)</td>
<td>2 452</td>
<td>6–36</td>
<td>12</td>
<td>8.4&lt;sup&gt;i&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Subset of data: children aged 12–48 months (original study followed children aged 1–9 years).
<sup>b</sup> Subset of data: children aged 6–36 months (original study followed children aged 1–36 months).
<sup>c</sup> Repeated measurements made on these children at 6-month intervals for 2 years. Data analysed by "child period" for a total of 9 861 observations.
<sup>d</sup> Severe: below 9th percentile of arm-circumference-for-height compared to above 50th percentile. Mild-to-moderate: 10th–50th percentile of arm-circumference-for-height compared to above 50th percentile.
<sup>e</sup> Severe: risk ratio below/above 60% Harvard standard median weight-for-age. Mild-to-moderate: risk ratio below/above 80% Harvard standard median weight-for-age.
<sup>f</sup> Severe risks could not be determined from published data.
<sup>g</sup> Severe: arm-circumference, 11 cm versus 13.5 cm. Mild-to-moderate: arm-circumference, 12.5 cm versus 13.5 cm.
<sup>h</sup> Severe: below 60% standard weight-for-age compared to above 80%. Mild-to-moderate: 60–80%.
<sup>i</sup> Severe: below 60% standard weight-for-age compared to above 75%. Mild-to-moderate: 60–75%.
<sup>j</sup> Severe: not documented. Mild-to-moderate: below 75% of expected weight-for-age compared to above 85% of expected weight-for-age.

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erence median weight-for-age were compared with those of the well-nourished children. Three studies (3, 7, 9) used the Harvard reference data, while two (6, 11) used the NCHS data.

Because the analysis only included children aged 6–60 months, the data in the Indian study (7) for children aged 1–6 months were excluded and the remaining two age groups in the study (6–11 months and 12–36 months) were combined into a single category.

Formal tests for heterogeneity were calculated to test whether there were significant differences among the relative risks reported within each nutritional status category from the various studies (14). Tests of heterogeneity that are significant would indicate that the individual relative risks should not be pooled.

The overall estimates of relative risk for the combined studies were estimated using precision-based weighting (13). This method calculates a weighted average of the individual relative risks (RR) using the following equation:

\[
\ln RR = \frac{\sum (\ln RR)}{\sum 1/\text{Var} (\ln RR)} / \sum 1/\text{Var} (\ln RR)
\]

where the pooled variance is given by

\[
\text{Var} (\ln RR) = \frac{1}{\sum 1/\text{Var} (\ln RR)}
\]

A Mantel–Haenszel summary \(\chi^2\) test (13) was used to test the overall association between each level of malnutrition and mortality.

**Estimation of global attributable risk of malnutrition-associated mortality**

Pooled relative risk estimates were used in conjunction with malnutrition prevalence data to obtain an estimate of the attributable risk of malnutrition for child mortality in developing countries. The expressions used to derive this estimate and the detailed calculations are shown in Annex 1.

The population of 6–60-month-olds in developing countries was calculated to be 90% of the total under-5-year-old population in those countries classified by UNICEF as having “under-5 mortality rates” greater than 70 per 1000 live births (15). This cut-off was selected in accordance with the World Summit for Children goal of reducing the under-5 mortality rate in all countries during the 1990s by a third or to 70 per 1000, whichever is less (15). Because accurate age-specific death rates are lacking for most of the poorest countries, historical data were used to estimate the proportion of under-5 mortality that occurs after the first 6 months of life. Published rates for the period 1948–82 for 36 of what are now mostly “middle” developed countries (16–20) were used to generate a regression equation of the association between infant mortality rate and the proportion of those deaths that occur during the first 6 months of life (Annex 2 and Fig. 1). Current infant mortality rates from the 64 countries that still have under-5 mortality rates greater than 70 per 1000 (15) were then substituted into this equation. The results, along with current under-5 mortality rates and populations, were then used to calculate a population-weighted average of the overall percentage of under-5 mortality among 6–60-month-olds.

Malnutrition prevalences were taken from a review by Haaga et al. of weight-for-age data from 22 developing countries (12). These workers estimated that 39% of children aged 6–60 months in developing countries weigh less than 80% of the WHO reference median weight-for-age. Of these 39%, we estimated the proportion who were either mild-to-moderately or severely malnourished using a population-weighted average of the 74 countries that had an under-5 mortality rate greater than 70 per 1000 in 1988, the last year UNICEF published comprehensive, percent of median (rather than z-score) weight-for-age data (27). According to these data, approximately 85% of those children who are less than 80% of the reference median weight-for-age are 60–80% of the reference value (mild-to-moderately malnourished), while the remaining 15% are less than 60% of the reference value (severely malnourished).

**Fig. 1. Plot of infant mortality rate (IMR) against percent of this mortality that occurs between 0 and 5.9 months of age** (Note: 97 observations are “hidden” by others).
These proportions and populations of children aged 6–60 months in developing countries were then used to calculate the number of children in each nutritional status category. As shown in Annex 1, these numbers were used in conjunction with the pooled relative risks to estimate a mortality rate for "normally" nourished children.

We used the mortality rate for nonmalnourished children to calculate the number of deaths occurring among malnourished children by multiplying the number of malnourished children by the product of the mortality rate among nonmalnourished children and the relative risk of malnutrition. The number of deaths that would have occurred in this group if the children had not been malnourished was then subtracted from the total to determine the total number of "excess deaths" attributable to malnutrition.

Classical attributable risk (AR) formulas, such as the following, led to comparable results:

\[ AR = \frac{P_1(RR_1-1) + P_2(RR_2-1)}{1 + P_1(RR_1-1) + P_2(RR_2-1)} \]

where \( P_1 \) = prevalence of mild-to-moderate malnutrition; \( P_2 \) = prevalence of severe malnutrition; \( RR_1 \) = relative risk of mild-to-moderate malnutrition; and \( RR_2 \) = relative risk of severe malnutrition.

Results

Relative risk of mortality by level of malnutrition

The relative risk of mild-to-moderate malnutrition was 1.2–3.5 compared with the reference categories of better nourished children, whose percent expected weight-for-age was greater than either 75% or 80% of the median value (Table 2). These relative risks were significantly greater than unity in all but one (3) of the five studies. The test for heterogeneity indicated that individual study relative risks were marginally different from each other (\( \chi^2 = 9.1; 4 \) degrees of freedom (df); \( 0.05<P<0.1 \)). The pooled relative risk was 2.2 (95% confidence interval (CI) = 1.7, 2.8). The test for overall association indicated that this pooled value was significantly different from the null hypothesis (Mantel–Haenszel \( \chi^2 = 37.9, P<0.001 \)).

The relative risk of severe malnutrition ranged from 3.1 to 19.2 compared with the reference categories. A test for heterogeneity indicated that there were significant differences between the study relative risks (\( \chi^2 = 18.0 \) (4 df); \( P<0.005 \)). The pooled relative risk was 6.8 (95% CI = 4.9, 9.4); the overall association was highly significant (\( \chi^2 = 140.0 \) (1 df); \( P<0.001 \)).

Attributable risk of malnutrition

Using historical data from 36 countries, along with current infant mortality rates, under-5 mortality rates and population values, we estimated that about 52% of the approximately 11 million deaths among under-5-year-olds occur after the first 6 months of life (Annex 2). Thus, approximately 5.654 million deaths occur among children aged 6–60 months of age in developing countries. Using this value, along with prevalences of mild-to-moderate and severe malnutrition (33% and 6%, resp.) and the pooled relative risk estimates for mild-to-moderate and severe malnutrition, we calculated that the mortality rate for nonmalnourished children was 10 per 1000 (see Annex 1). An estimated 1,251,280 excess deaths occur in mild-to-moderately malnourished children aged 6–60 months, while 1,067,268 excess deaths occur in severely malnourished children. In total, 2,318,548 deaths were calculated to be attributable to malnutrition. These malnutrition-associated excess deaths represent 41% of all deaths in this age group, or 21% of all deaths among under-5-year-olds.

Discussion

The objective of the study was to review and carry out a synthesis of published data on the mortality of children 6–24 months after their nutritional status had been determined. Specifically, pooled relative risk estimates associated with malnutrition and global attributable risk estimates were calculated.

Critique of methods used

Weight-for-age as the index of comparison. Weight-for-age was selected as the index of comparison since the majority of studies identified included this indicator of nutritional status, and data on the global prevalence of malnutrition based on this criterion are available. Weight-for-age is a robust predictor of long-term mortality (22). In contrast, growth velocity and weight-for-height more closely reflect current nutritional conditions and may be more extremely influenced by such events as a recent infectious disease (23) or seasonal differences in food availability (24). Both these indices may be more susceptible to the interpretational problems caused by reverse causality since, for example, an acute infectious disease may both result in low weight-for-height and lead to death. Weight-for-age is more resistant to transient conditions and therefore less subject to this problem (25).

Excluded studies and potential biases. Five of the studies identified were eliminated from the pool. These were compared in detail with those that were included in order to determine whether any selection
Table 2: Summary of data and risk of mortality associated with malnutrition in the five studies included in the analysis

<table>
<thead>
<tr>
<th>Study (ref.)</th>
<th>% of standard used to define:</th>
<th>Age (months)</th>
<th>No. malnourished:</th>
<th>No. not malnourished</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Malnourished</td>
<td>Not malnourished</td>
<td>Mortality rate (per 1 000)</td>
<td>Mortality rate (per 1 000)</td>
<td></td>
</tr>
<tr>
<td><em>Mild-to-moderate malnutrition</em></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Kielmann &amp; McCord (7)</td>
<td>60–79</td>
<td>≥80</td>
<td>6–36</td>
<td>47</td>
<td>3 753</td>
</tr>
<tr>
<td>Chen et al. (3)</td>
<td>60–74</td>
<td>≥75</td>
<td>12–23</td>
<td>44</td>
<td>1 042</td>
</tr>
<tr>
<td>Heywood et al. (9)</td>
<td>61–80</td>
<td>≥81</td>
<td>6–30</td>
<td>27</td>
<td>380</td>
</tr>
<tr>
<td>Alam et al. (6)</td>
<td>60–79</td>
<td>≥80</td>
<td>12–59</td>
<td>40</td>
<td>6 884</td>
</tr>
<tr>
<td>Yambi et al. (11)</td>
<td>60–79</td>
<td>≥75</td>
<td>6–36</td>
<td>33</td>
<td>492</td>
</tr>
<tr>
<td>Pooled</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><em>Severe malnutrition</em></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Kielmann &amp; McCord (7)</td>
<td>&lt;60</td>
<td>≥80</td>
<td>6–36</td>
<td>19</td>
<td>261</td>
</tr>
<tr>
<td>Chen et al. (3)</td>
<td>&lt;60</td>
<td>≥75</td>
<td>12–23</td>
<td>48</td>
<td>379</td>
</tr>
<tr>
<td>Heywood et al. (9)</td>
<td>&lt;61</td>
<td>≥81</td>
<td>6–30</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>Alam et al. (3)</td>
<td>&lt;60</td>
<td>≥80</td>
<td>12–59</td>
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<td>&lt;60</td>
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<td>26</td>
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<tr>
<td>Pooled</td>
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</tr>
</tbody>
</table>

* P value <0.01.
* Figures in parentheses are the 95% confidence interval.
* P value <0.05.
* Mantel-Haenszel summary $\chi^2 = 37.9$ (1 degree of freedom) = $P <0.001$; test for heterogeneity $\chi^2 = 9.1$ (4 degrees of freedom), 0.05<P<0.10.
* Mantel-Haenszel summary $\chi^2 = 140.0$ (1 degree of freedom) = $P <0.001$; test for heterogeneity $\chi^2 = 18.0$ (4 degrees of freedom), P<0.005.
biases may have influenced the findings (Table 1). In Bangladesh, Sommer et al. defined mild-to-moderate malnutrition as 10th–50th percentile of arm-circumference-for-height and “adequate” nutritional status as greater than the 50th percentile (2). The relative risk of mild-to-moderate malnutrition was 1.6 and of severe malnutrition (defined as less than the 9th percentile of arm-circumference-for-height) was 4.5.

In the study by Briend et al., crude data (e.g., the number at risk and the number who died) for each nutritional status category were not reported; instead, the “risk of death per 1000” at various arm-circumference cut-off points was given (5). Children whose arm-circumference measured 12.5 cm (the cut-off commonly used for mild-to-moderate malnutrition) at the start of the study period had a risk of death of 35 per 1000 and those who measured 13.5 cm had a risk of death of 16 per 1000. Based on these values, the relative risk of mild-to-moderate malnutrition would be 2.2. Similarly, severely malnourished children (arm-circumference, 11.5 cm) had a relative risk of mortality of 6.8 compared with those measuring 13.5 cm. Both of these relative risks are underestimates since they do not include children who were less than the cut-off value, only those exactly on the cut-off. For example, Briend et al. reported that children whose arm-circumference was 10.0 cm had a risk of death of 152 per 1000, almost twice that of those who measured 11.5 cm.

The Kosongo project did not report crude data; instead, the findings were presented as a risk ratio of 1.8 for children below 80% of the Harvard standard weight-for-age — roughly analogous to mild-to-moderate malnutrition — compared with those above 80% (8). For severely malnourished children (i.e., those <60% of the Harvard standard versus those >60% of the standard) the risk ratio reported was 3.3. This risk ratio would have been greater had the Kosongo project used “above 80%” of the standard as the comparison group, as is usually the case.

In Guinea-Bissau, Smedman et al. defined severe malnutrition as less than 75% of the expected weight-for-age rather than less than 60%, as in the other studies (10). Using this definition, they determined that the relative risk of malnutrition was 1.48 (95% CI = 0.86, 2.55), which is similar to the relative risks for mild-to-moderate malnutrition reported by many of the other studies.

The studies that were excluded therefore reported relative risks of malnutrition that were quite similar to those of the studies included in the final pooled analysis.

**Limiting the analysis to the 6–60-month age group.** Low weight-for-age during the first 6 months of life is generally more related to low birth weight than to postnatal nutritional conditions; thus, the analysis was restricted to older infants and children. Although analyses using narrower age strata would be preferable, of the studies selected only the investigation from India presented results disaggregated by age (7). In order to improve comparability among studies, data for infants less than 6 months of age in the Indian study were not pooled and the two older age groups were combined. This was reasonable since the test for heterogeneity by age group was not significant (13) ($\chi^2 = 0.24$ (1 df)).

The 6–60-month age range was selected because it was used by Haaga et al. to calculate the global prevalence of childhood malnutrition (11). Although four of the five studies selected measured weight-for-age of somewhat younger children (i.e., <36 months of age initially), the children’s ages were as high as 48 months after the follow-up period. It is unlikely that the relative risks for mortality vary much between 48 and 60 months of age.

**Pooling of relative risk estimates.** Pooled analyses of relative risk were carried out even though the tests for heterogeneity suggested that risk estimates differed significantly among the studies. Notably, only the study by Chen et al. caused the tests of heterogeneity to be statistically significant (3). Exclusion of this study results in even higher pooled estimates of the relative risk of malnutrition (2.7 (95% CI = 2.0, 3.6) for mild-to-moderate malnutrition; 11.7 (95% CI = 7.7, 17.7) for severe malnutrition).

The calculated pooled relative risk estimates of 6.8 for severe and 2.2 for mild-to-moderate malnutrition are very similar to those recently reported by Pelletier et al. (26). The latter analysis, which included four (6, 7, 9, 11) of the studies used in the present article as well as four additional data sets (4, 27, 28), reported pooled relative risks of 8.4, 4.6, and 2.5 for severe, moderate, and mild malnutrition, respectively. The analysis by Pelletier et al. also confirmed the lack of heterogeneity across studies, except for the study by Chen et al. (3), as discussed above.

**Prevalence data and estimates of 6–60-month mortality.** Estimating the rates of mortality for the 6–60-month age group was hindered by a lack of data for this age range. Plots of historical data from 36 of what are now mostly “middle-level” under-5-mortality-rate countries, however, demonstrated a clear relationship between infant mortality rate and the proportion of this rate that occurs during the first 6 months of life.

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(Fig. 1). As the infant mortality rate declines, a greater percentage of these deaths occur in the first few months after birth. The regression equation derived from these data (Annex 2), along with population-weighted values from the 64 countries that have under-5 mortality rates greater than 70 per 1000 (14), suggest that about 52% of such mortality occurs between the ages of 6 and 60 months.

Validity of results

Percentage of young-child deaths associated with malnutrition. The analysis found that 41% of all young childhood deaths were associated with some form of malnutrition. Using the pooled relative risk estimates of 11.7 (severe malnutrition) and 2.7 (mild-to-moderate), calculated after excluding the study by Chen et al. (3), we determined that the proportion of 6–60-month deaths associated with malnutrition was 52%. Similarly, using the pooled values of 8.0 (severe malnutrition) and 3.5 (mild-to-moderate) suggested by Pelletier et al. (26), we determined the attributable risk due to malnutrition to be 55%. These estimates are all consistent with those determined by Puffer & Serano (29), who reported that “nutritional deficiency” was associated with about 50% of deaths from infectious diseases among under-5-year-olds in the Americas. Similarly, Mosley (30) and Chen et al. (31), calculated that 38% and 45%, respectively, of the deaths in the Bangladesh study (3) were nutritionally related.

Is the association causal? Formal criteria to evaluate whether an association between a risk factor and a health outcome indicates a causal relationship often include the following: strength of the association; dose–response effect; consistency of the findings; lack of temporal ambiguity; and biological plausibility (32, 33). As described below, a review of the malnutrition–mortality association using these criteria strongly suggests a causal relationship.

The strength of association is reflected in the pooled relative risk estimates of 6.8 for severe and 2.2 for mild-to-moderate and severe malnutrition, respectively. As noted above, these are probably underestimates since the elimination of one study (3) resulted in pooled relative risk estimates of 11.7 and 2.7 for severe and mild-to-moderate malnutrition, respectively. Public health policy and programmatic decisions are often influenced by much lower risk estimates. A dose–response effect, with well-nourished children having less risk for mortality than mild-to-moderately malnourished children, who in turn have less risk than those who are severely malnourished, was observed in all the included and excluded studies. This similarity among studies carried out in different settings also confirms the consistency of findings criterion. Since only prospective studies were considered, temporal ambiguity is unlikely. The use of weight-for-age increased the probability that mortality was due to long-term nutritional status rather than an acute disorder. Finally, it is biologically plausible that malnutrition may cause mortality; protein–energy malnutrition compromises a myriad of human functions; for example, depressed immune function is associated with protein–calorie malnutrition (34), increasing susceptibility to infections that may lead to death. Numerous field studies have shown that poor nutritional status leads to more severe disease and higher case fatality (35, 36).

Are the results biased by confounding factors? Despite the above argument, it is conceivable that the association between malnutrition and mortality may be spurious, being caused instead by confounding factors that are associated with both nutritional status and mortality. The following are examples of potential confounders: age; infectious disease patterns; availability of medical services; socioeconomic factors; and nutritional conditions not captured by weight-for-age measures. Variations in some of these factors are probably responsible, in part, for the differences in relative risk estimates among studies. Unfortunately, few of the published studies presented results stratified by potentially confounding factors; hence, it is not possible to resolve this issue unequivocally.

We have discussed the stratification by age carried out by Kielmann & McCord (7). The homogeneity of the two older age groups in Kielmann & McCord’s study, and the fact that other studies did not identify age as a confounder, suggests that our use of the 6–60 month age grouping is acceptable.

Differences in morbidity patterns according to study location may have influenced the relative risk estimates. Heywood noted that diarrhoea is the leading cause of death in Bangladesh, while pneumonia is the chief cause of death in the highlands of Papua New Guinea (37). Importantly, the fact that infectious diseases are often the final cause of death does not diminish the significance of malnutrition as the predisposing cause of more severe illnesses.

The availability of nutrition and medical services may have contributed to the differences in relative risk estimates between studies, though complete information on this issue was unavailable. Also, socioeconomic variations may have affected the relationship between malnutrition and mortality. In the study by Chen et al. (3), maternal nutritional status and the socioeconomic conditions of families were closely correlated with mortality; the authors suggested that “background noise” (e.g., general child
care and parental response to illness) may have obscured differences between subgroups of the population and between populations (38).

Finally, differential micronutrient deficiencies may have affected mortality rates. Vitamin A deficiency, for example, has been associated with increased childhood mortality in Indonesia (39), India (40), and Nepal (41). It is unclear whether anthropometric indicators reflect nutritional status with regard to specific micronutrients.

In summary, it would be preferable to have more complete information on potential confounding variables in order to isolate better the malnutrition–mortality association of interest. Nevertheless, all of the other tests of the relationship suggest that malnutrition is responsible, at least in part, for the excess mortality observed in association with low weight-for-age.

**Suggestions for future studies**

The present article has emphasized the difficulties of comparing available longitudinal field studies to draw causative rather than simply associative conclusions. An important lesson of this exercise is that, while nutritional status is generally recognized to be an important component of child survival, few investigations have quantified its impact using optimal methods. To achieve better understanding of causal relationships, it is necessary to conduct randomized, controlled community trials of interventions that produce improved nutritional status. In order to minimize potential confounding of results, data on socioeconomic conditions (particularly maternal education), illnesses, medical treatments, etc. should be collected. Analyses should consider these potentially confounding factors, and the presentation of results should be sufficiently detailed to permit critique and assessment.

**Significance of the analysis and programmatic implications**

The above analysis verifies the strong association between malnutrition and mortality: 40–55% of young children who die in developing countries are malnourished. Current global health programmes, however, do not reflect the magnitude of the role that nutrition plays in child survival. Specific disease control programmes to improve child survival have been developed for diarrhoeal diseases (42) and acute respiratory infections (43), which currently have similar attributable risk estimates. Although we do not necessarily ascribe to the approach used in “vertical programmes” for control of malnutrition, a similar level of effort should be directed to eliminate or reduce it. In addition, the evidence for the poten-}

tiating effect of malnutrition on child mortality supports the concept that health and nutrition interventions should be integrated within the same programmes in order to take advantage of the multiplicative impact on mortality and the associated improvements in cost-effectiveness (44).

In summary, we believe that at the beginning of the second decade of child survival programmes, current public health strategies have lost sight of the overwhelming impact of malnutrition on children’s well-being. Intensified efforts are therefore needed to develop more effective and cost-efficient nutrition interventions. These are likely not only to reduce current rates of child mortality in developing countries, but also to improve children’s behavioural development, school performance, and future productivity (45, 46).

**Résumé**

L’état nutritionnel, facteur prédictif de la survie chez l’enfant: récapitulation des données et estimation de l’impact mondial

Les tentatives visant à réduire la mortalité infantile dans les pays en développement grâce à des soins de santé primaires sélectifs sont principalement axées sur la prévention et le traitement de maladies infectieuses déterminées, en n’accordant qu’une importance plus faible à l’amélioration de l’état nutritionnel sous-jacent.

Afin de récapituler l’ensemble des informations disponibles sur la relation entre l’état nutritionnel préexistant, évalué par des indicateurs anthropométriques, et la mortalité à long terme, nous avons réanalysé les données publiées et établi des estimations groupées du risque relatif pour divers degrés de malnutrition, en utilisant quatre études comparables. Ces données ont été combinées avec les estimations de la prévalence de la malnutrition pour calculer le nombre de décès chez l’enfant qui, dans les pays en développement, peuvent être «attribués» à la malnutrition.

Les jeunes enfants (6–60 mois) souffrant de malnutrition légère à modérée (60–80% de la médiane du poids de référence pour l’âge) avaient un risque 2,2 fois plus élevé de décéder au cours de la période de suivi que leurs équivalents mieux nourris (>80% de la médiane du poids de référence pour l’âge), alors que les jeunes enfants gravement dénutris (<60% de la médiane du poids de référence pour l’âge) avaient un risque 6,8 fois plus élevé de décéder pendant cette période.

On estime que, dans les pays en développement, 52% de l’ensemble des décès chez les
moins de 5 ans survivent après l’âge de 6 mois. Sur ce nombre, environ 2,3 millions de décès (soit 41% des décès pour ce groupe d’âge) sont chaque année imputables à la malnutrition.

L’ampleur du risque attribuable est, pour la malnutrition, du même ordre que pour les autres maladies actuellement visées par les programmes mondiaux de survie de l’enfant. Ces programmes devraient donc accorder une priorité plus élevée à la lutte contre la malnutrition de l’enfance.

Dans le présent article sont également examinés la comparabilité des études, les méthodes utilisées pour obtenir les données globales, les éventuels facteurs confondants susceptibles d’influer sur les estimations du risque, et la validité des résultats.

References


**Annex 1**

**Deaths associated with malnutrition**

The following expression was used to determine the total under-5-year-old mortality:

\[
\text{Total mortality (children aged 6–60 months)} = (\text{Relative risk of severe malnutrition} \times \text{(No. severely malnourished)} \times (\text{"normal" mortality rate}^4) + \\
(\text{Relative risk of mild-to-moderate malnutrition} \times \text{(No. of mild-to-moderately malnourished)} \times (\text{"normal" mortality rate}) + \\
(\text{No. of "normally" nourished)} \times (\text{"normal" mortality rate})
\]

The terms in this expression were determined as shown below.

- Total under-5-year-old population in 64 countries with USMR of ≥70 per 1000 × (% of under-5-year-olds aged 6–60 months) = 349 500 000 × 90%

Population of 6–60-month-olds = 314 550 000

- Total under-5-year-old mortality in 64 countries with USMR of 70 per 1000 × (% of under-5-year-old deaths after first 6 months) = 10 873 000 × 52%

i.e., Mortality among 6–60-month-olds = 5 653 960

Relative risk of severe malnutrition = 6.8

- Total population of 6–60-month-olds) × (total % malnourished) × (% of the malnourished who are severely malnourished) = 314 550 000 × 39% × 15%

i.e., No. of severely malnourished = 18 401 175

Relative risk of mild-to-moderate malnutrition = 2.2

- Total population of 6–60-month-olds) × (total % malnourished) × (% of the malnourished who are mild-to-moderately malnourished) = 314 550 000 × 39% × 85%

i.e., No. of mild-to-moderately malnourished = 104 273 325

- 6–60-month normal mortality rate = "normal" mortality rate

\[
(\text{Total population of 6–60-month-olds)} \times (\% \text{ normally nourished) = 314 550 000 × 61%}
\]

i.e., No. of normally nourished = 191 875 500

Substituting these calculated values in the above expression for total mortality among 6–60-month-olds gives

Total mortality (children aged 6–60 months) = 6.8 × ("normal" mortality rate) × (18 401 175) + (2.2) × ("normal" mortality rate) × (104 273 325) + ("normal" mortality rate) × (191 875 500)

and "normal" mortality rate = 0.01

- (Relative risk for mild-to-moderate malnutrition) × ("normal" mortality rate) = 2.2 × 0.010

i.e., Mortality risk with mild-to-moderate malnutrition = 0.022.

- (Relative risk for severe malnutrition) × ("normal" mortality rate) = 6.8 × 0.010

i.e., Mortality risk with severe malnutrition = 0.068

No. of deaths of children with mild-to-moderate malnutrition = 2 294 013c

\[\text{minus}\]
Nutritional status and child survival

No. of these children who would have died anyway = 1 042 733\(^d\)

No. of excess deaths associated with mild-to-moderate malnutrition = 1 251 280

No. of deaths of children with severe malnutrition = 1 251 279\(^e\)

\(\text{minus} \)

No. of these children who would have died anyway = 184 011\(^f\)

No. of excess deaths associated with severe malnutrition = 1 067 268

Total excess young child deaths in least-developed countries associated with malnutrition = 2 318 548

This last figure represents 41% of all deaths of children aged 6–60 months in the 64 least-developed countries.

\(^a\) "Normal" mortality rate = mortality rate of "normally" nourished children.

\(^b\) U5MR = under-5-year-old mortality rate.

\(^c\) (No. of mild-to-moderately malnourished) \(\times\) (mortality risk) = 104 273 325 \(\times\) 0.022.

\(^d\) (No. of mild-to-moderately malnourished) \(\times\) (normal risk) = 104 273 325 \(\times\) 0.010.

\(^e\) (No. of severely malnourished) \(\times\) (mortality risk) = 18 401 175 \(\times\) 0.068.

\(^f\) (No. of severely malnourished) \(\times\) (normal risk) = 18 401 175 \(\times\) 0.010.

Annex 2

Percent of under-5-year-old mortality involving 6–60-month-olds

The regression formula for modelling the relationship between infant mortality rate \((\text{IMR})\) and the percent of this rate that occurs in months 0–5 \((\text{PIMR05})\), as shown in Fig. 1, is given by the following expression:

\[
\text{PIMR05} = [10 809 - 60.76 (\text{IMR})]^{0.5}
\]

The proportion of the under-5-mortality rate \((\text{U5MR})\) that is \(\text{IMR}\), i.e., \(\text{PIMR}\) is given by the expression

\[
\text{PIMR} = \frac{\text{IMR}}{\text{U5MR}}
\]

Finally, the percent of \(\text{U5MR}\) after the first 6 months of life \((\text{P6-60})\) is given by the expression

\[
\text{P6-60} = 1 - ((\text{PIMR05}/100) \times \text{PIMR})
\]

Example: India

Current values (ref. 15): \(\text{IMR} = 84; \text{U5MR} = 126\)

Percent of \(\text{IMR}\) that occurs in months 0–5: 75.5% = \(10809 - 60.76 (84))^{0.5}\)

Percent of \(\text{U5MR}\) that is \(\text{IMR}\): 0.66 = 84/126

Percent of \(\text{U5MR}\) that occurs in months 6–60:

\[0.50 = 1 - (0.76 \times 0.66)\]