EDITORIALS

Ebola virus disease outbreak: incorporating ethical analysis into the health system response

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The current outbreak of Ebola in western Africa has been unprecedented for various reasons, mostly because of its magnitude, its expansion across the borders of several countries of the region, and its propagation in capital cities. The outbreak initially involved no more than a few hundred people mainly in the rural parts of Africa, but by mid-September it had affected more than 5800 persons and caused more than 2500 deaths in four countries (mainly in urban locations). It is still not showing any signs of decreasing in intensity. This epidemic has brought to the fore many issues which have implications that go beyond just Ebola and western Africa. For example, it has highlighted the ever-widening social and economic inequalities within and between countries; the globalisation and interconnectedness of our world today; and the dire economic consequences of epidemics – this outbreak of Ebola has had the power to close down ports and airports, as well as seal borders. The outbreak has also brought to the fore a number of ethical issues, some of which have been raised during earlier epidemics, and some of which are novel.

The response to any outbreak entails being prepared to limit individual rights and civil liberties in the interest of public health (1). The principles of such limitations are enshrined in the Siracusa Principles (2). When required to do so, the least restrictive and intrusive measures available should be used for tracing contacts and imposing quarantine measures, without placing unfair burdens on particular segments of the population. The Government of Liberia resorted to community quarantine to contain the outbreak, while Sierra Leone imposed a nationwide three day curfew. These measures limited the movement of people for several days, resulting in food shortages and poor access to essential services, including health. This, together with the fact that the people could no longer earn their livelihood, placed a huge burden on the community.

The epidemic has also highlighted the crucial role of the health systems in controlling the outbreak. The three main countries afflicted by Ebola virus disease (EVD) – Liberia, Guinea and Sierra Leone – have witnessed years of armed conflict, which has weakened their health systems tremendously. Though the health systems of these countries were in the process of recovering in the early days of the EVD outbreak, it put a colossal burden on their limited capacities and they were unable to cope with the public health crisis, despite external donor aid. This has not only resulted in a health crisis; it has also had a huge impact on development, the economy and trade, pushing these countries further into poverty. The experience of these three countries shows that there are important lessons to be learnt by other low- and low-middle-income countries. An investment in developing a robust health system that can take care of its people not only during "normal" times, but also during outbreaks of disease and epidemics will pay huge dividends in the long run. An investment in a strong health system is well worth making.

An understanding of the cultural aspects of health and disease and the traditions associated with the business of living and dying is equally important. It has been particularly difficult to contain EVD (a highly contagious disease) when a majority of the population does not consider it to be infectious and engages in cultural practices such as the traditional burial rites, that result in the spread of the disease to the relatives and friends of the deceased. In such a situation, the engagement with the community needs to be particularly robust and inclusive of all stakeholders, especially community leaders and traditional healers so that ways of modifying cultural practices can be identified that are acceptable to the population.

A lack of resources for the diagnostic and supportive services required to manage EVD is another key issue. The absence of diagnostic kits means that the quarantine period is lengthened, as a result of which people's rights of movement are curtailed and their ability to earn is limited for periods much longer than if they had been tested during contact tracing and declared Ebola-free. This is an ethical issue. The lack of adequate protective gear as well as other simple articles, such as gloves and single-use syringes, is also a matter of ethical concern. No health system should ask its healthcare and ancillary workers to take unusually high risks (including that of contracting EVD) and governments and external aid agencies have a moral obligation to provide them with basic protective articles.

When resources for the usual activities of containment, such as contact tracing and quarantine are scarce, their utilisation can be optimised through coordination, trust and a robust communication strategy. Wide public discourse and engagement are needed to maintain trust and to minimise social disruption and economic loss in times of crisis. Governments have a moral obligation to foster such engagement. In addition, they have a moral obligation to coordinate internal resources and external aid in their

response to the outbreak. They must ensure that priority-setting mechanisms are in place to guide the optimal use of resources. For example, those who provide essential services such as healthcare providers and workers, ancillary staff and burial staff, should be preferentially equipped with the means to protect themselves from the disease so that they can continue to deliver the services and, in the spirit of reciprocity, should be preferentially offered vaccines and therapeutics when these become available.

Of course, the story might have been different if vaccines and therapeutics to counter EVD had been available. This brings us to the wider ethical concern of why promising therapeutic interventions or vaccines remained at a pre-clinical stage of development for years, even though Ebola outbreaks have been occurring regularly for the past 40 years. In the past, outbreaks started among rural communities that were hard to reach, and instances of nosocomial transmission remained geographically limited. The relatively simple public health measures of case-finding, isolation, social mobilisation and contact tracing sufficed to contain the outbreaks. The disease never became endemic and was forgotten after each episode, and never attracted enough attention from either the drug developers or, indeed, the global community, except for the fact that it was seen as a potential bioterrorism risk. The lack of curative and preventive interventions becomes all the more tragic when one considers that this highly contagious disease, with a high fatality rate, has now spread to urban areas, and the capacity to contain it through isolation and quarantine is no longer sufficient to stop the outbreak.

The good news is that there are several products in the pipeline. Some, such as ZMapp and other RNA-based molecules, have been tested for their safety and efficacy in non-human primates, and some have undergone limited testing for safety in humans. However, they are still way behind the normal regulatory cycle for registration. How ethical is it, then, to offer these products to patients when neither their safety, nor their efficacy in humans is known? This was the question put to the Ethics Panel convened by the World Health Organization on August 11, 2014. The panel, which included eminent ethicists and members of ethics committees from around the world, agreed that in the exceptional situation created by the Ebola outbreak, it is ethically permissible and acceptable to offer the experimental interventions that have shown promising results in the laboratory and in relevant animal models to patients and people at high risk of developing the disease, with the proviso that certain conditions are met (3). While the panel listed many conditions, the key conditions included that ethical criteria based on universal norms of research ethics, professional ethics, public health ethics and global health ethics must be respected. Further, appropriate scientifically useful data generated on the clinical and other relevant outcomes resulting from the use of these agents must be collected and shared transparently and rapidly with the scientific community. The decision of the panel was not an easy one, and it came after careful deliberations on the circumstances of the outbreak, and evaluation of the risks and benefits. The risks were on several levels. On the one hand, there was a risk that the affected population would consider itself deprived of potentially life-saving vaccines (the two test vaccines – Chimpanzee adenovirus serotype 3 (ChAd3) vaccine and Recombinant Vesicular Stomatitis Virus (rVSV) vaccine – have protected 100% of the animals later exposed to Ebola virus) and drugs. On the other hand, there was a risk that the affected population would feel that the scientific community was taking advantage of their vulnerability for commercial gain through the use of "experimental" drugs and vaccines or for testing counter-terrorism measures.

There was also the concern that the data generated by the use of the experimental drugs and vaccines would not be gathered and analysed, so that nothing would be learnt about their use in the future. The panel, therefore, recommended that, to the extent possible, these drugs/vaccines should be used in a research context, through well-designed studies – preferably using a randomised controlled or adaptive trial design – that could be implemented in the settings in which the drugs were being used, without jeopardising the normal clinical care that the patients otherwise received or putting the healthcare workers at risk. Thus, the imperative to collect data scientifically should not be at the expense of supportive clinical care.

At another level, there was the risk that the experimental vaccines and therapeutics may prove not to be efficacious in humans, or may have adverse effects that were not seen in the animal model. How could such uncertainties be conveyed to a desperate population that was looking for solutions – any solution? Even though the panel recommended that ethical principles such as informed consent be upheld, how valid would informed consent be in a climate of fear? How could healthcare providers convey uncertainties, especially when the person was sick and feared for her/his life? Further, uncertainties could endanger trust – something that was already compromised in the affected areas. In this context, although the panel did not make this explicit recommendation, the onus of carrying out a benefit–risk analysis and ensuring that the patients' interests were protected might best fall on an appropriately constituted ethics committee. Since most ethics committees, especially those in the developing countries, are essentially research ethics committees, they would have to take on this new role until enough clinical care ethics committees or national ethics committees were established. Support from experienced ethics groups from other countries with the relevant expertise may be required.

Transparency – in an atmosphere of uncertainty and lack of trust – was also emphasised by the Ethics Panel. Transparency would be vital to the successful deployment of drugs and vaccines that have not yet been proven to be safe and efficacious in human beings and is relevant at several levels, such as in decision-making, communication, data-gathering, and sharing of data with other scientists It is also important to be transparent about the uncertainties and to communicate those uncertainties in a "language" that is understood by the affected communities. The fact that communities in the affected countries rely on their

traditional concepts of disease and contagion and have greater trust in traditional healers should be kept in mind when planning communication and communication messages. Efforts to help the community should also take into account the people's values and concerns. All stakeholders must be involved in a truly participatory fashion, their concerns, doubts and fears must be heard, and solutions must be found together. Social mobilisation and engagement of the community are vital for the success of any public health programme and even more important in the context of an emergency.

One of the major ethical concerns in an emergency situation relates to the allocation of resources. The number of interventions available is invariably limited and during any epidemic, governments and policy-makers need to make hard decisions on how to prioritise their use when planning a response (1). WHO convened a consultation on September 4 and 5, 2014, on potential therapeutic and preventive interventions to counter Ebola, keeping issues of safety and efficacy in mind. In addition, there were discussions on innovative models for rapidly informative clinical trials, possible ways to ramp up the production of the most promising products, and innovative financing models, among other issues. The more than 150 participants, including participants from the affected countries in West Africa, had a wide range of expertise – from pharmaceutical research and the clinical demands of Ebola care, to expertise on ethical, legal and regulatory issues – which is reflected in their recommendations (4). This is another unprecedented aspect of this current epidemic. Never before has such a sense of solidarity and urgency been demonstrated. The consultation epitomised ethics in action. It also highlighted that it is essential for all countries to invest in global efforts to support research and development for new medical interventions for diseases that affect predominantly poor people and low-income countries, and in particular, for infectious diseases and epidemics, so that drugs and vaccines are available when and where needed.

What lessons, if any, can all countries draw from the current outbreak? This outbreak has demonstrated, like nothing before, that in today's world – which is characterised by interconnectedness, increasing globalisation and easier means of transportation, and in which pathogens no longer respect the borders of countries – no country can remain immune to the risk of pathogens, whatever their origin, whether it is the jungles of Africa or a metropolitan city of India. Countries should, therefore, make it a priority to strengthen their health systems to manage health and disease in normal times as well as in times of emergency. A major guiding principle for action should be solidarity, whether it is the solidarity of the rich with the poor, the urban with the rural, or the rich countries with the poor countries. This is also the basis for the International Health Regulations (5), which have been agreed to by most countries, and which bind all signatory countries – through legal agreements - to enforce travel restrictions and exit screening, as well as to share relevant data.

Finally, national preparedness plans for the control of epidemics raise a host of ethical questions that need local solutions, with inputs from all communities. There are some guiding principles and mechanisms that can be helpful in this context. While *ad-hoc* ethics panels and groups can be established to quickly put such mechanisms in place and advise local and national policy-makers, they are unlikely to have long-term legitimacy. They would lack the institutional memory and the consistency associated with an established national or sub-national ethics committee. There is a tradition in Europe, the Americas and more recently, in countries in other regions of the world of establishing national ethics/bioethics committees/commissions that are independent and have the responsibility to carry out an ethical analysis based on ethical principles, and to advise policy-makers on the pros and cons of particular actions that they are contemplating, so that the policies are ethically sound and robust. The governments of countries in which such committees do not exist may consider establishing similar independent bodies which would have the legitimacy to support policy-makers and health administrators in developing ethically sound policies and healthcare plans. The assurance that health policies and plans are supported by robust ethical frameworks will go a long way in engendering trust among the public, especially during public health emergencies such as epidemics. Trust, in turn, will promote compliance with and acceptance of the public health policies and plans.

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References

1. World Health Organization. Research ethics in international epidemic response. WHO technical consultation [Meeting Report] [Internet]. Geneva, Switzerland: WHO; 2009 Jun 10–11[cited 2014 Sep 13]. Available from: www.who.int/ethics/gip_research_ethics_.pdf
2. UN Commission on Human Rights. United Nations Economic and Social Council. The Siracusa Principles on the Limitation and Derogation provisions in the International Covenant on Civil and Political Rights. UN Doc. E/CN.4/1985/4. Annex – 1985 [Internet]. Geneva: UNESC;1984 Sep 28 [cited 2014 Sep 13]. Available from: http://www.refworld.org/docid/4672bc122.html (accessed on 10 September 2014)
3. World Health Organization. Ethical considerations for use of unregistered interventions for Ebola virus disease [Report of an advisory panel to WHO] [Internet]. Geneva: WHO; 2014 [cited 2014 Sep 13]. Available from: http://www.who.int/csr/resources/publications/ebola/ethical-considerations/en/ (accessed on 10 September 2014)
4. World Health Organization. Statement on the WHO Consultation on potential Ebola therapies and vaccines [Internet]. Geneva: WHO; 2014 Sep 5 [cited 2014 Sep 13]. Available from: http://www.who.int/mediacentre/news/statements/2014/ebola-therapies-consultation/en/
5. World Health Organization. Alert, response, and capacity building under the International Health Regulations (IHR) [Internet]. Date unknown [cited 2014 Sep 13]. Available from: http://www.who.int/ihr/about/en/