

## EDITORIAL

# Global epidemiology of infections due to *Shigella*, *Salmonella* serotype Typhi, and enterotoxigenic *Escherichia coli*

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Enteric infections are a leading cause of disease and death in young children, particularly in the developing world [1]. In 1990, the World Health Organization (WHO) Global Burden of Disease estimated that diarrhoea contributed to 2·5 million deaths in children aged <5 years, representing 19·4% of total mortality in that age group [2]. Preliminary estimates from WHO for 2000 indicate that 1·6–2·1 million deaths occurred in children aged <5 years during that year [3–5]. While the declines are promising, and suggest that progress was made in the intervening decade, the confidence intervals surrounding these estimates are wide, especially at the national and sub-national levels, and pathogen-specific morbidity and mortality are poorly characterized. Although mortality rates due to diarrhoea have decreased globally, diarrhoea morbidity rates have not followed the same trend, especially in poor regions experiencing rapid population growth, where morbidity due to diarrhoea may actually have increased in recent years [6]. Furthermore, diarrhoea morbidity and mortality are probably greatest in areas where resources for surveillance, diagnosis, prevention, and treatment are most scarce, areas that are often under-represented in national estimates of diarrhoea incidence that are based on data from health facilities.

New tools for the prevention and treatment of enteric infections have become available in recent years. These include pathogen-specific interventions such as new vaccines and improved diagnostics with

which to target treatment [7], as well as interventions that may affect a variety of pathogens, such as new approaches to household water treatment and storage [8], new strategies for the promotion of sanitation [9] and hand hygiene [10], nutritional supplementation [11], integrated case management with low-osmolarity oral rehydration solution [12], and zinc supplementation [13]. However, little is known about the relative or combined impact of these interventions on enteric infections in general, or about their pathogen-specific effectiveness, in terms of health and economic benefits. The rational allocation of resources for treatment and prevention by policy-makers and funders requires accurate information on the pathogen-specific burden of disease and death, and on the cost-effectiveness of available interventions on pathogen-specific morbidity and mortality.

Financial and human resource constraints have limited the opportunities to perform accurate assessments of the disease burden caused by specific enteric pathogens and of the effectiveness of various interventions, especially in the developing world. Estimates of pathogen-specific disease burden are rarely population-based, inclusive of all age groups, or designed to capture all relevant health outcomes. Public health policy is frequently based on extrapolation of findings from limited controlled trials and may not accurately reflect localized variations, which influence the more relevant measure of practical effectiveness. For example, age-specific data are required to determine the potential preventable fraction by a vaccine given during infancy. Intervention studies often do not have the power to measure

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impacts on illnesses caused by specific pathogens, or on specific sequelae of enteric infections such as malnutrition. In addition, assessments of specific interventions are frequently constrained by the potential bias of short-term perspectives and advocacy, and may not reflect longer term biological and ecological factors or changes resulting from economic development.

To identify more clearly the gaps in our understanding of the epidemiology of enteric infections in the developing world, with support from the Bill and Melinda Gates Foundation, we conducted extensive literature reviews of three aetiological agents, *Shigellae*, *Salmonella enterica* serotype Typhi, and enterotoxigenic *Escherichia coli*. For each, we also reviewed data on specific interventions and diagnostic tools that can be used to better assess efforts to reduce mortality and morbidity associated with these pathogens.

For each pathogen, we searched the PubMed database using the same set of keywords and certain pathogen-specific terms. We restricted the results to studies conducted in low- and medium-income countries, and published between 1984 and 2005. Population-based studies with culture confirmation of cases were considered primary data sources; when these were lacking, hospital-based studies were considered.

This series of reviews can serve as a guide to our current knowledge of the epidemiology of these three major bacterial enteric pathogens [14–16]. A fourth review paper on infections due to *Vibrio cholerae* has been published elsewhere [17]. The knowledge gaps identified can serve as a roadmap of research activities for those who are interested in funding efforts to better control these diseases with targeted or general interventions.

Of particular note, our findings indicate that most, if not all, of the bacterial enteric infections are environmentally determined and respond to secular changes in hygiene and sanitation. Studies that were conducted in populations 20 years ago and indicate a high incidence of infection cannot be extrapolated to the same populations today, as they may have undergone substantial development. For example, the 14 500 deaths from diarrhoea in children aged <5 years in Mexico in 1990 was reduced to 5095 by 1995, and has been reduced even further in recent years, with a change from summertime deaths, thought to result from bacterial infections, to wintertime deaths, presumably caused by rotavirus [18, 19]. Municipal

water and sanitation services greatly contributed to the reduction that occurred during this period [20, 21].

While a significant portion of worldwide diarrhoeal disease mortality can be attributed to the pathogens reviewed in these articles, they are among a diverse group of pathogens responsible for global morbidity resulting from enteric infections. Among these, *G. lamblia*, *C. parvum*, and enteroaggregative *E. coli* (EAEC) have received increasing attention in recent years because of their effects on child development [22–27]. Development of new diagnostics and investigation of host and microbial genetic factors will further elucidate the complex relationships between enteric pathogens, diarrhoeal illnesses, and child development.

The papers in this series provide background on the demographic and geographic distributions and knowledge gaps of the epidemiology of three major bacterial enteric infections. We hope that these reviews will help to optimize the implementation of targeted approaches to disease control.

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## DECLARATION OF INTEREST

None.

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