The global burden of diarrhoeal disease, as estimated from studies published between 1992 and 2000

Margaret Kosek,[1] Caryn Bern,[2] & Richard L. Guerrant[1]

Abstract Current estimates of the global burden of disease for diarrhoea are reported and compared with previous estimates made using data collected in 1954–79 and 1980–89. A structured literature review was used to identify studies that characterized morbidity rates by prospective surveillance of stable populations and studies that characterized mortality attributable to diarrhoea through active surveillance. For children under 5 years of age in developing areas and countries, there was a median of 3.2 episodes of diarrhoea per child-year. This indicated little change from previously described incidences. Estimates of mortality revealed that 4.9 children per 1000 per year in these areas and countries died as a result of diarrhoeal illness in the first 5 years of life, a decline from the previous estimates of 13.6 and 5.6 per 1000 per year. The decrease was most pronounced in children aged under 1 year. Despite improving trends in mortality rates, diarrhoea accounted for a median of 21% of all deaths of children aged under 5 years in these areas and countries, being responsible for 2.5 million deaths per year. There has not been a concurrent decrease in morbidity rates attributable to diarrhoea. As population growth is focused in the poorest areas, the total morbidity component of the disease burden is greater than previously.

Keywords Diarrhea/epidemiology; Child; Cost of illness; Developing countries; Longitudinal studies; Meta-analysis (*source: MeSH, NLM*).

Mots clés Diarrhée/épidémiologie; Enfant; Coût maladie; Pays en développement; Etude longitudinale; Méta-analyse (*source: MeSH, INSERM*).

Palabras clave Diarrea/epidemiología; Niño; Costo de la enfermedad; Países en desarrollo; Estudios longitudinales; Meta-análisis (*fuente: DeCS, BIREME*).

Bulletin of the World Health Organization 2003;81:197-204.

Voir page 201 le résumé en français. En la página 202 figura un resumen en español.

Introduction

Diarrhoea is one of the principal causes of morbidity and mortality among children in the developing world. In 1982, on the basis of a review of active surveillance data from studies conducted in the 1950s, 1960s and 1970s, it was estimated that 4.6 million children died annually from diarrhoea (*1*). In 1992, a review of studies conducted in the 1980s suggested that diarrhoeal mortality had declined to approximately 3.3 million annually (*2*). Both reviews estimated that children in the developing world experienced a median of between two and three episodes of diarrhoea every year. Neither review included data from China.

Since 1993 more complex methodologies have been applied to a wider range of data sources in order to estimate the global disease burden attributable to specific conditions, including diarrhoea (*3–5*). The strengths of recent approaches to disease burden modelling include the ability to compare figures for multiple diseases and the inclusion of the disability-adjusted life year, which takes into account both morbidity and mortality (*6*). However, for diseases that have been studied closely over time in many locations, such as diarrhoea among young children in developing countries, our understanding may also be deepened by a more detailed review of the most rigorously conducted studies. The purpose of the present review is to examine recent data from studies meeting the same stringent criteria as were applied in the 1982 and 1992 reviews, and to look at trends and patterns in the light of current thinking on diarrhoeal diseases and related causes of morbidity and mortality.

Methods

The studies included in this review were identified through MEDLINE searches for English language sources published since 1990 by using the following keywords: morbidity and diarrhoea; longitudinal studies and diarrhoea; mortality and diarrhoea; and verbal autopsy and diarrhoea.

Further sources were located by cross-referencing, consultation with experts in the field, and the use of the related articles link. Morbidity studies were included if active surveillance had been conducted for at least one year in a stable population of children under 5 years of age in developing countries, including China. For intervention studies, only the placebo or non-intervention group was included in the estimates. In order to allow comparison over time we utilized the methods of the two previous reviews (*1*, *2*). Whenever

[1] Division of Geographic and International Medicine, University of Virginia, Charlottesville, VA, USA. Correspondence should be addressed to Dr Guerrant at the following address: Box No. 485, Health Sciences Center, Charlottesville, Virginia 22908, USA (email: RGL9A@hscmail.mcc.virginia.edu).

[2] Division of Parasitic Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA.

Ref. No. **01-1194**

possible, data were stratified by age categories (0–5 and 6–11 months, and 1, 2, 3 and 4 years). Morbidity was expressed as episodes of diarrhoea per person-year. Because longitudinal data for older persons were sparse, estimates were calculated only for children aged under 5 years.

Studies were included in the mortality estimates if deaths due to diarrhoea were ascertained through active surveillance. Our estimates included prospective and retrospective studies but not ones based on vital statistics only. Death was considered to have been caused by diarrhoea only if this was listed as the primary cause. Studies that assigned equal weight to multiple causes of death were not included in the mortality estimates. If two sources described mortality rates in the same population with overlapping observation periods, only data from the more recent source were included.

Demographic data were obtained from the 1995 UNESCO estimates for countries in the following WHO regions: African, Americas, Eastern Mediterranean, South-East Asia, and Western Pacific (*7*). In contrast to the two earlier reviews, which excluded China from their calculations, three studies provided data from this country.

Results

Morbidity

Twenty-seven studies were included in the morbidity analysis (*8–38*) (Table 1). The studies varied in their definitions of diarrhoea and the frequency of surveillance. One study defined diarrhoea as two or more loose stools per day; 16 studies defined it as three or more loose stools per day; three studies defined it as four or more loose stools per day; in nine studies a local definition or that of the principal carer was used. Four studies also included episodes of bloody stool as diarrhoeal illness. The frequency of surveillance varied from once per day (n = 1) to once per month (n = 2), but most studies interviewed carers between two and three times weekly (n = 16) or weekly (n = 8). The incidence of diarrhoea was highest among children aged 6–11 months, who experienced a median of 4.8 episodes per child per year (Fig. 1). The incidence fell progressively to 1.4 episodes per child per year for 4-year-olds. The median incidence for all children aged under 5 years was 3.2 episodes per child-year.

The calculated median incidences were similar to those of the two previous reviews (Fig. 1). The slightly higher estimates in the current review may reflect more frequent surveillance of smaller populations in recent studies, resulting in more complete detection of mild episodes of illness (*1*, *39*). Of 18 morbidity studies reviewed by Snyder & Merson in 1982, only five involved at least weekly follow-up of study populations smaller than 600; the median incidence was 3.0 episodes per child-year in these studies, whereas it was 2.2 for all the studies in the review. In the 1992 review, populations smaller than 600 were followed up at least twice weekly in 17 of 22 studies. The present review included studies comparable to those covered by the 1992 review: a group of fewer than 600 children was followed up in 15 of 27 studies and surveillance was at least weekly in 24 studies and at least twice weekly in 15 studies.

Mortality

Mortality estimates were derived from 34 studies in 21 countries (Table 2) (*40–73*). The age categories varied. In 22 studies, relevant data were provided for children younger than 5 years as a single category. Only 15 studies provided mortality data for children aged under 1 year, while 10 provided data for children aged 1–4 years. Data from 30 studies were available for estimating the fraction of deaths attributable to diarrhoea. For children aged under 1 year and 1–4 years the median mortalities were 8.5 and 3.8 per 1000 children per year, respectively. Among children aged under 5 years the median mortality was 4.9 per 1000 per year and 21% of deaths were estimated to be attributable to diarrhoea.

The diarrhoea-specific mortality rates in infants and children aged 1–4 years and under 5 years in the developing world only were chosen in order to compare the summary statistics of the present study with those of the previous reviews (Fig. 2). This allowed the mortality burden to be expressed independently from the effects of population growth. Although the 1982, 1992, and current reviews used somewhat different age categories for their summary measures, there was a clear declining trend. Diarrhoea-specific mortality rates for children younger than 5 years steadily fell from 13.6 per 1000 per year in studies published between 1955 and 1979 to 5.6 per 1000 per year in 1980–89 and to 4.9 per 1000 per year in studies published between 1992 and 2000. For children aged under 1 year, mortality fell from 23.3 per 1000 per year in 1982 to 19.6 per 1000 per year in the 1992 review, and to 8.2 per 1000 per year in the current analysis. For children aged 1–4 years the fall was less marked, from 4.6 per 1000 per year in 1992 to 3.8 per 1000 per year in the current analysis.

The 1995 UNESCO estimates of the population of children aged under 5 years in the geographical areas of interest were multiplied by the specific mortality rate to obtain a yearly number of deaths from diarrhoea in this population. On the basis of this review, approximately 2.5 million children died from diarrhoeal disease each year in the 1990s (25th to 75th percentile, assuming a normal distribution of mortality rates: 2.1–4.7 million).

Case-fatality ratios

Case-fatality ratios were available from only two studies. One reported a case-fatality ratio of 0.11% in children under the age of 5 years (*38*). The other reported case-fatality ratios of 1.8% in children under the age of 1 year and 0.75% in children aged 1–3 years (*32*). The overall calculated case-fatality ratio obtained by dividing the estimated number of diarrhoea-related deaths by the estimated number of diarrhoea disease episodes in children under the age of 5 years was 0.15%, a quarter of that calculated in 1982 (0.6%) (*1*), half that reported in 1992 (0.3%) (*2*), and similar to the 0.2% estimated by the US Institute of Medicine in 1986 (*74*).

Discussion

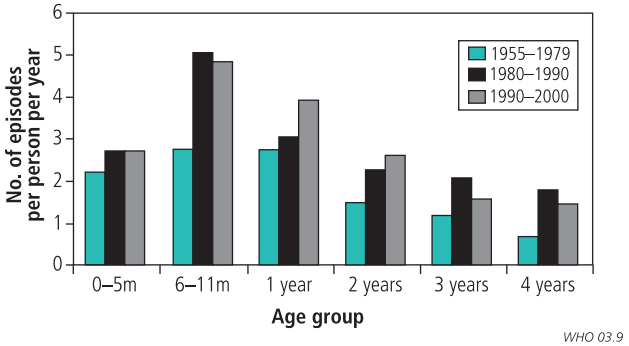
The 1982 review was one of the first analyses to use existing data to make explicit estimates of disease burden. During the past decade, composite estimates of disease and disability burden for a wide variety of conditions have been presented as providing a basis for priority-setting and resource allocation in the sphere of public health (*3–5*). Although such estimates are accepted as valuable, researchers have questioned the complex modelling used to derive them, the underlying social and economic assumptions, and the appropriateness of their use in regions where data are sparse (*75–78*). Focused reviews of primary research concerning specific diseases can provide a more transparent method of assessing and synthesizing the available data, and are an important complement to estimates based on composite measures such as the disability-adjusted life year.

Table 1. **Diarrhoea morbidity rates from prospective studies in 20 countries published between 1990 and 2000**

Region[a]	Country	Period	Population	No. of diarrhoea episodes per child at age						
				0–5 months	6–11 months	1 year	2 years	3 years	4 years	0–4 years
AFRO	Guinea-Bissau (*8*)	1987–90	1314							10.4
	Nigeria (*9*)	1989–90	351	3.3	4.1	2.9	2.2			
	Kenya (*10*)	1989–90	920	———	———	3.5	———	———[b]		
	Zaire (*11*)	1987–88	1914		7.3					6.3
	Zimbabwe (*12*)	1987–88	204	1.8	4.8					
AMRO	Brazil (*13*, *14*)	1989–93	189			6.8				5.25
	Brazil (*15*)	1990–91	620		———	———	7.1	———		
	Brazil (*16*)	1990–92	270	———	———	6.0	———			
	Chile (*17*)	1986–89	360	———	2.3	———	2.1	1.3	0.9	
	Honduras (*18*)	–	266	———	5.0	———	3.9	3.2	2.6	1.5	3.2
	Mexico (*19*)	1988–91	214	———	———	2.9	———			
	Guatemala (*20*)	1987–89	321	———	———	7.64	———	———	———	
	Peru (*21–23*)	1985–87	677	7.3	10.3	9.1	6.3			
EMRO	Egypt (*24*)	1995–98	397	7.3	8.8	5.5	3			
	Pakistan (*25*)	1995	227							7.1
	Pakistan (*26*)	1984–87	1476	———	———	3.6	———	———		
SEARO	Indonesia (*27*)	1989–91		———	———	0.84	———	———	———	
	Thailand (*28*)		449	2	2.4	1.2				0.9
	Bangladesh (*29*, *30*)	1988–89	705							4.6
	India (*31*)	1992–94	553	2	3.1	2	1.3	1.1		
	India (*32*)	1984–85	2278	———	6.0	———	5.5	4.2		
	India,Tamil Nadu (*33*)	1989	7655		———	———	5.6	———	———	
WPRO	China (*34*)	1989	74		1.8	1.8	1.7			
	China (*35*)	1986–87	270	———	4.2	———	3.8	2.3	1.6	1.7	2.5
	China (*36*)	1986–87								2.3
	Malaysia (*37*)	1988–89	156							0.24
	PNG[c] (*38*)	1986–89	1926	2.7	5.4	5	2.8	1.5	1.2	3
Median global estimates				2.7 (2.0–7.3)[d]	4.8 (2.8–8.1)	3.9 (2.0–5.5)	2.6 (1.7–3.5)	1.5 (1.2–2.1)	1.4 (1.0–1.7)	3.2 (2.3–6.3)

[a] AFRO = WHO African Region; AMRO = WHO Region of the Americas; EMRO = WHO Eastern Mediterranean Region; SEARO = WHO South-East Asia Region; WPRO = WHO Western Pacific Region.
[b] Solid lines indicate data for these ages combined.
[c] PNG = Papua New Guinea.
[d] Figures in parentheses are the 25th–75th percentiles.

Fig. 1. **Median age-specific incidences for diarrhoeal episodes per child per year from three reviews of prospective studies in developing areas, 1955–2000**



Estimates of disease burden from diarrhoea

Estimates of disease burden, however they may be derived, have substantial inherent uncertainty. In a detailed literature review the number of data points for any given region may be small, thus making regional estimates unreliable. The sites of the studies included may not be representative of the country or the region as a whole. In the present review the regional boundaries were defined on the basis of geographical and political considerations, and the countries in a region often varied widely in socioeconomic and health status. Summing across the countries of a region may obscure important differences. However, the stringent inclusion criteria of the current review ensured that the data provided the most valid information available for examining the morbidity and mortality caused by diarrhoeal disease in recent years. The most important results of this review may not be the precise numbers but rather the patterns and trends emerging from the analysis.

Our findings confirm that mortality from diarrhoea has fallen substantially but that morbidity has remained high over the last four decades. The estimated median number of annual deaths from diarrhoea fell from 4.6 million in 1982 to 3.0 million in 1992 and to 2.5 million in the current review, despite world population growth and the inclusion of China in the current analysis. This decreasing trend is corroborated by other recent reviews (*5*, *79*) and by vital registration data in Latin America (*80*).

Table 2. **Age-specific annual mortality rates from 34 studies in 21 countries published between 1992 and 2000**

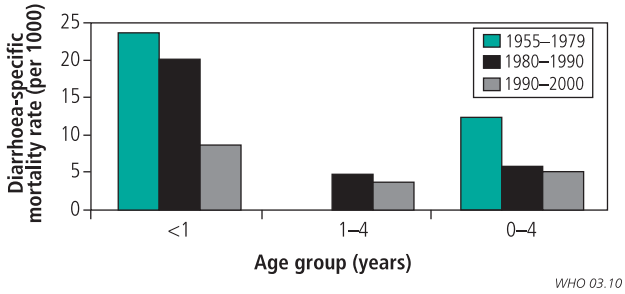
Region[a]	Country	Period	Population	Age-specific mortality rate (per 1000 per year)				% of 0–4 years mortality
				<1 year	1–4 years	0–4 years	under-5[b]	
AFRO	Gambia (*40*)	1989–93	155 000[c]	5.6	1.9			8.4
	Gambia (*41*)	1988–89	26 089	11	4.5	5.9		17
	Ghana (*42*)	1990	851			4.3		43
	Ghana (*43*)	1989–91	ca 11 000			5.2		27.8
	Ghana (*44*)	1993–95	16 495			4.2		15.3
	Guinea-Bissau (*45*)	1987–90	1426			18.9		30.7
	Nigeria (*46*)	1987	1928			20		33
	Senegal (*47*)	1985–89	6352[c]				15.1	18.6
	Ethiopia (*48*)	1994–95	5430		14.6			
	Ethiopia (*49*)	1986–88	5067	7.6	3.1	4.1		8.4
	South Africa (*50*)	1992–95	63 000[c]			1.5		20
AMRO	El Salvador (*51*)	1988–93	children of 5752 women	7	3	3.8		20
	Ecuador (*52*)	1979–89	children of 7961 women	7	5	5.4		23
	Nicaragua (*53*)	1982–93	children of 7150 women	12	15	14.4		31
EMRO	Egypt (*54*)	1992–96	1636	40.6			51.5	39.4
	Pakistan (*55*)	1988–91	4000[c]	13			22.7	35
	Pakistan (*56*)	1986	1194			8.8		22
	Sudan (*57*)	1988–90	14 149			3.5		43
SEARO	Indonesia (*58*)	1992–93	914	5.2				
	Indonesia (*59*)	1986–87	8624			9.9		23
	Thailand (*60*)	1991	824				20.1	14.1
	Bangladesh (*61*)	1986–87	189 700[c]			8.6		24.5
	India (*62*)	1987	3947			8.4		20
	India, Aligarh (*63*)	1989–90	2035	16.8	6.3	11.8		37.5
	India, Ballarbgarh (*64*)	1992–94	5000	8.5				16.7
	India, Lucknow (*65*)	1993–94	2796			4.6		18.3
	India, Pune (*66*)	1987–94	4129	7.8	0.64	2.1		15
	India, Tamil Nadu (*67*)	1989	7655			4.3		41
	India, West Bengal (*68*)	1988	46 913[c]	9.9				17
	Nepal (*69*)	1989–90	14 143			4.6		28
	Nepal (*70*)	1989–91	5832	—17.0[d]———[e]		20[c]		
WPRO	China, Guizhou (*71*)	1985–87	24 469	11.3				9
	Philippines (*72*)	1998–91	9942	—6.3[d]———		14.6[d]		
	Viet Nam (*73*)	1988	9691	3.4	0.68	1.4		13
Median global estimates					8.5 (7.0–12)[f]	3.8(1.6–8.4)	4.9(1.0–9.1)	21(16–32)

[a] See footnote a, Table 1.
[b] under 5 = cumulative mortality in children aged under 5 years.
[c] Total population.
[d] 0–2 years.
[e] Solid lines indicate that the data from these ages are combined.
[f] Figures in parentheses are the 25th–75th percentiles.

Estimates of mortality in developing countries should be interpreted with caution. In addition to the uncertainties inherent in extrapolation from relatively sparse data, there may be variations between studies in the methods of determining causes of death. For studies included in the 1982 review, the ascribed causes of death were based on physicians' clinical findings or on death certificates. The majority of the studies covered by the 1992 review and the current review used verbal autopsies, the sensitivity and specificity of which are reported to vary between sites (*81*–*83*). The Global Burden of Disease estimates (*3*, *4*) were derived from vital registration data, and, for regions with low coverage, from mathematical modelling based on such data (*84*). For the regions included in the current review, only countries in Latin America had vital registration coverage reaching 28% (*84*). For sub-Saharan Africa the coverage was estimated to be 0.4% (*84*), and this has led some authors to suggest that the estimates should not be used (*78*).

In contrast to mortality estimates, the incidence of diarrhoea appears to have remained remarkably stable over time. While the studies reviewed in 1982 may have underestimated incidence because of large study populations and infrequent surveillance (*39*), the 1992 review and the current one covered comparable groups of studies in these terms. Persistently high rates of morbidity are of concern, because early childhood diarrhoea may have long-term effects on linear growth (*85*, *86*) and physical and cognitive function (*87*).

Fig. 2. **Diarrhoea-specific mortality trends from three reviews of active surveillance in developing areas, 1955–2000.** Only two studies presented in the review covering 1955–79 described age-specific mortality for children aged 1–4 years. Consequently, no rate is shown for this age group



Interventions for diarrhoeal disease

Most interventions for diarrhoeal disease, e.g. increased breastfeeding, better weaning practices, improved sanitation and higher rates of measles immunization, would be expected to affect mortality and morbidity simultaneously. The use of oral rehydration therapy is an exception, its increased use over the past two decades probably having been responsible for some of the decrease in case-fatality rates, especially from acute dehydrating diarrhoea. Globally, the proportion of diarrhoeal episodes treated with oral rehydration therapy was estimated to have risen from less than 15% in 1984 to approximately 40% in 1993 (*88*). Diarrhoeal mortality has fallen more rapidly among children aged under 1 year than among those aged 1–4 years. This is consistent with the observation that infants are at higher risk for death from acute dehydrating diarrhoea (*89*). Where oral rehydration therapy is widely used, persistent diarrhoea or dysentery may cause an increasing proportion of diarrhoeal deaths relative to those associated with watery diarrhoea (*90*). In order to achieve further declines in mortality it may be necessary to adopt a more complex approach that would include distinguishing acute watery diarrhoea, dysentery and persistent diarrhoea, and ensuring appropriate case management for each syndrome. These issues are specifically addressed in the WHO/UNICEF initiative for the improved management of childhood illness (*91*). Furthermore, diarrhoea surveillance should classify diarrhoeal episodes as acute watery, dysenteric, or persistent so that interventions can be appropriately targeted at the population level.

Nutritional status is another factor that may help to explain the de-linking of diarrhoeal mortality and morbidity rates. There are conflicting data on the effect of malnutrition on the incidence of diarrhoea (*92–95*). However, investigators agree that malnutrition prolongs the duration of diarrhoea (*92*, *94*, *96*) and increases the risk of mortality from the condition (*72*, *97–99*). The past two decades have seen an impressive decrease in rates of stunting in all parts of the world except East Africa (*100*).

The interaction between malnutrition and diarrhoeal disease is bi-directional (*101*). Increases in immunization coverage, better health care access, improvements in water and sanitation, and other socioeconomic changes affect both diarrhoeal mortality and childhood nutrition. Recent trends in mortality from diarrhoea and the prevalence of malnutrition should be interpreted in the light of these complex relationships (*102*).

Diarrhoeal disease and HIV/AIDS

This review does not include data that might help to assess the potential impact of HIV/AIDS on the global burden of diarrhoeal disease. Nevertheless, one of the many consequences of the HIV/AIDS pandemic may be to halt the impressive decline in childhood diarrhoeal mortality seen over the past four decades. Diarrhoeal incidence (*103*, *104*), duration (*105*), severity (*103*, *105*) and mortality (*103*) are higher in children with HIV/AIDS than in others. Chronic diarrhoea is also a major cause of morbidity and death among adults with HIV (*106–108*). This review therefore substantially underestimates the burden of diarrhoeal disease in areas where HIV is highly endemic.

Conclusions

It is important to note that the decline in diarrhoeal mortality occurred in the context of a decrease in overall childhood mortality. It has been estimated that worldwide mortality rates in children aged under 5 years declined from 159 to 70 deaths per 1000 live births between the periods 1955–59 and 1995–99 (*109*). The Global Burden of Disease estimate for the number of deaths in children under 5 years of age was 12.8 million in 1990. Our estimate of 2.5 million deaths in children under 5 years of age accounts for 19.5% of these deaths, a proportion that correlates well with the median of 21% of all deaths among children aged under 5 years that were caused by diarrhoea as determined by active surveillance. This is reassuring, given the different methodologies used in arriving at these estimates. An analysis of 10.5 million deaths in 1999 attributed 1.6 million of them to diarrhoea only; many other diarrhoeal deaths in children who also had malaria or pneumonia were attributed to these conditions (*7*; R. Lozano, unpublished observations, 2001). Diarrhoea thus still accounts for 1.6–2.5 million deaths annually, and each child in the developing world experiences an average of three episodes of diarrhoea per year. Clearly, despite the decline in diarrhoeal mortality, diarrhoea remains one of the principal causes of morbidity and mortality in children. ■

Conflicts of interest: none declared

Résumé

La charge mondiale des maladies diarrhéiques, calculée d'après les résultats des études publiées entre 1992 et 2000

Le présent article rapporte les estimations actuelles de la charge mondiale des maladies diarrhéiques et les compare avec les estimations précédentes basées sur des données recueillies en 1954-1979 et en 1980-1989. On a procédé à une recherche documentaire structurée pour identifier les études ayant caractérisé les taux de morbidité au moyen d'une surveillance prospective des populations stables et les études ayant caractérisé la mortalité attribuable à la diarrhée au moyen d'une surveillance active. Dans

les zones et pays en développement, la médiane des épisodes de diarrhée chez les moins de 5 ans était de 3,2 par enfant-année. Ce résultat ne montre que peu de changement par rapport aux incidences décrites auparavant. Les estimations de la mortalité ont montré que dans ces zones et pays, le nombre d'enfants qui décédaient de maladie diarrhéique avant l'âge de 5 ans était de 4,9 pour 1000 par an, chiffre en diminution par rapport aux précédentes estimations, respectivement de 13,6 et 5,6 pour 1000 par an. La baisse était plus prononcée chez les enfants de moins d'un an. Malgré une amélioration des tendances de la mortalité, les maladies diarrhéiques étaient responsables, en valeur médiane, de 21 % de l'ensemble des décès chez les enfants de moins de 5 ans dans ces zones et pays, avec 2,5 millions de décès par an. Il n'y a pas eu de baisse concomitante des taux de morbidité imputables à la diarrhée. Comme la croissance démographique est principalement concentrée dans les régions les plus pauvres, la part de la morbidité que représentent les maladies diarrhéiques dans la charge totale est plus importante qu'auparavant.

Resumen

La carga mundial de enfermedades diarreicas, según estimaciones de estudios publicados entre 1992 y 2000

Se informa de las actuales estimaciones de la carga mundial de morbilidad por diarrea, comparándolas con estimaciones anteriores realizadas durante 1954-/1979 y 1980-/1989.

Se hizo una revisión estructurada de la literatura para localizar estudios que hubieran determinado las tasas de morbilidad mediante la vigilancia prospectiva de poblaciones estables y estudios que hubieran determinado la mortalidad atribuible a la diarrea mediante medidas de vigilancia activa.

Para los niños menores de 5 años de los países y áreas en desarrollo, se observó una mediana de 3,2 episodios de diarrea por niño y año, lo que indica, si se consideran las tasas de incidencia notificadas con anterioridad, que la situación apenas ha cambiado. Las estimaciones de la mortalidad revelaron que 4,9 niños por 1000 fallecieron cada año en esos países y áreas como resultado de enfermedades diarreicas en los 5 primeros años de vida, lo que supone una reducción respecto a las estimaciones anteriores de 13,6 y 5,6 por 1000 cada año. La disminución más pronunciada es la observada en los menores de un año.

Pese a la mejora de las tendencias de las tasas de mortalidad, la diarrea fue la causa de un 21% (valor mediano) de todas las defunciones de menores de 5 años en esos países y áreas, con 2,5 millones de muertes anuales. No ha habido una disminución paralela de las tasas de morbilidad por diarrea. Como el crecimiento demográfico se centra en las zonas más pobres, la contribución de esa enfermedad a la morbilidad total ha aumentado.

References

1. Snyder JD, Merson MH. The magnitude of the global problem of acute diarrhoeal disease: a review of active surveillance data. *Bulletin of the World Health Organization* 1982;60:604-13.
2. Bern C, Martines J, de Zoysa I, Glass RI. The magnitude of the global problem of diarrhoeal disease: a ten-year update. *Bulletin of the World Health Organization* 1992;70:705-14.
3. World Bank. *World development report 1993*: *investing in health.* New York: Oxford University Press; 1993.
4. Murray CJL, Lopez AD. *The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020.* Cambridge (MA): Harvard School of Public Health on behalf of the World Health Organization and the World Bank; 1996.
5. World Health Organization. *The world health report 1999: making a difference.* Geneva: World Health Organization; 1999.
6. Murray CJ. Quantifying the burden of disease: the technical basis for disability-adjusted life years. *Bulletin of the World Health Organization* 1994;72: 429-45.
7. World Health Organization. *The world health report 2000*-health systems: improving performance: Geneva: World Health Organization; 2000.
8. Molbak K, Jensen H, Ingholt L, Aaby P. Risk factors for diarrheal disease incidence in early childhood: a community cohort study from Guinea-Bissau. *American Journal of Epidemiology* 1997;146:273-82.
9. Oni GA, Schumann DA, Oke EA. Diarrhoeal disease morbidity, risk factors and treatments in a low socioeconomic area of Ilorin, Kwara State, Nigeria. *Journal of Diarrhoeal Diseases Research* 1991;9:250-7.
10. Mirza NM, Caulfield LE, Black RE, Macharia WM. Risk factors for diarrheal duration. *American Journal of Epidemiology* 1997;146:776-85.
11. Manun'ebo MN, Haggerty PA, Kalengaie M, Ashworth A, Kirkwood BR. Influence of demographic, socioeconomic and environmental variables on childhood diarrhoea in a rural area of Zaire. *Journal of Tropical Medicine and Hygiene* 1994;97:31-8.
12. Moy RJ, Booth IW, Choto RG, McNeish AS. Recurrent and persistent diarrhoea in a rural Zimbabwean community: a prospective study. *Journal of Tropical Pediatrics* 1991;37:293-9.
13. Newman RD, Sears CL, Moore SR, Nataro JP, Wuhib T, Agnew DA, et al. Longitudinal study of *Cryptosporidium* infection in children in northeastern Brazil. *Journal of Infectious Diseases* 1999;180:167-75.
14. Lima AM, Moore SR, Barboza MS, Soares AM, Schleupner MA, Newman RD, et al. Persistent diarrhea signals a critical period of increased diarrhea burdens and nutritional shortfalls: A prospective cohort study among children in northeastern Brazil. *Journal of Infectious Diseases* 2000;181:1643-51.
15. Barreto ML, Santos LM, Assis AM, Araujo MP, Farenzena GG, Santos PA, et al. Effect of vitamin A supplementation on diarrhoea and acute lower-respiratory-tract infections in young children in Brazil. *Lancet* 1994;344: 228-31.
16. Linhares AC, Gabbay YB, Mascarenhas JD, de Freitas RB, Oliveira CS, Bellesi N, et al. Immunogenicity, safety and efficacy of tetravalent rhesus-human, reassortant rotavirus vaccine in Belem, Brazil. *Bulletin of the World Health Organization* 1996;74:491-500.
17. Ferreccio C, Prado V, Ojeda A, Cayyazo M, Abrego P, Guers L, et al. Epidemiologic patterns of acute diarrhea and endemic *Shigella* infections in children in a poor periurban setting in Santiago, Chile. *American Journal of Epidemiology* 1991;134:614-27.
18. Kaminsky RG. Parasitism and diarrhoea in children from two rural communities and marginal barrio in Honduras. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1991;85:70-3.
19. Guerrero ML, Noel JS, Mitchell DK, Calva JJ, Morrow AL, Martinez J, et al. A prospective study of astrovirus diarrhea of infancy in Mexico City. *Pediatric Infectious Disease Journal* 1998;17:723-7.
20. Cruz JR, Bartlett AV, Mendez H, Sibrian R. Epidemiology of persistent diarrhea among Guatemalan rural children. *Acta Paediatrica. Supplement* 1992;381:22-6.
21. Lanata CF, Black RE, Gilman RH, Lazo F, Del Aguila R. Epidemiology, clinical, and laboratory characteristics of acute vs. persistent diarrhea in periurban Lima, Peru. *Journal of Pediatric Gastroenterology and Nutrition* 1991;12:82-8.
22. Yeager BA, Lanata CF, Lazo F, Verastegui H, Black RE. Transmission factors and socioeconomic status as determinants of diarrhoeal incidence in Lima, Peru. *Journal of Diarrhoeal Diseases Research* 1991;9:186-93.

23. Lanata CF, Black RE, Maurtua D, Gil A, Gabilondo A, Yi A, et al. Etiologic agents in acute vs persistent diarrhea in children under three years of age in peri-urban Lima, Peru. *Acta Paediatrica. Supplement* 1992;381:32-8.
24. Naficy AB, Rao MR, Holmes JL, Abu-Elyazeed R, Savarino SJ, Wierzba TF, et al. Astrovirus diarrhea in Egyptian children. *Journal of Infectious Diseases* 2000;182:685-90.
25. Chavasse DC, Shier RP, Murphy OA, Huttly SR, Cousens SN, Akhtar T. Impact of fly control on childhood diarrhoea in Pakistan: community-randomised trial. *Lancet* 1999;353:22-5.
26. Mahmud A, Jalil F, Karlberg J, Lindblad BS. Early child health in Lahore, Pakistan: VII. Diarrhoea. *Acta Paediatrica. Supplement* 1993;390:79-85.
27. Dibley MJ, Sadjimin T, Kjolhede CL, Moulton LH. Vitamin A supplementation fails to reduce incidence of acute respiratory illness and diarrhea in preschool-age Indonesian children. *Journal of Nutrition* 1996;126:434-42.
28. Punyaratabandhu P, Vathanophas K, Varavithya W, Sangchai R, Athipanyakom S, Echeverria P, et al. Childhood diarrhoea in a low-income urban community in Bangkok: incidence, clinical features, and child caretaker's behaviours. *Journal of Diarrhoeal Diseases Research* 1991;9:244-9.
29. Baqui AH, Black RE, Sack RB, Chowdhury HR, Yunus M, Siddique AK. Malnutrition, cell-mediated immune deficiency, and diarrhea: a community-based longitudinal study in rural Bangladeshi children. *American Journal of Epidemiology* 1993;137:355-65.
30. Baqui AH, Sack RB, Black RE, Haider K, Hossain A, Alim ARMA, et al. Enteropathogens associated with acute and persistent diarrhea in Bangladeshi children <5 years of age. *Journal of Infectious Diseases* 1992;166:792-6.
31. Gupta DN, Sircar BK, Sengupta PG, Ghosh S, Banu MK, Mondal SK, et al. Epidemiological and clinical profiles of acute invasive diarrhoea with special reference to mucoid episodes: a rural community-based longitudinal study. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1996; 90:544-7.
32. Lal S. Surveillance of acute diarrhoeal diseases at village level for effective home management of diarrhoea. *Indian Journal of Public Health* 1994;38:65-8.
33. Rahmathullah L, Underwood BA, Thulasiraj RD, Milton RC. Diarrhea, respiratory infections, and growth are not affected by a weekly low-dose vitamin A supplement: a masked, controlled field trial in children in southern India. *American Journal of Clinical Nutrition* 1991;54:568-77.
34. Lie C, Ying C, Wang EL, Brun T, Geissler C. Impact of large-dose vitamin A supplementation on childhood diarrhoea, respiratory disease and growth. *European Journal of Clinical Nutrition* 1993;47:88-96.
35. Yang CR, Meng ZD, Wang X, Li YL, Zhang YX, Zhao QP. Diarrhoea surveillance in children aged under 5 years in a rural area of Hebei Province, China. *Journal of Diarrhoeal Diseases Research* 1990;8:155-9.
36. Chen KC, Lin CH, Qiao QX, Zen NM, Zhen GK, Chen GL, et al. The epidemiology of diarrhoeal diseases in southeastern China. *Journal of Diarrhoeal Diseases Research* 1991;9:94-9.
37. Yap KL, Yasmin AM, Wong YH, Ooi YE, Tan SC, Jegathesan M, et al. A one year community-based study on the incidence of diarrhoea and rotavirus infection in urban and suburban Malaysian children. *Medical Journal of Malaysia* 1992;47:303-8.
38. Wyrsch M, Coakley K, Alexander N, Saleu G, Taime J, Kakazo M, et al. Diarrhoea morbidity in children in the Asaro Valley, Eastern Highlands Province, Papua New Guinea. *Papua New Guinea Medical Journal* 1998;41:7-14.
39. Alam N, Henry FJ, Rahaman MM. Reporting errors in one-week diarrhoea recall surveys: experience from a prospective study in rural Bangladesh. *International Journal of Epidemiology* 1989;18:697-700.
40. Jaffar S, Leach A, Greenwood AM, Jepson A, Muller O, Ota MO, et al. Changes in the pattern of infant and childhood mortality in Upper River Division, The Gambia, from 1989 to 1993. *Tropical Medicine and International Health* 1997;2:28-37.
41. De Francisco A, Hall AJ, Schellenberg JR, Greenwood AM, Greenwood BM. The pattern of infant and childhood mortality in Upper River Division, The Gambia. *Annals of Tropical Paediatrics* 1993;13:345-52.
42. Afari EA, Nkrumah FK, Nakana T, Sakatoku H, Hori H, Binka F. Impact of primary health care on child morbidity and mortality in rural Ghana: the Gomoa experience. *The Central African Journal of Medicine* 1995;41:148-53.
43. Ghana VAST Study Team. Vitamin A supplementation in northern Ghana: effects on clinic attendances, hospital admissions, and child mortality. *Lancet* 1993;342:7-12.
44. Binka FN, Kubaje A, Adjuik M, Williams LA, Lengeler C, Maude GH, et al. Impact of permethrin impregnated bednets on child mortality in Kassena-Nankana district, Ghana: a randomized controlled trial. *Tropical Medicine and International Health* 1996;1:147-54.
45. Molbak K, Aaby P, Ingholt L, Hojlyng N, Gottschau A, Andersen H, et al. Persistent and acute diarrhoea as the leading causes of child mortality in urban Guinea-Bissau. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1992;86:216-20.
46. Jinadu MK, Olusi SO, Agun JI, Fabiyi AK. Childhood diarrhoea in rural Nigeria. I. Studies on prevalence, mortality and socio-environmental factors. *Journal of Diarrhoeal Diseases Research* 1991;9:323-7.
47. Pison G, Trape JF, Lefebvre M, Enel C. Rapid decline in child mortality in a rural area of Senegal. *International Journal of Epidemiology* 1993;22:72-80.
48. Fantahun M. Patterns of childhood mortality in three districts of north Gondar Administrative Zone. A community based study using the verbal autopsy method. *Ethiopian Medical Journal* 1998;36:71-81.
49. Shamebo D, Muhe L, Sandstrom A, Wall S. The Butajira rural health project in Ethiopia: mortality pattern of the under fives. *Journal of Tropical Pediatrics* 1991;37:254-61.
50. Kahn K, Tollman SM, Garenne M, Gear JS. Who dies from what? Determining cause of death in South Africa's rural north-east. *Tropical Medicine and International Health* 1999;4:433-41.
51. Salvadorian Demographic Association and Centers for Disease Control and Prevention. *National family health survey, San Salvador, El Salvador, 1994.* San Salvador: Salvadorian Demographic Association; 1994.
52. Centers for Disease Control and Prevention. *Family planning and child survival survey.* Atlanta (GA): Centers for Disease Control and Prevention; 1992.
53. Profamilia, Centers for Disease Control and Prevention. [*Study of family health, Nicaragua, 92-93*].Managua: Profamilia; 1993. In Spanish.
54. Yassin KM. Indices and sociodemographic determinants of childhood mortality in rural Upper Egypt. *Social Science and Medicine* 2000;51:185-97.
55. Marsh D, Majid N, Rasmussen Z, Mateen K, Khan AA. Cause-specific child mortality in a mountainous community in Pakistan by verbal autopsy. *Journal of the Pakistan Medical Association* 1993;43:226-9.
56. Khan AJ, Khan JA, Akbar M, Addiss DG. Acute respiratory infections in children: a case management intervention in Abbottabad District, Pakistan. *Bulletin of the World Health Organization* 1990;68:577-85.
57. Herrera MG, Nestel P, el Amin A, Fawzi WW, Mohamed KA, Weld L. Vitamin A supplementation and child survival. *Lancet* 1992;340:267-71.
58. Humphrey JH, Agoestina T, Wu L, Usman A, Nurachim M, Subardja D, et al. Impact of neonatal vitamin A supplementation on infant morbidity and mortality. *Journal of Pediatrics* 1996;128:489-96.
59. Roesin R, Sutanto A, Sastra K, Winarti. ARI intervention study in Kediri, Indonesia (a summary of study results). *Bulletin of the International Union against Tuberculosis and Lung Disease* 1990;65:23.
60. Omori K, Greksa LP, Chomngandu P, Noimoung S, Sila S. Morbidity and mortality patterns, health beliefs, and health risk factors of Karen highlanders of northwest Thailand. *Southeast Asian Journal of Tropical Medicine and Public Health* 1999;30:789-803.
61. Fauveau V, Yunus M, Zaman K, Chakraborty J, Sarder AM. Diarrhoea mortality in rural Bangladeshi children. *Journal of Tropical Pediatrics* 1991;37:31-6.
62. Bang AT, Bang RA, Tale O, Sontakke P, Solanki J, Wargantivar R, et al. Reduction in pneumonia mortality and total childhood mortality by means of community-based intervention trial in Gadchiroli, India. *Lancet* 1990;336:201.
63. Khalique N, Sinha SN, Yunus M, Malik A. Early childhood mortality – a rural study. *Journal of the Royal Society of Health* 1993;113:247-9.
64. Anand K, Kant S, Kumar G, Kapoor SK. ''Development''is not essential to reduce infant mortality rate in India: experience from the Ballabgarh project. *Journal of Epidemiology and Community Health* 2000;54:247-53.
65. Awasthi S, Pande VK, Glick H. Under fives mortality in the urban slums of Lucknow. *Indian Journal of Pediatrics* 1996;63:363-8.
66. Hirve S, Ganatra B. A prospective cohort study on the survival experience of under five children in rural western India. *Indian Pediatrics* 1997;34:995-1001.
67. Rahmathullah L, Underwood BA, Thulasiraj RD, Milton RC, Ramaswamy K, Rahmathullah R, et al. Reduced mortality among children in southern India receiving a small weekly dose of vitamin A. *New England Journal of Medicine* 1990;323:929-35.

68. Biswas AB, Basu M, Das KK, Biswas R. Infant and early childhood mortality in some rural ICDS blocks of west Bengal. *Indian Journal of Public Health* 1993;37:81-6.
69. West KP, Pokhrel RP, Katz J, LeClerq SC, Khatry SK, Shrestha SR, et al. Efficacy of vitamin A in reducing preschool child mortality in Nepal. *Lancet* 1991;338:67-71.
70. West KP, Katz J, Shrestha SR, LeClerq SC, Khatry SK, Pradhan EK, et al. Mortality of infants < 6 mo of age supplemented with vitamin A: a randomized, double-masked trial in Nepal. *American Journal of Clinical Nutrition* 1995;62:143-8.
71. Huang W, Yu H, Wang F, Li G. Infant mortality among various nationalities in the middle part of Guizhou, China. *Social Science and Medicine* 1997;45:1031-40.
72. Yoon PW, Black RE, Moulton LH, Becker S. The effect of malnutrition on the risk of diarrheal and respiratory mortality in children < 2 years of age in Cebu, Philippines. *American Journal of Clinical Nutrition* 1997;65:1070-7.
73. van Tran D, van Thuan C, Tuan T, Dung PH, Persson L, Grabe M. Survey on immunization, diarrhoeal disease and mortality in Quang Ninh Province, Viet Nam. *Journal of Tropical Pediatrics* 1991;37:280-5.
74. Institute of Medicine , Committee on Issues and Priorities for New Vaccine Development, National Institute of Allergy and Infectious Diseases. *The burden of disease resulting from various diarrheal pathogens. New vaccine development: establishing priorities.* Washington (DC): National Academy Press; 1985.
75. Sen K, Bonita R. Global health status: two steps forward, one step back. *Lancet* 2000; 356:577-82.
76. Ustun TB, Rehm J, Chatterji S, Saxena S, Trotter R, Room R, et al. Multiple-informant ranking of the disabling effects of different health conditions in 14 countries. WHO/NIH Joint Project CAR Study Group. *Lancet* 1999;354:111-5.
77. James KC, Foster SD. Weighing up disability. *Lancet* 1999;354:87-8.
78. Cooper RS, Osotimehin B, Kaufman JS, Forrester T. Disease burden in sub-Saharan Africa: what should we conclude in the absence of data? *Lancet* 1998;351:208-10.
79. Martines J, Phillips M, Feachem RG. Diarrheal diseases. In: Jamison DT, NetLibrary I, World B, editors. *Disease control priorities in developing countries: a summary.* Washington (DC): World Bank; 1993. p. 91-116.
80. Pan American Health Organization. *Health statistics from the Americas.* Washington (DC): Pan American Health Organization; 1999.
81. Mobley CC, Boerma JT, Titus S, Lohrke B, Shangula K, Black RE. Validation study of a verbal autopsy method for causes of childhood mortality in Namibia. *Journal of Tropical Pediatrics* 1996;42:365-9.
82. Kalter HD, Gray RH, Black RE, Gultiano SA. Validation of postmortem interviews to ascertain selected causes of death in children. *International Journal of Epidemiology* 1990;19:380-6.
83. Snow RW, Armstrong JR, Forster D, Winstanley MT, Marsh VM, Newton CR, et al. Childhood deaths in Africa: uses and limitations of verbal autopsies. *Lancet* 1992;340:351-5.
84. Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. *Lancet* 1997;349:1269-76.
85. Guerrant RL, Kirchhoff LV, Shields DS, Nations MK, Leslie J, de Souza MA, et al. Prospective study of diarrheal illnesses in northeastern Brazil: patterns of disease, nutritional impact, etiologies, and risk factors. *Journal of Infectious Diseases* 1983;148:986-97.
86. Black RE, Brown KH, Becker S. Effects of diarrhea associated with specific enteropathogens on the growth of children in rural Bangladesh. *Pediatrics* 1984;73:799-805.
87. Guerrant DI, Moore SR, Lima AAM, Patrick P, Schorling JB, Guerrant RL. Association of early childhood diarrhea and cryptosporidiosis with impaired physical fitness and cognitive function four-seven years later in a poor urban community in Northeast Brazil. *American Journal of Tropical Medicine and Hygiene* 1999;61:707-13.
88. Victora CG, Bryce J, Fontaine O, Monasch R. Reducing deaths from diarrhoea through oral rehydration therapy. *Bulletin of the World Health Organization* 2000;78:1246-55.
89. Rahaman MM, Aziz KMS, Patwani Y, Munshi MH. Diarrhoeal mortality in two Bangladeshi villages with and without community-based oral rehydration therapy. *Lancet* 1979;2:809-12.
90. Victora CG, Huttly SR, Fuchs SC, Barros FC, Garenne M, Leroy O, et al. International differences in clinical patterns of diarrhoeal deaths: a comparison of children from Brazil, Senegal, Bangladesh, and India. *Journal of Diarrhoeal Diseases Research* 1993;11:25-9.
91. Gove S. Integrated management of childhood illness by outpatient health workers: technical basis and overview. *Bulletin of the World Health Organization* 1997;75 Suppl 1:7-24.
92. Schorling JB, McAuliffe JF, de Souza MA, Guerrant RL. Malnutrition is associated with increased diarrhoea incidence and duration among children in an urban Brazilian slum. *International Journal of Epidemiology* 1990; 19:728-35.
93. Sepúlveda J, Willett W, Munoz A. Malnutrition and diarrhoea. A longitudinal study among urban Mexican children. *American Journal of Epidemiology* 1988;127:365-76.
94. Black RE, Brown KH, Becker S. Malnutrition is a determining factor in diarrheal duration, but not incidence, among young children in a longitudinal study in rural Bangladesh. *American Journal of Clinical Nutrition* 1984;39:87-94.
95. Chen LC, Huq E, Huffman SL. A prospective study of the risk of diarrheal diseases according to the nutritional status of children. *American Journal of Epidemiology* 1981;114:284-92.
96. Baqui AH, Sack RB, Black RE, Chowdhury HR, Yunus M, Siddique AK. Cell-mediated immune deficiency and malnutrition are independent risk factors for persistent diarrhea in Bangladeshi children. *American Journal of Clinical Nutrition* 1993;58:543-8.
97. Sachdev HP, Kunar S, Singh KK, Satyanarayana L, Puri RK. Risk factors for fatal diarrhea in hospitalized children in India. *Journal of Pediatric Gastroenterology and Nutrition* 1991;12:76-81.
98. Fauveau V, Henry FJ, Briend A, Yunus M, Chakraborty J. Persistent diarrhea as a cause of childhood mortality in rural Bangladesh. *Acta Paediatrica Scandinavica* 1992;381 Suppl:12-4.
99. Rice AL, Sacco L, Hyder A, Black RE. Malnutrition as an underlying cause of childhood deaths associated with infectious diseases in developing countries. *Bulletin of the World Health Organization* 2000;78:1207-21.
100. de Onis M, Frongillo EA, Blossner M. Is malnutrition declining? An analysis of changes in levels of child malnutrition since 1980. *Bulletin of the World Health Organization* 2000;78:1222-33.
101. Guerrant RL, Schorling JB, McAuliffe JF, de Souza MA. Diarrhea as a cause and effect of malnutrition: diarrhea prevents catch-up growth and malnutrition increases diarrhea frequency and duration. *American Journal of Tropical Medicine and Hygiene* 1992;47:28-35.
102. Rutstein SO. Factors associated with trends in infant and child mortality in developing countries during the 1990s. *Bulletin of the World Health Organization* 2000;78:1256-70.
103. Pavia AT, Long EG, Ryder RW, Nsa W, Puhr ND, Wells JG, et al. Diarrhea among African children born to human immunodeficiency virus 1- infected mothers: clinical, microbiologic and epidemiologic features. *Pediatric Infectious Disease Journal* 1992;11:996-1003.
104. Kotloff KL, Johnson JP, Nair P, Hickman D, Lippincott P, Wilson PD, et al. Diarrheal morbidity during the first 2 years of life among HIV-infected infants. *Journal of the American Medical Association*1994;271:448-52.
105. Johnson S, Hendson W, Crewe-Brown H, Dini L, Frean J, Perovic O, et al. Effect of human immunodeficiency virus infection on episodes of diarrhea among children in South Africa. *Pediatric Infectious Disease Journal* 2000;19:972-9.
106. Colebunders RL, Latif AS. Natural history and clinical presentation of HIV-1 infection in adults. *AIDS* 1991;5 Suppl 1:S103-12.
107. Malebranche R, Arnoux E, Guerin JM, Pierre GD, Laroche AC, Pean-Guichard C, et al. Acquired immunodeficiency syndrome with severe gastrointestinal manifestations in Haiti. *Lancet* 1983;873-6.
108. King R, Fox E, Twagirakristu JB, Karita E, Allen S. Excess morbidity related to HIV infection. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1994;88:295.
109. Ahmad OB, Lopez AD, Inoue M. The decline in child mortality: a reappraisal. *Bulletin of the World Health Organization* 2000;78:1175-91.