Incomplete use of global data for aetiological attribution of diarrhoeal disease in the Global Burden of Disease study

The Global Burden of Disease study (GBD) for 2016 makes a bold attempt to estimate the aetiology of diarrhoeal disease for all ages.[1] Understanding of this burden, especially among non-paediatric populations, has been inadequate, and these necessary estimates will influence policy and prioritisation. However, we are concerned that GBD estimates are highly sensitive to key assumptions, some of which seem arbitrary and do not integrate all relevant data.

In the GBD approach to aetiological attribution, age-specific episodes and deaths for each aetiology are estimated as the product of three variables: the incidence of diarrhoea, the proportion of diarrhoeal episodes in which a given pathogen is detected, and the odds that detection of that pathogen indicates the cause of diarrhoea.[1] It is the third variable, known as attributable fraction, that merits further consideration.

The odds ratios for the attributable fraction used by GBD come solely from the Global Enteric Multicenter Study (GEMS).[2] GEMS was a rigorous multicentre study with comprehensive aetiological testing of moderate to severe diarrhoea among children aged 0–4 years in four African and three Asian low-income and middle-income countries. In GBD, the attributable fraction from GEMS is extrapolated to all age groups, countries, and the full clinical spectrum of diarrhoeal disease. Such a generalisation presents some serious limitations and potentially results in inaccurate burden estimates for several key pathogens.

However, GEMS is not the only source of data available to inform attributable fraction. For example, the English Infectious Intestinal Disease study could provide data across the age range and would have led to different estimates.[3] That study found the presence of *Campylobacter* spp, enteroaggregative *Escherichia coli*, sapovirus, and norovirus to be strongly associated with diarrhoea, whereas GEMS did not. Another example is our systematic review of norovirus, in which we identified 20 studies worldwide with data on the relative frequency of norovirus among cases of acute gastroenteritis versus controls without acute gastroenteritis.[4] Data from that review were used to generate the WHO Foodborne Disease Burden Epidemiology Reference Group global norovirus estimates of 685 million episodes and 212 000 deaths annually.[5] By comparison, the GBD estimates are an order of magnitude lower, at 140 million episodes and 19 000 deaths annually. These sources, and others, could collectively provide a diverse set of study populations and represent a more complete spectrum of ages, disease severity, and development levels. Future estimates of the global burden of diarrhoeal disease should integrate this wider range of data.

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Attributable deaths caused by infections with antibiotic-resistant bacteria in France

We read with interest the paper by Alessandro Cassini and colleagues[1] on deaths attributable to antibiotic-resistant bacterial infections in the EU in 2015, in which it was estimated that 33 110 deaths each year are caused by infections with antibiotic-resistant bacteria. The method used to provide this estimation is based on mathematical constructs developed in the EU as part of the Burden of Communicable Disease in Europe project, in the context of widespread anxiety about antibiotic resistance and the risk of present and future mortality due to antibiotic-resistant bacteria.

In the report by Cassini and colleagues,[1] the number of deaths due to multidrug-resistant bacteria in France was estimated to be 5543 per year (out of 29 000 deaths due to bacterial infections per year). At the IHU Méditerranée Infection (Marseille, France), we examine, on a weekly basis, the microbiological results of most hospital and private laboratories in the southern region of France (which has around 5 million inhabitants), accounting for about 300 000 bacterial isolates per year.[2,3] We also examine the results of antibiotic susceptibility testing of all isolated bacteria in the University