A new twenty-first century science for effective epidemic response

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With rapidly changing ecology, urbanization, climate change, increased travel and fragile public health systems, epidemics will become more frequent, more complex and harder to prevent and contain. Here we argue that our concept of epidemics must evolve from crisis response during discrete outbreaks to an integrated cycle of preparation, response and recovery. This is an opportunity to combine knowledge and skills from all over the world—especially at-risk and affected communities. Many disciplines need to be integrated, including not only epidemiology but also social sciences, research and development, diplomacy, logistics and crisis management. This requires a new approach to training tomorrow's leaders in epidemic prevention and response.

When *Nature* published its first issue in 1869[1], a new understanding of infectious diseases was taking shape. The work of William Farr[2], Ignaz Semmelweis[3], Louis-René Villermé[4] and others had been published; John Snow had traced the source of a cholera epidemic in London[5] (although Robert Koch had not yet isolated the bacterium that caused it[6]). The science of epidemiology has described patterns of disease in human populations, investigated the causes of those diseases, evaluated attempts to control them[7] and has been the foundation for public health responses to epidemic infections for over 100 years. Despite great technological progress and expansion of the field, the theories and practices of infectious disease epidemiology are struggling to keep pace with the transitional nature of epidemics in the twenty-first century and the breadth of skills needed to respond to them.

Epidemiological transition theory has focused mostly on the effects of demographic and socioeconomic transitions on well-known preventable infections and a shift from infectious diseases to non-communicable diseases[8]. However, it has become clear that current demographic transitions—driven by population growth, rapid urbanization, deforestation, globalization of travel and trade, climate change and political instability—also have fundamental effects on the dynamics of infectious diseases that are more difficult to predict. The vulnerability of populations to outbreaks of zoonotic diseases such as Ebola, Middle East respiratory syndrome (MERS) and Nipah has increased, the rise and spread of drug-resistant infections, marked shifts in the ecology of known vectors (for example, the expanding range of *Aedes* mosquitoes) and massive amplification of transmission through globally connected, high-density urban areas (particularly relevant to Ebola, dengue, influenza and severe acute respiratory syndrome-related coronavirus SARS-CoV). These factors and effects combine and interact, fuelling more-complex epidemics.

Although rare compared to those diseases that cause the majority of the burden on population health, the nature of such epidemics disrupts health systems, amplifies mistrust among communities and creates high and long-lasting socioeconomic effects, especially in low- and middle-income countries. Their increasing frequency demands attention. As the Executive Director of the Health Emergencies Program at the World Health Organization (WHO) has said: "We are entering a very new phase of high-impact epidemics… This is a new normal, I don't expect the frequency of these events to reduce."[9].

We have to act now but act differently: a broader foundation is required, enhancing traditional epidemiology and public health responses with knowledge and skills from a number of areas (Table 1). Many of these areas have long been associated with epidemic preparedness and response, but they must now stop being seen as esoteric 'nice things to have', and instead become fully integrated into the critical planning and response to epidemics.

This will require considerable changes by the global public health community in the way that we respond to epidemics today and how we prepare for and seek to prevent those of tomorrow. It will mean reshaping the global health architecture of the response to epidemics and transforming how we train new generations of researchers and practitioners for the epidemics of the future[10].

The modern research culture—often shaped by the behaviour of funders—has required many researchers to specialize in narrow fields, with less emphasis on translation than on field-specific innovations. Although this siloed landscape has brought major advances in global health, it is not fit for the transitional phase of epidemic diseases: rapidly evolving, high-impact events bring together communities, responders and researchers who do not routinely interact. Different assumptions, cultures and practices, each of which may be widely accepted within a

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Table 1 | Selected key areas to integrate into twenty-first century epidemic responses

Area	Key areas and/or disciplines
Governance and infrastructure	Local, national and international organizations; integrate accountability and transparency across multiple stakeholders; improve data sharing, improve logistics and crisis management
Engagement and communication	Encourage a community-led response, community engagement and health diplomacy
Social sciences	Anthropology, political science, human geography, linguistics
Ethics	Consent, clinical trial designs
Emerging technologies	Pathogen genomics, metagenomics, systems serology and analytics, data science and artificial intelligence
Research and development	Diagnostics, therapeutics and vaccines
One Health	Ecology and environmental, veterinary and agricultural sciences

particular community, make working together in outbreak situations more challenging. Fundamental to success is respect and understanding of the contribution each party brings. In a successfully integrated approach, we each have to realize that our knowledge and skills are a small part of a rapidly expanding toolkit (Box 1). We need to understand major trends in research and how and when they may influence the response to an epidemic, develop new research to strengthen the support that we can provide across other areas and learn to operate in multi-stakeholder situations—including, at times, as part of a critical debate to bring better practices to the fore.

Central to this approach must be the communities who are at risk and those affected by epidemics: local people are the first responders to any outbreak and their involvement in the preparation and response activities is essential. From communities, through local and regional health authorities, national public health institutes and international organizations—including many essential partners in sectors beyond public health—the integrated approach must be supported. The WHO, in particular, has a critical part to play, using its unique mandate not to lead every aspect of preparation, response and recovery, but to change its practices, facilitate integration with and among others, and ensure accountabilities are built in from the bottom to the top.

Nineteenth and twentieth century epidemiology

A wave of cholera epidemics across Europe in the 1830s and 1840s catalysed a new era of 'infectious disease diplomacy'[11] globally. Nations recognized that infections do not stop at borders and that therefore multilateral collaboration is essential to protecting citizens from lethal epidemics. The development of germ theory through the second half of the nineteenth century[12] transformed ideas about the causes of infections, informing scientific research as well as clinical responses. Scientific understanding translated into vaccines[13] and antibiotics, while programmes for child health, hygiene, clean water and sanitation became common in the twentieth century. As a result, childhood diseases such as measles and mumps became rare, smallpox was eventually eradicated[14] and polio was eliminated from all but a handful of countries[15]. Many people thought that infectious diseases would soon be history. Sir Frank Macfarlane Burnet is often cited for his remark in the 1970s that, with the emergence of new diseases being a distant prospect, "the future of infectious diseases will be very dull"[16].

Although the focus in high-income nations turned to non-communicable diseases, which constituted a considerable and increasing burden on the health of their citizens, infectious diseases did not disappear. Some endemic infections such as malaria and tuberculosis were not susceptible to elimination strategies, and new diseases with epidemic and pandemic potential emerged. Ebola virus disease was first identified in the 1970s, HIV/AIDS in the 1980s, Nipah virus in the 1990s, SARS and MERS at the start of the twenty-first century, and many more have since been identified. Far from becoming 'very dull', the field of infectious disease epidemiology has sometimes struggled to adapt: as late as 1990, respected researchers used a nineteenth century 'law' of epidemiology to make predictions about the AIDS epidemic—these turned out to be vast underestimates[17]. Advances in other fields gave epidemiology the chance to evolve. In 2001, when the editors of the *International Journal of Epidemiology* provocatively asked whether it was time to 'call it a day'[18] given the putative power of genomics to explain diseases over the capacity of epidemiologists to describe them, their conclusion was that it had the potential to positively transform epidemiology as much as the rise of germ theory a century earlier.

The new normal

At least 150 pathogens that affect humans have been identified as emerging, re-emerging or evolving since the 1980s[19], while increasing rates of antimicrobial resistance threaten to make formerly controlled infections, such as malaria, untreatable[20]—this also limits our ability to control their epidemic potential. The demographic transition is driving much of this: human society is becoming more urban than rural for the first time in our history, bringing large numbers of people (and often animals) together in densely populated areas[21]. Agricultural and forestry practices are changing the relationships between people, animals and our respective habitats[22]. Travel is more accessible around the world,

Box 1

Non-traditional tools for epidemics

Artificial intelligence
Advances in computer science and computing speeds have led to a number of applications of artificial intelligence across society[84]. Applications in epidemiology include tracking online searches about disease symptoms to aid early detection of epidemics, although more sophisticated methods may be required before artificial intellegence becomes a reliable detection tool[85].

Crystallography
Modern X-ray diffraction and electron microscopy can reveal structures of viruses and antibodies in such detail that it is possible to identify specific sites of vulnerability on the virus. A previous study showed how such techniques identified an antibody that was much more potent against respiratory syncytial virus than the only currently available intervention[86].

Platform vaccine technology
Developing vaccines for emerging infectious diseases has many challenges, including the time it takes, a limited market and strict regulatory requirements for products that will be given to healthy people[87]. Platform technologies use one underlying approach with standardized processes and some antigen-specific optimization to speed up both development and manufacture of vaccines. For example, vector-based platforms combine an antigen, or a gene for an antigenic protein or peptide, in a virus-like particle or liposome. Such platform technologies have the potential to deliver vaccines a few months after an emerging pathogen is identified and sequenced, rather than years[88].

so migration, trade and tourism bring more people into contact and thus affect disease transmission[23]. Climate change has many effects on ecosystems and environments, not least in changing the habitats and migratory habits of disease vectors[24]. States with weak health systems are far less likely to cope with or recover from multiple emergent demands without damaging routine services[25]. Inequalities[26], inequities and distrust in national structures and institutions compound people's vulnerabilities[27]. Conflict increases the risk of epidemics and makes responding to them close to impossible[28].

Since 2000, there have been several outbreaks of Ebola (including the two biggest in history), not to mention outbreaks of SARS, MERS, Nipah, influenza A subtype H5N1, yellow fever, Zika and the continued spread of dengue. Epidemics overlap and run into each other, yet the world is not currently equipped to cope with this increasing burden of multiple public health emergencies. Preparing for epidemics, therefore, requires global health, economic and political systems to be integrated just as much as infectious disease epidemiology, translational research and development, and community engagement.

Essential areas in epidemic response

Governance and infrastructure

Epidemics represent shared risks that cross borders and all of society. Health systems, routine care, trust in governments, travel, trade, business—all are disrupted during an epidemic. With such broad risks, the preparation and response must be nationally owned and led, internationally supported and undertaken with a whole-of-society approach. Some initiatives have started to build frameworks for this to happen in a coordinated way. For example, the WHO's Pandemic Influenza Preparedness Framework brings together nation states, industry, other stakeholders and the WHO to implement a global approach to pandemic preparedness and response[29].

A focus must be building coordinated regional and country expertise, resources and capacity through national and regional public health institutions[30]. This brings its own challenges—governance of institutions, leadership, collaborations and interventions have to be impeccable or misconduct can thrive[31]. Unwelcome in itself, misuse of funding, resources or people within efforts intended to support an epidemic response will also undermine trust in the organizations that respond to an outbreak and, in turn, prolong the outbreak.

Key governance components include drafting policies in advance and being willing to implement those policies for data collection and sharing during epidemics. They must be flexible enough to enable affected communities and nations to retain ownership of the response, while drawing on international expertise to find the best possible response. Governance should also include processes for vaccine and therapeutic approvals during outbreaks. However, it is clear that the centre of gravity for leadership, governance and implementation must be where the need is greatest if these are to truly deliver.

In 1971, Julian Tudor Hart proposed the inverse care law: "The availability of good medical care tends to vary inversely with the need for it in the population served."[32]. An analogue of the inverse care law can be applied to public health and epidemiology. Expertise in these fields has traditionally gravitated towards centres of excellence in Europe and the United States. Of course, high-income countries are not immune to the disruption associated with epidemics, especially in an era of misinformation and growing mistrust in authorities and public health initiatives. However, the centre of gravity must shift so that globally representative distributed networks of collaborating centres can jointly ensure coverage in the regions that urgently need these skills on the ground[33]. International collaborations remain important; however, strengthening epidemiology, public health and laboratory capacity in low- and middle-income countries is essential[34]. Collaborative interventions should not be limited to when there is a major outbreak, but be integrated into regular interactions.

Capacity, resources, expertise and governance can be supported by the increasing role for regional and national centres of disease control. The US Centers for Disease Control (CDC) lends its expertise all around the world in addition to protecting the US population. In 2004, the European CDC started, followed by the China CDC in 2015 and by the Africa CDC in 2017. Although more can be done to improve data sharing and access to laboratories, the networks and connections between these centres have strengthened all of their work, as well as having a positive effect on public health systems in low- and middle-income countries.

Engagement and communication

During the pan-European wave of cholera in the 1830s, there were riots across the continent: doctors, nurses and pharmacists were murdered, hospitals and medical equipment destroyed[27]. Similar reports today usually come from communities that have not had positive prior interactions with public health initiatives, and thus the encounter with national or international teams who arrive only in response to a 'new' disease means that trust can never be assumed and has to be earned on both sides. Engagement needs to start before an outbreak—ensuring that patients, their families and their communities are at the centre of all public health is essential for the successful prevention and response to epidemics. There is no public health without the support of the community.

For example, the early detection of disease events will be improved if more national and regional public health institutions establish community event-based surveillance systems. Communities are the first to know when something unusual happens[35]—therefore training and mobilizing community volunteers to report such occurrences is a cost-effective way to rapidly detect diseases and contain them at the source. This will also help to sustain engagement between communities and the organizations that respond to outbreaks. Furthermore, improved information flow between the community and the public health system should provide a better understanding of local social networks to complement other means of tracking chains of transmission between individuals and places. This can be the community themselves, or it might be veterinarians who see clusters of sick animals, or nurses and doctors who care for patients in primary care—or it may be teams that are often forgotten in public health initiatives, such as those working in critical care facilities; it is striking how the first cases of Nipah, SARS, MERS and influenza A subtype H5N1 were all first identified by clinical teams in critical care facilities.

An inclusive, whole-of-society approach is challenging, and the challenges may be magnified in a conflict or post-conflict zone. Wars and conflicts not only increase the risk of epidemics as people move to escape violence and health services become harder to maintain[36], but also make public health responses vulnerable to interruption, thus making them less effective. Then, miscommunication, mistrust, disease and violence can fuel each other in a vicious cycle. Engaging local communities remains the highest priority, even in unstable contexts such as North Kivu and Ituri provinces of the Democratic Republic of the Congo (DRC)[37], where an Ebola epidemic started in August 2018. It seems inevitable that responding to epidemics in politically unstable environments will become more common, and skilled negotiators and peacekeepers will have to be better integrated in response teams. Equally essential, therefore, will be an improved understanding of these challenging operational contexts among affected communities and external responders alike.

Social sciences

Social scientists have long applied their skills and knowledge in epidemic responses, although their roles have become more visible in recent years[38]. By focusing on communities, social science humanizes the epidemic response[39], helps to increase understanding of context and may uncover associations between the context or local practices and the risk of transmission. The Social Science in Humanitarian Action Platform[40] has successfully produced rapid reports and

Box 2

Precision public health

Precision medicine refers to the use of genomic sequencing to retrace the specific course of a disease in individual patients, with the aim of being able to choose the best treatment option for each person. In public health, the analogous idea of precisely directing the right intervention to the right population is equally appealing.

The potential of such an approach has been illustrated by the identification of two areas in the United States in 2016 that were at risk of Zika transmission[89]. Rather than the whole country, or even only Florida, being declared at risk, these two areas each measured less than 5 km^2, and the response focused only on these specific neighbourhoods. By contrast, a campaign against yellow fever, also in 2016, defined risk 'at the level of entire nations'.

A broad interpretation of precision public health[90] incorporates many different types of data to increase the power of epidemiology[91]. Such data would not only include genomic information, but also satellite imaging, mobile phone data, social media use data and so on. For example, a study published in 2019 combined epidemiological surveillance data, travel surveys, parasite genetics and anonymized mobile phone data to measure the spread of malaria parasites in southeast Bangladesh[92]. A retrospective analysis of mobile phone call data in Sierra Leone from 2015 showed how it might have been used to assess the impact of travel restrictions on mobility during the Ebola epidemic[46].

The principle of selecting the most relevant information from all available data seems within the scope of good epidemiological practice already. The challenge is recognizing and incorporating new types of data when they become available.

briefings on regions in which an epidemic has been identified, and the Global Research Collaboration for Infectious Disease Preparedness includes a social science research funders' forum to 'propel research in this area'[41], acknowledging that its integration in the preparation and response to outbreaks is often missing or added as an afterthought to solve a problem that could have been forseen. There is still much to learn about how epidemic responders and social scientists can make the most of each other's expertise[42] and how data from social science can fit into the wider information architecture of epidemic response.

As an example, behavioural surveillance[43] will be critical in twenty-first century responses to disease outbreaks[44]. Just as behavioural surveillance to improve the understanding of HIV was crucial in identifying high-risk groups for HIV infection, so human behaviours will continue to be important as we respond to future infectious diseases. For instance, the Ebola virus outbreak in West Africa probably began before December 2013, but it took several months before hospital transmission and traditional burial practices were found to be the leading causes of its rapid spread.

Emerging technologies

The increasing prevalence of mobile phones, wireless internet connectivity and social media activity raises the possibility of using these tools to gather data for epidemiological studies, diagnostics[45], population mobility during an Ebola epidemic[46] or influenza incidence in real time[47]. Future developments in predictive technology, machine learning and artificial intelligence will bring more opportunities to move towards 'precision public health' (Box 2).

The use of data from people is becoming strictly controlled, however, and it will be a challenge to persuade countries to invest in a new surveillance system, for example, before its general effectiveness has been demonstrated at a country level[48]. Even then, technology-based solutions should be integrated with community-based programmes and other existing epidemic preparedness and response systems because surveillance is more effective when standardized among different countries, districts and communities. To this end, suites of guidance and open-access standardized tools are being developed for reporting cases of disease, as well as consent forms, standard operating procedures and training materials[49], properly validated diagnostic assays and access to quality-assurance panels in public[50] and veterinary[51] health. The rising trend of engaging citizens in data gathering is also welcome—the use of mosquito-recognition apps enables the collection of data far beyond the capacity of routine mosquito surveillance[52]. This way, citizens feed information into the public health system and the feedback loop offers a fast and direct way to provide citizens with details of potential actions that they can take.

As well as potentially supporting diagnosis and surveillance[53], the fast-developing field of genomic epidemiology[54] can yield information to track the evolution of a virus such as Ebola during an epidemic[55,56]. There will be times when it can detect outbreaks better than traditional epidemiology, illustrating the need to have these tools available in the same toolbox. During the large Lassa fever outbreak in Nigeria in 2018, real-time genomic sequencing provided clear evidence that the rapid increase was not due to a single Lassa virus variant, nor attributable to sustained human-to-human transmission. Rather, the outbreak was characterized by vast viral diversity defined by geography, with major rivers acting as barriers to migration of the rodent reservoir[57]. These findings were crucial in containing the outbreak.

Developing and sustaining the capacity to conduct real-time sequencing with adequate bioinformatics analyses at regional and national levels will be challenging in low- and middle-income countries. Moreover, investments in relatively high-tech capacity (such as real-time sequencing) are competing with other, arguably more fundamental needs, such as equipment and training in primary laboratories. Political engagement must be nurtured between epidemics: it is not enough to offer technological and laboratory support during a crisis, even with the promise of building capacity, if the political will is not there. However, with proper preparation, and accessible and trusted data sharing and governance mechanisms, laboratories with limited resources may be able to leap-frog into the twenty-first century[58,59].

Research and development

Vaccination is one of the most effective public health interventions and innovative strategies for research and development of vaccines, such as using ring vaccination as a trial design during Ebola epidemics since 2015[60–62], must be encouraged. At the start of the 2013–2015 epidemic in West Africa, vaccine candidates were already in development, based on a long history of preclinical research, although a lot of work was still required to get clinical trials underway in time to be useful[63]. In 2015, when Zika was first internationally recognized as a pathogen that could cause birth defects[64], there was hardly any research and no vaccines in late-stage development. Two-and-a-half years later, results from three phase I clinical trials had been reported[65], although challenges remained for further development. The lack of a profitable market for such products means that pharmaceutical companies lack the incentives to push this work between epidemics. Initiatives such as the Coalition for Epidemic Preparedness Innovations are attempting to positively disrupt financing models for vaccines against epidemic diseases[66], and stockpiles of meningococcal vaccine, yellow fever vaccine and oral cholera vaccine are maintained by the International Coordinating Group to minimize potential delays due to limited manufacturing capacity[67].

Similarly, if investigational treatments or vaccines are to be used as part of the response to an epidemic, ethical protocols[68] for managing informed consent and introducing them in clinical settings must be planned in advance with at-risk communities (Box 3). Trial designs[69]

Box 3

Epidemic ethics

In 2016, the PREVENT project received Wellcome funding to provide ethics guidance "at the intersection of pregnancy, vaccines, and emerging and re-emerging epidemic threats"[93]. This was in response to the newly recognized association between infection with Zika virus during pregnancy and microcephaly in the newborn. Developing a vaccine was an obvious route to explore, but many researchers felt that they could not conduct clinical trials with pregnant women because it is generally assumed that the risk to the woman, the fetus or both outweighs any potential benefit. However, as Heyrana et al. argue: "Preventing pregnant women from participating in clinical trials is well intentioned but misguided."[94].

PREVENT rapidly developed guidance for including pregnant women and their babies in Zika vaccine research[95], and has since extended their scope to "a roadmap for the ethically responsible, socially just, and respectful inclusion of the interests of pregnant women in the development and deployment of vaccines against emerging pathogens."[88].

Integrating ethics in the preparation and response to epidemics does not close off avenues of research; it opens up possibilities and expedites progress.

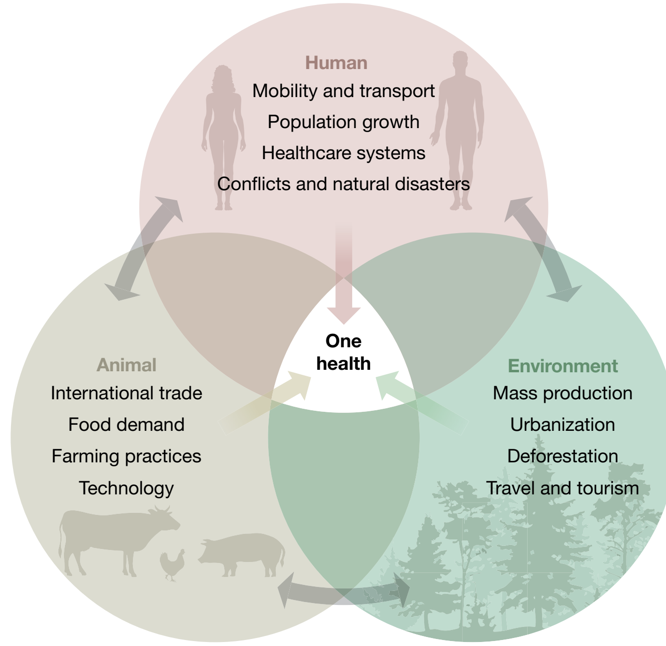

Fig. 1 | An ecosystem of interactions. The tightly interconnected nature of human, animal and environmental health makes the emergence and decline of epidemics difficult to predict. One Health integrates multiple perspectives in a framework that emphasizes the need to consider any particular aspect in this broader context.

should be created as soon as the option becomes viable. The essential consideration is how the resulting data can add to previous trials and influence the approach to trials in future epidemics. For example, research during the 2013–2015 Ebola epidemic enabled progress on therapeutic agents[70] that are now being trialled in the ongoing outbreak in DRC[71]. Scientific progress during and between epidemics must be matched by other workstreams, such as the preparation of supply chain logistics and communication with at-risk populations. Plans have to be made for a series of future outbreaks, enabling adaptive, multi-year, multi-country studies[72]. Similar plans are needed for continual preclinical research to ensure that future vaccine and therapeutic pipelines will be filled.

One Health

The term 'One Health'[73] is used to acknowledge that human, animal and ecosystem health are tightly interconnected and need to be studied in the context of each other (Fig. 1). Changes in the environment—whether natural or anthropogenic—affect interactions between pathogens, vectors and hosts in multiple and complex ways, making the emergence or decline of endemic, epidemic and zoonotic diseases difficult to predict, while epidemics of animal diseases can challenge a community's access to food. The fact that pools of viruses, bacteria and parasites are maintained in wild and domesticated animals[74] makes surveillance of potentially zoonotic diseases an intrinsic part of One Health epidemic planning. Many agencies and nations around the world now use prioritization tools such as those developed by the US CDC[75] or the United Nations (UN) Food and Agriculture Organization (FAO)[76] to identify and prioritize zoonotic diseases of concern. An early precedent was a joint consultation on emerging zoonotic diseases by the WHO, the FAO and the World Organisation for Animal Health in 2004[77]. Understanding disease ecology in the zoonotic reservoir could potentially lead to ways to predict the risk of human disease, thus providing the basis for smart early-warning surveillance systems.

Individual countries with limited resources for epidemiological studies and epidemic preparation and response must decide their own priorities. However, infectious diseases do not respect borders. Similarly, the interdisciplinary nature of One Health means there are several different lenses through which different sectors assess risks and priorities. For One Health approaches to work, these multiple perspectives must be taken into account, whether human health or animal health, ecology or social sciences[78].

Recovery

Epidemics do more than cause death and debilitation: they increase pressure on healthcare systems and healthcare workers and draw resources from services not directly linked to the epidemic. This can leave a legacy of distrust between people, governments and health systems, although more-positive outcomes have been found to strengthen relations between communities and public authorities. The full social and economic costs of the Ebola outbreak in West Africa have been estimated[79] to be as high as US$53 billion when including the effect on health workers, long-term conditions suffered by 17,000 Ebola survivors, and costs of treatment, infection control, screening and deployment of personnel beyond West Africa. As healthcare resources became increasingly allocated to the Ebola response, hospital admissions fell and deaths from other diseases rose markedly, adding US$18.8 billion to the estimated cost. Such pressure can be withstood in high-income countries with strong health systems, but in low-income countries the pressure can quickly reach a breaking point.

Ebola killed almost 1.5% of doctors, nurses and midwives in Guinea, 6.85% in Sierra Leone and just over 8% in Liberia[80]. This is compared to mortality between 0.02% and 0.11% of the whole population of these countries. Estimates of the effect of this loss on maternal mortality suggest that thousands more women may have died in childbirth each year since the epidemic ended. Beyond the tragic deaths of so many healthcare workers, people were less likely to use health services for children or adults during the epidemic, suggesting decreased trust or even fear of healthcare settings[81]. More recently, in some areas affected by the 2018 Ebola outbreak in DRC, the introduction of free non-Ebola healthcare led to unprecedented demand. However, healthcare facilities were not given sufficient additional resources to care for the number of people, which may have contributed to nosocomial infections.

Survivors, too, need to be cared for long after the epidemic is declared over. A cohort of more than 3,000 children is growing up in Brazil after being born with microcephaly because their mothers were infected with Zika during pregnancy. Tracking the development of these children increases understanding of the effects of Zika infection and helps to define what medical and social support the affected families may need as many of the children will grow up with severe developmental delays[82].

Outlook

The challenges posed by twenty-first century epidemics are real and changing: future epidemics will be fuelled by conflict, poverty, climate change, urbanization and the broader demographic transition. In our response we must consider epidemics not as discrete events, but rather as connected cycles for which we can prepare, even if we cannot predict specific outbreaks. The challenge is then to choose the right response at the right scale in the right area at the right time. There needs to be a greater emphasis on absorbing and using positive lessons from each episode and avoiding those that led to negative outcomes[83].

The way that we train practitioners and researchers working in all fields relevant to today's epidemic landscape has to change. A modern approach that is capable of characterizing epidemics and the best ways to control them must go beyond a narrow definition of epidemiology that sustains artificial barriers between disciplines. Instead, it must be able to integrate tools and practices from a diverse range of established and emerging scientific, humanistic, political, diplomatic and security fields. We believe that such an approach needs to become the norm for the curriculums of schools of public health around the world.

As well as training new generations of epidemiologists so that they have the skills, knowledge and networks to recognize and make use of every tool available to help them to do their work effectively, the entire architecture of the response to epidemics has to be adapted. Only then will we be able to maintain the comprehensive and effective response—including prevention and research—needed to stop epidemics and protect people's lives, no matter what the circumstances.

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It is an ethical imperative to consider and implement research in an epidemic setting as, for many epidemic diseases, it is the only time at which to conduct the research that will inform and improve the lives of the individuals affected during epidemic and to ensure that future generations are better prepared; however, such research is challenging at many levels and it is critical to have an ethical framework that guides the research, places individuals and communites at the heart of the research and facilitates the maximum benefit for the maximum number of people, in an equitable way, that is independent of the ability to pay—such a framework is outlined in this paper and is put into the context of social justice and equity.
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