

Fail to prepare no more

While deaths from leading infectious diseases have decreased since the millennium, the threat from potential new outbreaks means that complacency is not an option. The global health community is grossly underprepared to meet new epidemic challenges, but signs suggest that improvement is underway.

A recent summary of the ten leading causes of death globally in 2015 provides a snapshot on the changing dynamics of disease around the world (<http://www.who.int/mediacentre/factsheets/fs310/en/>). Ischaemic heart disease and stroke account for the largest number of deaths, causing 15 million of the 56.4 million total deaths in 2015, an increase on the 12.3 million deaths caused by these diseases in 2000. Notably, 2015 also witnessed 1.6 million deaths related to diabetes, a substantial increase from the 1 million in 2000, as well as 1.5 million deaths related to Alzheimer's disease and other dementias, more than double the number in 2000. The picture is a little brighter for infectious diseases. Deaths from lower respiratory tract infections were down from 3.4 million in 2000 to 3.2 million in 2015, and those from diarrhoeal diseases down from 2.2 million to 1.4 million. Substantial decreases were also seen for tuberculosis (1.4 million, down from 1.7 million) and HIV/AIDS (1.1 million, down from 1.5 million), with the latter no longer scoring among the ten leading causes of death. Overall deaths from these leading communicable diseases were down from 8.75 million at the turn of the century to 7.07 million in 2015, a very positive trend. However, if the numbers are broken down by the income of each country, a less encouraging picture emerges. In low-income countries, lower respiratory tract infections and diarrhoeal diseases displace stroke and heart disease as the two leading causes of death and together with HIV/AIDS, tuberculosis and malaria account for five of the top seven.

Infectious diseases collectively remain among the leading causes of death in a substantial proportion of the world, while also inflicting a heavy economic and societal burden. However, they cannot be seen as a challenge solely for those in low- and middle-income countries to deal with. Infectious diseases do not respect international borders, and require a global response both to drive endemic diseases back and to tackle newly emerging epidemics. Coupled with the looming threat from antimicrobial resistance, which will disproportionately affect low- and middle-income economies but also have a substantial impact on

high-income economies, it is clear that coherent structuring of healthcare efforts and the active involvement of high-income-economy countries remains of fundamental importance. As John-Arne Røttingen puts it in an illuminating interview in this issue (article no. 17023), “wealthier countries have the responsibility to contribute to the protection of vulnerable populations far from their own border”.

Røttingen is the director of the Division of Infectious Disease Control at the Norwegian Institute of Public Health, and was recently announced as the interim chief executive officer for the Coalition of Epidemic Preparedness Innovations (CEPI), an alliance of governments, health bodies and philanthropic and industrial partners with the mandate to fund the development of new vaccines to prevent epidemics. With an initial investment of US\$540 million, CEPI will coordinate funding and research for vaccines against three emerging viral diseases — Middle East respiratory syndrome, Nipah virus and Lassa fever — and take development through until they are ready for phase III clinical trials, which can only take place in an outbreak setting. As discussed by Røttingen, CEPI was conceived to fill a hole in the system for epidemic preparedness, namely the lack of vaccine development against emerging viruses that pose potential epidemic threats. Because the market for these vaccines is extremely limited, there is little to no incentive for industry to undertake the task of developing vaccines from late preclinical stages up to phase III readiness. The 2014 Ebola outbreak in West Africa exposed this flaw. Of the numerous potential vaccines, none had progressed from testing in animal models and it took a year for the rVSV (recombinant vesicular stomatitis virus–Zaire Ebola virus) vaccine to pass through initial human safety trials and to be deployed in the field. By previous standards this is incredibly fast, but if the initial development work had already been carried out, many of the 11,000 lives lost could potentially have been saved.

With finite resources available, developing vaccines for future epidemics will always be a bit of a gamble. The three viruses to be initially targeted were selected using criteria

including the current health impact of the disease and the risk of an outbreak, as well as the preclinical pipeline and tools available for vaccine development. Focusing on a limited number of viruses rather than spreading their efforts too thinly is the correct approach for CEPI to take; however, it leaves us less prepared to cope with many other potential epidemic viruses, should they emerge instead. If CEPI is successful in developing the initial three vaccines, the global community should provide additional funding to expand the list of pathogens in their portfolio for vaccine development. While taking vaccine candidates through development to phase III readiness is not cheap, the collective financial impact of an epidemic would dwarf this initial investment.

Vaccine development is by no means the only area in which work is needed to close gaps in epidemic preparedness, as outlined in a recent analysis (S. Moon *et al.*, *BMJ* 356, j280; 2017). Suerie Moon and colleagues examined seven major reports assessing what went wrong in the global response to the Ebola outbreak and what needs to be done to improve for future outbreaks. The authors identified several priority gaps that need to be addressed, including ensuring that all countries have the basic core capacities for identifying and responding to outbreaks; preventing unnecessary restrictions on trade and travel during an outbreak, which can hamper responses and economically punish countries experiencing an outbreak; developing international standards for sharing of data and samples, for clinical trial protocols and for regulatory processes; ensuring access to diagnostic technologies, vaccines and drugs for all countries; and lastly, tackling the organizational and operational problems at the World Health Organization and the United Nations to better enable rapid and coordinated emergency responses.

While much of this work is underway, as demonstrated by the formation of CEPI, Moon and colleagues conclude that “the world remains grossly underprepared for outbreaks of infectious disease, which are likely to become more frequent in the coming decades”. Failing to be better prepared for future outbreaks will lead to countless thousands of people dying unnecessarily. □