
REVIEW ARTICLE

Diarrhoea morbidity and mortality in older children, adolescents, and adults

C. L. FISCHER WALKER* AND R. E. BLACK

Johns Hopkins Bloomberg School of Public Health, Department of International Health, Baltimore, MD, USA

(Accepted 17 February 2010; first published online 22 March 2010)

SUMMARY

Diarrhoea is a leading cause of morbidity and mortality yet diarrhoea specific incidence and mortality rates for older children, adolescents, and adults have not been systematically calculated for many countries. We conducted a systematic literature review to generate regional incidence rates by age and to summarize diarrhoea specific mortality rates for regions of the world with inadequate vital registration data. Diarrhoea morbidity rates range from 29·9 episodes/100 person-years for adults in the South East Asian region to 88·4 episodes/100 person-years in older children in the Eastern Mediterranean region and have remained unchanged in the last 30 years. Diarrhoea mortality rates decline as the child ages and remain relatively constant during adulthood. These data are critical for improving estimates worldwide and further highlight the need for improved diarrhoea specific morbidity and mortality data in these age groups.

Key words: Diarrhoea, epidemiology.

INTRODUCTION

Diarrhoea is a leading cause of morbidity and mortality in children aged <5 years [1], but much less is known about the burden of disease in older children, adolescents, and adults. Past efforts to estimate the burden of disease have relied on combining limited morbidity and mortality data. Mortality estimates were obtained from countries where vital registration data were available. Morbidity estimates were generated from limited outbreak surveillance data [2, 3]. Although these methods provide important information they only address mortality in countries that use standard medical certification for the cause of registered deaths and thus do not include many low- and middle-income countries. For morbidity, outbreak surveillance or physician reports do not

detect all episodes of community-acquired diarrhoea. In addition, routine surveillance systems are not in place in most of the developing world where evidence has shown that diarrhoea incidence is greatest and mortality remains one of the top five causes of death in young children [4, 5].

The 2004 Global Burden of Disease update estimates that diarrhoeal diseases account for a reported 72·8 million disability adjusted life years (DALYs) (4·8% of all DALYs) which encompasses the 2 163 000 diarrhoea deaths and 4·6 billion diarrhoea episodes each year [3]. The original methods for deriving these estimates were developed as part of the 1990 Global Burden of Disease Report based on a systematic literature review of childhood diarrhoea from 1980 to 1990, but have not been updated since then and separate estimation based on data from older children and adults has never been incorporated [6]. We conducted a systematic review of diarrhoea morbidity and mortality in children aged ≥ 5 years, adolescents, and adults. To our knowledge this is the

* Author for correspondence: C. L. Fischer Walker, Ph.D., M.H.S., Assistant Scientist, Department of International Health, 615 N. Wolfe Street/Suite E5608, Baltimore, MD 21205, USA.
(Email: cfischer@jhsph.edu)

first systematic literature review designed to summarize diarrhoea incidence rates in all regions of the world and diarrhoea mortality rates in developing countries for these age groups.

METHODS

Systematic review

We searched PubMed/Medline, CAB abstracts, System for Information on Grey Literature in Europe (SIGLE), and all World Health Organization (WHO) regional databases for studies published from 1 January 1980 to 31 December 2008 using all combinations of the following search terms: *diarrhoea*, *morbidity*, *incidence*, *prevalence*, *mortality*, *etiology*, *cause of death*, and *gastroenteritis*. The objective of the search was to identify all papers reporting diarrhoea specific morbidity and mortality rates that met our inclusion and exclusion criteria. We also included unpublished studies for which full reports including a clear description of methods and results were available and when authors permitted inclusion of results in this analysis. We included studies published in all languages which contained data with at least 12 months of surveillance for morbidity or of recall for mortality studies to rule out seasonality bias. For the morbidity analyses we included prospective studies with a recall period of <2 weeks and cross-sectional surveys with a recall period of <4 weeks conducted in more developed countries. For the mortality analyses we included only studies with at least 20 total deaths in persons aged ≥ 5 years and limited the studies to those conducted after 1980. We excluded studies conducted in special populations, such as travellers, cancer patients, HIV-positive patient populations and conflict zones, and studies of generalized gastroenteritis symptoms, such as nausea or vomiting without differentiating incidence of symptomatic diarrhoea. Because diarrhoea in adults is not widely studied and there is not a standard definition of self-reported community diarrhoea, we included all definitions of symptomatic diarrhoea. We also excluded studies designed to detect antibiotic-associated diarrhoea or hospital-acquired diarrhoea, individual case reports, and outbreak studies.

We conducted the initial searches in all databases and combined the search results dropping all duplicate titles by using RefWorks Reference Manager [7]. We then screened all titles for relevance and all abstracts of papers passing the initial title and

abstract review. We trained two abstractors to read the full papers of all remaining studies in order to determine final eligibility for morbidity or mortality analyses. Any paper excluded after reading the full manuscript was logged and the reasons for exclusion were documented. We developed a standardized data abstraction sheet that included all relevant study characteristics and results. Both data abstractors completed the abstraction sheet for each included study; we then cross-checked the abstraction sheets and rectified any differences to create a final database of included studies.

Morbidity analytical methods

The objective of the morbidity analyses was to generate diarrhoea incidence rates by age and sex for all regions of the world. Only two studies conducted prospective daily diarrhoea surveillance, therefore to meet this objective we approximated diarrhoea incidence rates using 1-, 2-, and 4-week prevalence rates per 100 person-years (p-yr) assuming prevalence approximates incidence when the duration of the episode is short (typically <3 days). Because studies report various age categories we created standardized age categories and generated incidence rates for each year of age based on the individual study data. We then generated a mean incidence rate for each study according to our standardized age bands. For example, if a study reported diarrhoea incidence to be x for age 10–12 years and y for age 13–14 years, we calculated the mean for age band 10–14 years to be $(3x + 2y)/5$. Many studies did not provide narrow age bands, therefore overall incidence rates were applied to all ages included in the study. For example, if a study reported an incidence rate of z for all ages ≥ 15 years, this rate was then applied to the 15–19 years age band and all subsequent ages. We then aggregated the data from multiple narrow age bands to generate three broad age categories, 5–14, 15–54, and ≥ 55 years for regions of the world where we had at least one representative study. We generated median incidence rates, by broad age band, and calculated the interquartile range (IQR) (3rd quartile minus 1st quartile) for each age band within each region. Age-specific incidence rates were then applied to the 2005 reference population for each age within the age band to generate regional and global estimates for total annual diarrhoea episodes in all persons aged ≥ 5 years [8].

In this review we included studies published as early as 1980 including data from the mid-1960s to the

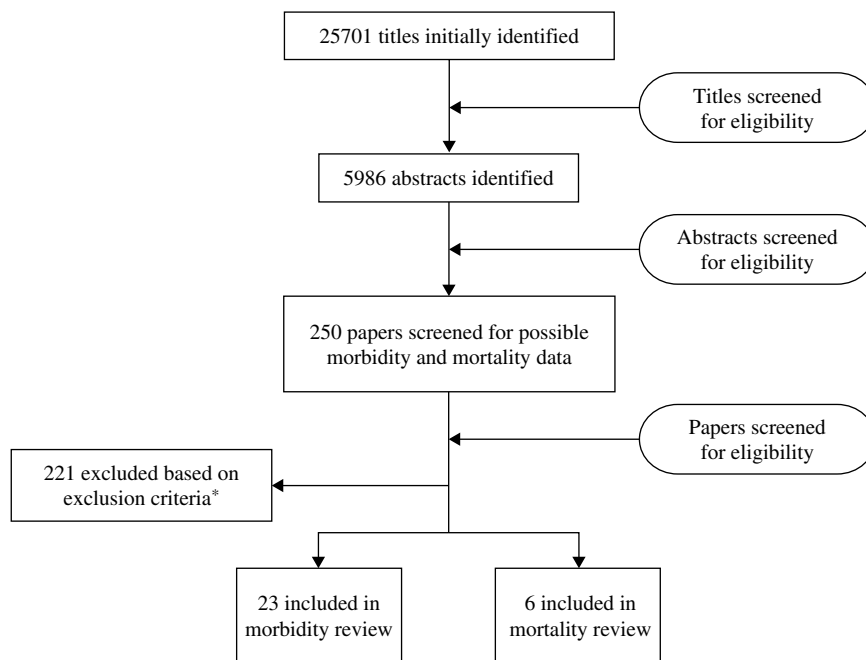


Fig. 1. Results of the systematic review. * Inclusion criteria: any children aged > 5 years and adults; all languages; prospective studies with at least 12 months of surveillance or cross-sectional surveys conducted over a period of a year. Exclusion criteria: studies conducted among travellers, special populations (e.g. cancer patients, only HIV-positive individuals); case reports; hospitalized-acquired diarrhoea or antibiotic-associated diarrhoea; studies lacking appropriate information regarding study population; reports of outbreaks; prospective morbidity studies with recall beyond 2 weeks; and cross-sectional studies with recall beyond 4 weeks; mortality studies with fewer than 20 deaths.

mid-2000s. We plotted the categorical age-specific incidence rates for each study based on the year of data collection. We then fitted an unweighted polynomial curve to the individual data points within each age band. Although we used strict inclusion and exclusion criteria for this review, there is still much variability in studies with regard to sample size, length of recall and variation in definition of diarrhoea. Unfortunately we did not identify an adequate number of studies to assess how these variables influence the precision of the estimated incidence rate. Typically studies are weighted according to sample size, but this assumes equality and consistency with regard to all other aspects of the study design. Because these studies have great variability, we chose not to weight studies by sample size when fitting the polynomial curve.

Mortality analytical methods

The objective of the mortality review was to summarize age- and sex-specific diarrhoea specific mortality rates for regions of the world where there are inadequate or non-existent vital registration data. To meet this objective we applied the same age

standardization technique described above for incidence rates to the diarrhoea mortality rates to generate standardized age strata. We generated regional median mortality rates based on all available data in each region for 11 discrete age categories in 5-year increments until age 25 years and then in subsequent 10-year age bands until age 85 years.

RESULTS

We identified a total of 25 701 titles during the initial systematic review with contributions from all databases (Fig. 1). After initial review of titles and abstracts and complete review of more than 250 papers, we included 23 papers [9–30], (Liu, unpublished observations) that met our inclusion and exclusion criteria for the morbidity review and six papers [9, 31–35] which met our inclusion and exclusion criteria for the mortality review.

Morbidity

Study characteristics of all papers included in the final morbidity analyses are described in Table 1. The

Table 1. *Characteristics of studies included in the morbidity analyses*

First-named author [ref.]	Country	WHO region	Study site and population description	Study type	Date of data collection	Study duration (months)	Sample size, <i>n</i> (p-yr)	Recall period	Diarrhoea definition
el Alamy [10]	Egypt	EMR	All ages living in rural, eastern border of the Nile Delta, 55 km east of Cairo; mostly farming community	Prospective cohort	1981–1983	24	(2556)	4 days	n.g.
Van der Hoek [28]	Pakistan	EMR	All ages living in rural, irrigated area of southern Punjab	Prospective cohort	1998–1999	12	(1470)	1 wk	≥3 non-bloody/ loose stools or ≥1 bloody loose stools/24 h
Luby [16]	Pakistan	EMR	Children (0–15 yr) living in low-income, urban squatter settlements in Karachi	Cluster randomized controlled trial	2002–2003	12	1528 (1320)	1 wk	≥3 loose stools/24 h
Lerman [15]	Israel	EUR	Children 0–18 yr living in rural communal settlement in the central region	Prospective cohort	1988–1992	48	284 (1005·3)	1 day	≥3 stools/day and increase in liquidity of fecal discharges
Scallan [24]	Ireland	EUR	All ages living in Northern Ireland and Republic of Ireland	Population-based cross-sectional survey	2000–2001	12	9903	4 wk	≥3 loose stools/24 hr period
Nygaard [20]	Norway	EUR	All ages from randomly selected households not exposed to low water pressure	Prospective cohort	2003–2004	12	(1334)	7 days	≥3 loose stools/24 hr
Monto [18]	USA	AMR	Complete households including all ages from small town outside Detroit	Prospective cohort	1965–1971	72	(4905)	1 wk	n.g.
Rodriguez [22]	USA	AMR	All ages from middle class of suburban northern VA	Prospective cohort	1977–1980	29	145	2 wk	Increase in number of stools/day over the normal pattern, with stools tending towards liquid consistency, as reported by the family
Jones [14]	USA	AMR	All ages with varied SES living in urban and rural areas; FoodNet Surveillance areas in 9 states	Multi-site, telephone, population-based, cross-sectional survey	1996–2003	48	50 757	4 wk	≥3 loose stools /24 h with impairment of daily activities or duration of diarrhoea > 1 day in the last month
Majowicz [17]	Canada	AMR	All ages living in urban centre, Hamilton	Population-based, randomly selected telephone, cross-sectional survey	2001–2002	12	3213	4 wk	≥3 loose stools/24 h

Table 1 (cont.)

First-named author [ref.]	Country	WHO region	Study site and population description	Study type	Date of data collection	Study duration (months)	Sample size, <i>n</i> (p-yr)	Recall period	Diarrhoea definition
Thomas [27]	Canada	AMR	All ages living in urban and rural, British Columbia	Representative convenience sample; cross-sectional telephone survey	2002–2003	12	4309	4 wk	Any loose stool or stool with abnormal liquidity
Sargeant [23]	Canada	AMR	All ages, English-speaking residents of urban Ontario	Randomly selected cross-sectional telephone survey	2005–2006	12	2090	4 wk	Stool with abnormal liquidity or any loose stool
Islam [13]	Bangladesh	SEAR	All ages living with low literacy in Matlab farming community	Prospective cohort Demographic Surveillance System (DSS)	1975–1976	12	1577	1 wk	≥2 watery stools/ day
Rahaman [45]	Bangladesh	SEAR	All ages living in rural, southeast Teknaf Region	Longitudinal surveillance	1977–1978	12	46 283	1 wk	≥3 loose, watery, mucoid or bloody-mucoid motions/ 24 h
Mathan [29]	India	SEAR	All ages living in rural villages, 20 km south of Vellore	Prospective cohort	1980–1981	12	311	1 wk	≥3 loose stools/ day; a single large watery stool; or presence of mucus and blood in stool
Nazir [19]	Indonesia	SEAR	All ages ≥5 yr living in rural villages in South Sumatra Province with low literacy rates	Prospective cohort and cross-sectional survey	1983–1984	12	3811	2 wk	Passing loose or watery stools
Shahid [25]	Bangladesh	SEAR	All ages living in low-income, peri-urban slum of Dhaka	Cluster randomized controlled trial	1983	12	695	1 day	≥2 loose stools or ≥4 watery stools/24 h
Tarleton [26]	Bangladesh	SEAR	Children 6–9 yr living in urban slum of Dhaka	Prospective cohort	NG	48	191	1 day	n.g.
Hellard [12]	Australia	WPR	All ages, families who drink tap water, own their homes and have children in large urban city	Randomized controlled trial	1997–1999	17	2297	1 wk	≥3 loose stools/24 h
Hall [11]	Australia	WPR	All ages, general population	Cross-sectional telephone survey	2001–2002	12	6087	4 wk	≥3 loose stools/24 h

Table 1 (cont.)

First-named author [ref.]	Country	WHO region	Study site and population description	Study type	Date of data collection	Study duration (months)	Sample size, <i>n</i> (p-yr)	Recall period	Diarrhoea definition
Do [30]	Vietnam	WPR	Adults ≥ 15 yr living in rural, farming community in Hanoi	Prospective cohort	2002–2004	18	636 (902.2)	1 wk	≥ 3 loose/watery stools/24 h, or ≥ 2 loose stools with GI symptoms, or single loose stool with blood/mucous
Macgregor-Skinner [37]	Vietnam	WPR	Random sample of all age residents in 4 districts	In-person cross-sectional surveys	2002–2003	12	2925	30 days	≥ 3 loose or watery stools/24 h
Liu (personal communication)	China	WPR	All ages living in urban and rural Henan Province	Population based cross-sectional survey (4 survey/12 months)	2006–2007	12	42 912	2 wk	n.g.

EMR, Eastern Mediterranean region; EUR, Europe; AMR, Region of the Americas; SEAR, South and South East Asia region; WPR, Western Pacific region; n.g., not given, SES, socioeconomic status; GI, gastrointestinal.

23 studies were conducted in 14 different countries from five WHO regions. No studies were identified from Africa (AFR) or Central/South America. The studies included all ages starting at age 5 years, but many studies provided either very wide age bands or no age bands. None provided incidence rates by sex, therefore we were not able to identify possible differences in sex-specific morbidity rates.

We calculated diarrhoea incidence rates by age and region (Table 2) and found that for older children and adolescents, aged 5–14 years, the highest median rate was found in the Eastern Mediterranean region (EMR) (88.4/100 p-yr). This estimate is based on three studies in the region. The lowest regional incidence rate was observed in the Western Pacific region (WPR) (26.5/100 p-yr). For adolescents and adults, aged 15–54 years, the highest median morbidity rate was again observed in the EMR (88.4/100 p-yr). The lowest morbidity rate for ages 15–54 years was observed in the South and South East Asia region (SEAR) (29.9/100 p-yr). For adults aged ≥ 55 years, the highest reported median incidence rate was found in Europe (EUR) (78.7/100 p-yr) and the lowest was observed in the SEAR (30.1/100 p-yr). Applying the annual incidence rates to the 2005 [36] population in each region, we estimated more than 2.8 billion episodes of diarrhoea per year in children aged ≥ 5 years, adolescents and adults. The largest burden occurs in the WPR where there are an estimated 691 million episodes of diarrhea each year in this age group.

Overall there has been little change in diarrhoea morbidity over time as can be observed in Figure 2. Although the shape of the curve is suggestive of a slight increase this may be the result of many more additional studies since the late 1990s. We excluded one study which emerged as an outlier from the trend lines. In this Vietnamese study, the authors reported incidence rates of 280/100, 135/100, and 170/100 p-yr for ages 5–14, 15–54, and ≥ 55 years, respectively [37]. Overall, although there are not adequate data to suggest an increase in morbidity, the data do indicate that rates have at least remained constant rather than declining over the last 30 years in persons aged ≥ 5 years.

Mortality

Table 3 presents the characteristics of studies included in the mortality analyses. We identified studies from six countries in two WHO regions, AFR and SEAR. Although the studies span the entire age

Table 2. Median diarrhoea incidence by age group and world region

Author [ref.]	Diarrhoea incidence rate per 100 person-years			Annual number of diarrhoea episodes
	Age			
	5–14 yr	15–54 yr	≥ 55 yr	
SEAR				
Mathan [29]	43.9	29.9	30.1	
Nazir [19]	5.9	2.9	2.9	
Islam [13]	91.1	47.7	88.0	
Tarleton [26]	166.1			
Rahaman [21]	5.7	7.6	7.6	
Shahid [25]	91.9	59.9	59.9	
Median (IQR)	67.5 (15.4–91.7)	29.9 (7.6–47.7)	30.1 (7.6–59.9)	
2005 population	357 317 134	971 678 168	184 244 910	587 178 556
EMR				
Luby [16]	88.4	88.4		
Van der Hoek [28]	132.0	119.0	119.0	
el Alamy [10]	29.9	13.7	13.7	
Median (IQR)	88.4 (59.1–110.2)	88.4 (59.1–103.7)	66.4 (40.0–92.7)	
2005 population	124 858 076	295 820 561	44 416 140	410 372 323
AMR				
Rodriguez [22]	44.0	43.0	43.0	
Monto [18]	47.5	57.4	36.0	
Jones [14]	54.0	66.8	30.6	
Sargeant [23]	70.0	103.7	97.2	
Thomas [27]	14.3	24.4	10.6	
Majowicz [17]	66.7	96.0	81.6	
Median (IQR)	50.8 (44.9–63.5)	62.1 (46.6–88.7)	39.5 (32–72)	
2005 population	155 216 381	507 705 749	143 409 745	455 987 342
EUR				
Lerman [15]	10.6	2.6		
Scallan [24]	56.4	37.2	21.6	
Nygaard [20]	156.8	112.0	135.8	
Median (IQR)	56.4 (33.5–106.6)	37.2 (19.9–74.6)	78.7 (50.2–107.3)	
2005 population	109 401 561	511 731 632	213 126 523	419 797 221
WPR				
Do [30]	20.4	25.9	38.6	
Macgregor-Skinner [37]	280.0	135.0	170.0	
Liu (personal comm.)	26.5	44.3	45.9	
Hall [11]	62.4	93.0	54.9	
Hellard [12]	13.1	37.7		
Median (IQR)	26.5 (20.4–62.4)	44.3 (37.7–93)	50.4 (44.1–83.7)	
2005 population	271 577 620	1 073 121 273	285 051 126	691 026 561
AFR				
Median (incidence data not available from review, assume SEAR incidence rates to calculate total number of annual episodes)				263 995 522
2005 population	200 103 311	377 773 828	53 061 171	
Global total				2 839 357 525

SEAR, South and South East Asia region; EMR, Eastern Mediterranean region; AMR, Region of the Americas; EUR, Europe; WPR, Western Pacific region; AFR, Africa; IQR, Interquartile range.

range of interest, i.e. ≥ 5 years, only two studies included children and adolescents aged 5–14 years [31, 35].

We observed that diarrhoea mortality decreases drastically as the child ages in Asia but is more consistent across the adolescent and adult lifespan in

Table 3. *Characteristics of studies included in the mortality analyses*

First-named author [ref.]	Country	WHO region	Study site and population description	Study type	Date of data collection	Study duration (months)	Sample size, <i>n</i> (p-yr)	Age group	Recall period	Overall mortality rate (/100 p-yr)	% deaths attributable to diarrhoea
Etard [31]	Senegal	AFR	Rural, prospective DSS in Fatick District	Prospective DSS	1989–2000	144	(159 016)	5–14	Constant surveillance	0.48	12.5
Centers for Disease Control [9]	Tanzania	AFR	Multi-site: affluent in Hai District; poor rural in Morogoro District; poor urban in Dar-es-Salaam	Community-based prospective surveillance	1992–1998	72	n.g.	15–59	1 month	0.85	4.6
Kelly [32]	Zambia	AFR	Urban city dwellers in poor townships outside Lusaka	Retrospective, cross-sectional survey	1995	24-month survey	6440	> 15	2 yr	4.06	20
Tollman [33]	South Africa	AFR	Rural, Agincourt	Prospective DSS	1995–1997	24	n.g.	> 65	1 yr	3.55	n.g.
Adjuik [34]	South Africa	AFR	Rural, Agincourt	Prospective DSS	1999–2003	60	(342 906)	≥ 15	n.g.	0.86	1.2
Adjuik [34]	Senegal	AFR	Rural, prospective DSS in Niakhar	Prospective DSS	1999–2003	60	(123 314)	≥ 15	n.g.	1.47	8.1
Anwar [35]	Indonesia	SEAR	Rural, South Sumatra	Cross-sectional survey	1984	1	1658	5–14	1 yr	0.54	22.2
Adjuik [34]	Bangladesh	SEAR	Rural, Matlab	Prospective DSS	1999–2003	60	(878 800)	≥ 15	n.a.	0.69	3.7

AFR, Africa; SEAR, South and South East Asia region; DSS, Demographic surveillance site; n.a., not available; n.g., not given.

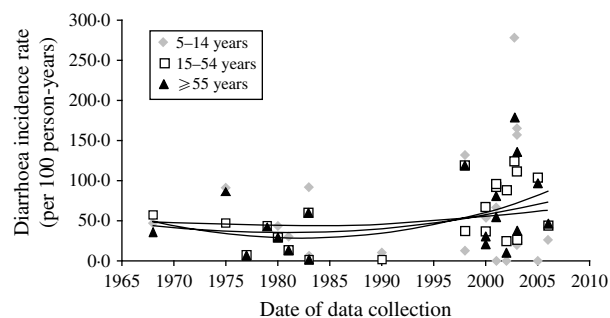


Fig. 2. Mean diarrhoea incidence rates and trend lines in stratified age groups for each included study (trend lines represent unweighted polynomial trend by age). Macgregor-Skinner was excluded from the trend lines as an extreme outlier [37].

Africa (Fig. 3). In Africa, there were five studies contributing data for age ≥ 15 years. In this age group the lowest diarrhoea mortality rate was found in South Africa (0.01/100 p-yr) and the highest in the rural poor in Tanzania (0.288/100 p-yr). In Asia one study provided data for age < 15 years (0.12/100 p-yr) [35] and one study provided data for age ≥ 15 years (0.03/100 p-yr) [34].

DISCUSSION

This is the first systematic review of diarrhoea morbidity and mortality in children aged ≥ 5 years, adolescents, and adults designed to determine diarrhoea incidence rates for all regions of the world and diarrhoea mortality rates where vital registration data are lacking. We conducted an extensive literature search, identified 23 morbidity studies, and found that although there is variability by age, there is not a consistent pattern between regions as has been observed in children aged < 5 years [38]. This review suggests that diarrhoea morbidity rates have remained constant in all ages since the 1980s in both developed and developing countries and estimates more than 2.8 billion episodes of diarrhoea per year in children aged ≥ 5 years, adolescents, and adults. This is significantly greater than previous burden-of-disease estimates [3].

For young children diarrhoea mortality is one of the most important causes of death [5]. In Asia, this risk remains high from ages 5–14 years, and then reaches a low and constant plateau throughout adolescence and adulthood while in Africa it declines less dramatically after age 5 years and remains relatively constant throughout the lifespan. Although extremely sparse especially for Asia, these data might be used to

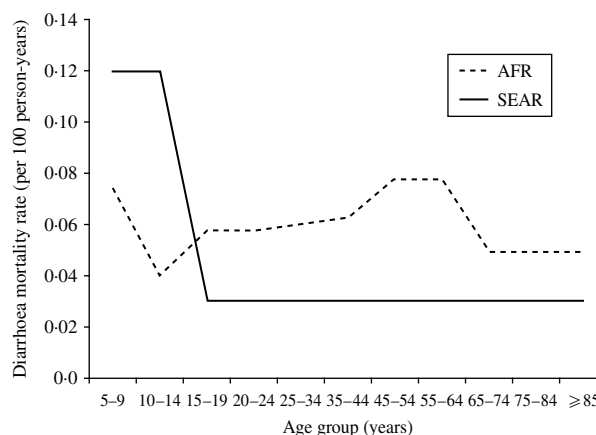


Fig. 3. Diarrhoea mortality rates by age and world region. AFR, Africa; SEAR, South and South East Asia region.

better inform adult mortality estimates for regions of the world lacking vital registration data. Previous estimates were based solely on data from regions of the world with vital registration data so although great caution must be exercised when interpreting these data, they add important information for regions of the world where adult cause-specific mortality evidence remains sparse.

We used strict inclusion and exclusion criteria to avoid potential biases in our estimates including seasonal variation and recall bias. All studies had at least 12 months of data collection to minimize seasonal bias. We recognize that this is a limitation because otherwise well-designed studies, such as outbreak studies, may have been excluded. For this reason, the estimates of diarrhoea morbidity from this review and analysis may underestimate the true burden and might be regarded as the minimum burden. Although we were not able to model diarrhoea seasonality for this global analysis at the local level, studies with seasonal data may be useful for national-level analyses where knowledge regarding site-specific diarrhoea seasonality would allow for extrapolation to annual estimates.

We limited the morbidity recall period to 2 weeks for developing countries and included studies with up to 4 weeks for more developed countries. There are no studies regarding appropriate recall period for diarrhoea morbidity in adults. Studies in children have shown that reported diarrhoea prevalence falls by half if a mother is asked to recall an episode after more than a week [39]. However, it has also been shown that literate mothers report higher diarrhoea morbidity rates for their children than illiterate mothers, despite decreased mortality rates in a more educated

population [40]. In this review we observed that cross-sectional surveys with 4-week recall in both developed countries and in Vietnam found higher rates of reported diarrhoea than many prospective studies, therefore it does not appear that a longer recall in these populations leads to an underestimate of morbidity. Alternatively, there may be over-reporting of morbidity by recalling episodes where more than 4 weeks have elapsed. Because we do not have prospective studies from similar settings to compare rates it is difficult to make assumptions with regard to potential reporting bias. Higher rates in more developed countries might be expected as children in developing countries experience higher diarrhoea rates and thus are actively building immunity at an early age whereas young children in more developed countries are exposed to fewer diarrhoea pathogens and may experience higher incidence rates later in life [41]. Because appropriate studies from South and Central America were not identified, this may be a limitation for the estimate for diarrhoea morbidity for the Region of the Americas (AMR) where only data from the USA and Canada was available.

We found an increasing number of studies reporting morbidity data since the 1990s, including more in high-income countries with increased attention to surveillance of possible foodborne diseases. Unfortunately, many large-scale studies conducted in developed countries were excluded from our analysis because aggregate data of all gastroenteritis symptoms were reported without specific reference to diarrhoea symptoms [12, 42–44]. Although attempts were made to contact authors to provide the incidence of diarrhoea symptoms, in many cases this was not possible.

Overall we recovered limited data from which to derive regional morbidity and mortality estimates. For many regions of the world, such as Latin America and Africa we identified no morbidity studies, thus making the generalization of diarrhoea incidence rates in older children and adults in these regions difficult. The strict inclusion and exclusion criteria did not prove to discriminate against studies from any particular region, thus we are confident that the final database represents the best possible studies for estimating the burden of diarrhoea in older children and adults. The few data points limit the possibility of using more advanced modelling techniques to construct improved estimates for countries where data are missing. The mortality data are particularly scarce and it appears that very little research is being done

outside of the Demographic Surveillance Sites (DSS) around the world to determine cause of death in adults in countries where civil registration of mortality does not exist. Improved cause-specific mortality estimates are crucial for the planning of health services, therefore every effort should be made to publish the results from surveillance sites as well as new efforts to establish vital registration systems in countries where current mortality data are scarce. Diarrhoea is often considered to be an important disease only in young children. However, we have shown that although mortality rates may have declined in the past 15 years, morbidity rates have remained constant and thus more aggressive efforts will be needed to ensure every person, both young and old, has access to clean water, sanitation facilities, and food sources free from contamination in order to minimize risk factors for diarrhoeal diseases.

ACKNOWLEDGEMENTS

This work was undertaken as a part of the Global Burden of Diseases, Injuries, and Risk Factors Study. A grant from the Bill and Melinda Gates Foundation supported the Study's core activities and partially supported the epidemiological reviews in this paper. This work was jointly funded by the World Health Organization – Foodborne Disease Burden Epidemiology Reference Group. The authors thank the members of the WHO Foodborne Disease Burden Epidemiology Reference Group (FERG) for their invaluable feedback and assistance in identifying unpublished data sources. We also thank the Melinda Munos, Hilda Ndirangu, and Ramya Amyakutty for help with the initial literature review and data abstraction. The results in this paper are prepared independently of the final estimates of the Global Burden of Diseases, Injuries, and Risk Factors Study.

DECLARATION OF INTEREST

None.

REFERENCES

1. **Bryce J, et al.** WHO estimates of the causes of death in children. *Lancet* 2005; **365**: 1147–1152.
2. **Flint JA, et al.** Estimating the burden of acute gastroenteritis, foodborne disease, and pathogens commonly transmitted by food: an international review. *Clinical Infectious Diseases* 2005; **41**: 698–704.

3. **WHO.** *The Global Burden of Disease: 2004 Update.* Geneva: World Health Organization, 2008.
4. **Kosek M, Bern C, Guerrant RL.** The global burden of diarrhoeal disease, as estimated from studies published between 1992 and 2000. *Bulletin of the World Health Organization* 2003; **81**: 197–204.
5. **Boschi-Pinto C, Velebit L, Shibuya K.** Estimating child mortality due to diarrhoea in developing countries. *Bulletin of the World Health Organization* 2008; **86**: 710–717.
6. **Murray CJL, Lopez AD (eds).** *The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability from Diseases, Injuries, and Risk Factors in 1990 and Projected to 2020.* Boston: Harvard University Press, 2006.
7. **RefWorks.** *RefWorks: Scopus Edition,* 2009. RefWorks: North America.
8. **United Nations.** *World Population Prospects, 2006 Revision.* New York: United Nations, 2007.
9. **CDC.** Cause-specific adult mortality: evidence from community-based surveillance – selected sites, Tanzania, 1992–1998. *Morbidity and Mortality Weekly Reports* 2000; **49**: 416–419.
10. **el Alamy MA, et al.** The incidence of diarrheal disease in a defined population of rural Egypt. *American Journal of Tropical Medicine and Hygiene* 1986; **35**: 1006–1012.
11. **Hall GV, et al.** Frequency of infectious gastrointestinal illness in Australia, 2002: regional, seasonal and demographic variation. *Epidemiology and Infection* 2006; **134**: 111–118.
12. **Hellard ME, et al.** A randomized, blinded, controlled trial investigating the gastrointestinal health effects of drinking water quality. *Environmental Health Perspective* 2001; **109**: 773–778.
13. **Islam MS, Bhuiya A, Yunus M.** Socioeconomic differentials of diarrhoea morbidity and mortality in selected villages of Bangladesh. *Journal of Diarrhoeal Disease Research* 1984; **2**: 232–237.
14. **Jones TF, et al.** A population-based estimate of the substantial burden of diarrhoeal disease in the United States; FoodNet, 1996–2003. *Epidemiology and Infection* 2007; **135**: 293–301.
15. **Lerman Y, Slepon R, Cohen D.** Epidemiology of acute diarrheal diseases in children in a high standard of living rural settlement in Israel. *Pediatric Infectious Disease Journal* 1994; **13**: 116–122.
16. **Luby SP, et al.** Effect of intensive handwashing promotion on childhood diarrhea in high-risk communities in Pakistan: a randomized controlled trial. *Journal of the American Medical Association* 2004; **291**: 2547–2554.
17. **Majowicz SE, et al.** Magnitude and distribution of acute, self-reported gastrointestinal illness in a Canadian community. *Epidemiology and Infection* 2004; **132**: 607–617.
18. **Monto AS, Koopman JS.** The Tecumseh Study. XI. Occurrence of acute enteric illness in the community. *American Journal of Epidemiology* 1980; **112**: 323–333.
19. **Nazir M, Pardede N, Ismail R.** The incidence of diarrhoeal diseases and diarrhoeal diseases related mortality in rural swampy low-land area of south Sumatra, Indonesia. *Journal of Tropical Pediatrics* 1985; **31**: 268–272.
20. **Nygard K, et al.** Breaks and maintenance work in the water distribution systems and gastrointestinal illness: a cohort study. *International Journal of Epidemiology* 2007; **36**: 873–880.
21. **Rahaman MM, et al.** A diarrhea clinic in rural Bangladesh: influence of distance, age, and sex on attendance and diarrheal mortality. *American Journal of Public Health* 1982; **72**: 1124–118.
22. **Rodriguez WJ, et al.** Longitudinal study of rotavirus infection and gastroenteritis in families served by a pediatric medical practice: clinical and epidemiologic observations. *Pediatric Infectious Disease Journal* 1987; **6**: 170–176.
23. **Sargeant JM, Majowicz SE, Snelgrove J.** The burden of acute gastrointestinal illness in Ontario, Canada, 2005–2006. *Epidemiology and Infection* 2008; **136**: 451–460.
24. **Scallan E, et al.** Acute gastroenteritis in northern Ireland and the Republic of Ireland: a telephone survey. *Communicable Disease and Public Health* 2004; **7**: 61–67.
25. **Shahid NS, et al.** Hand washing with soap reduces diarrhoea and spread of bacterial pathogens in a Bangladesh village. *Journal of Diarrhoeal Disease Research* 1996; **14**: 85–89.
26. **Tarleton JL, et al.** Cognitive effects of diarrhea, malnutrition, and Entamoeba histolytica infection on school age children in Dhaka, Bangladesh. *American Journal of Tropical Medicine and Hygiene* 2006; **74**: 475–481.
27. **Thomas MK, et al.** Population distribution and burden of acute gastrointestinal illness in British Columbia, Canada. *BMC Public Health* 2006; **6**: 307.
28. **van der Hoek W, et al.** Irrigation water as a source of drinking water: is safe use possible? *Tropical Medicine and International Health* 2001; **6**: 46–54.
29. **Mathan VI, Rajan DP.** The prevalence of bacterial intestinal pathogens in a healthy rural population in southern India. *Journal of Medical Microbiology* 1986; **22**: 93–96.
30. **Do TT, et al.** Epidemiology and aetiology of diarrhoeal diseases in adults engaged in wastewater-fed agriculture and aquaculture in Hanoi, Vietnam. *Tropical Medicine and International Health* 2007; **12** (Suppl. 2): 23–33.
31. **Etard JF, et al.** Childhood mortality and probable causes of death using verbal autopsy in Niakhar, Senegal, 1989–2000. *International Journal of Epidemiology* 2004; **33**: 1286–1292.
32. **Kelly P, et al.** High adult mortality in Lusaka. *Lancet* 1998; **351**: 883.
33. **Tollman SM, et al.** Implications of mortality transition for primary health care in rural South Africa: a population-based surveillance study. *Lancet* 2008; **372**: 893–901.

34. **Adjuik M, et al.** Cause-specific mortality rates in sub-Saharan Africa and Bangladesh. *Bulletin of the World Health Organization* 2006; **84**: 181–188.
35. **Anwar Z, et al.** The pattern of the causes of death in children in rural swampy area of South Sumatra, Indonesia. *Paediatr Indonesiana* 1987; **27**: 93–98.
36. **World Health Organization.** Population, death rates, and reproductive rates, 2009. (http://www.who.int/choice/demography/pop_death_rates/en/print.html). Accessed 1 September 2009.
37. **Macgregor-Skinner GJ, et al.** Who seeks treatment for diarrhea in Vietnam? Results from a population-based survey (unpublished report).
38. **Boschi-Pinto C, Lanata C, Black RE.** The global burden of childhood diarrhoea. In: Ehiri J, ed. *Maternal and Child Health: Global Challenges, Problems, and Policies*. Washington, DC: Springer Publishers (in press).
39. **Byass P, Hanlon PW.** Daily morbidity records: recall and reliability. *International Journal of Epidemiology* 1994; **23**: 757–763.
40. **Manesh AO, et al.** Accuracy of child morbidity data in demographic and health surveys. *International Journal of Epidemiology* 2008; **37**: 194–200.
41. **Malik J, Bhan MK, Ray P.** Natural immunity to rotavirus infection in children. *Indian Journal of Biochemistry & Biophysics* 2008; **45**: 219–228.
42. **Wheeler JG, et al.** Study of infectious intestinal disease in England: rates in the community, presenting to general practice, and reported to national surveillance. The Infectious Intestinal Disease Study Executive. *British Medical Journal* 1999; **318**: 1046–1050.
43. **de Wit MA, et al.** Sensor, a population-based cohort study on gastroenteritis in the Netherlands: incidence and etiology. *American Journal of Epidemiology* 2001; **154**: 666–674.
44. **Payment P, et al.** A randomized trial to evaluate the risk of gastrointestinal disease due to consumption of drinking water meeting current microbiological standards. *American Journal of Public Health* 1991; **81**: 703–708.
45. **Rahman M, et al.** Cryptosporidiosis: a cause of diarrhea in Bangladesh. *American Journal of Tropical Medicine and Hygiene* 1990; **42**: 127–130.