Op-Ed

Ethical Allocation of Drugs and Vaccines in the West African Ebola Epidemic

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THE WEST AFRICAN EPIDEMIC OF EBOLA VIRUS DISEASE (EVD) is spiraling out of control, with an exponential increase in cases, projected to infect 10,000 people per week by December.¹ Despite the rising death toll and regional spread, a major international response did not occur until 2 US aid workers and a Spanish priest were treated with the investigational drug ZMapp, a monoclonal antibody developed by Mapp Biopharmaceutical.

Vaccines and drugs that have never been tested in humans, and are in scarce supply, could never have contained this outbreak. Nonetheless, what if good evidence emerged demonstrating their safety and efficacy? What would be an ethical method of allocating scarce beneficial resources? The apparent preference given to foreign aid workers over West Africans provoked a firestorm. Before discussing the ethical allocation of scarce drugs, we should ask a more fundamental question: Why did it take nearly 40 years after the first outbreak in 1976 to launch clinical trials?

After more than 20 outbreaks of EVD and 5 months after its international spread, governments and industry have begun to ramp up research, with expedited regulatory processes and clinical protocols. On September 5, 2014, a World Health Organization (WHO) expert committee reviewed, and vowed to accelerate development of, promising drug and vaccine candidates, including blood transfusions from recovered Ebola patients and antibody treatments.² Days earlier, the National Institutes of Health (NIH) launched vaccine safety trials, and preliminary clinical trial results for a GlaxoSmithKline vaccine are expected by November. The US Department of Health and Human Services promised Mapp Biopharmaceutical up to \$42.3 million to develop ZMapp.

Although these therapeutic agents offer some hope, with Ebola treatment centers currently overwhelmed, the global community must assist countries in building domestic health systems. Countries will require

more human resources and technical assistance with, for example, transfusing whole blood, plasma, or serums derived from recovered Ebola patients. At the same time, the global community must help transport and deliver therapeutics to local facilities, while rigorously maintaining a cold-storage supply chain.

Many factors have dissuaded investment in EVD countermeasures. Ebola outbreaks are sporadic, with an unpredictable market for interventions. These outbreaks typically occur in countries ranked lowest in economic development, which cannot afford the high price of patented medications. Rich countries have had other international funding priorities that better reflect the global burden of disease (eg, AIDS, tuberculosis, and malaria). But EVD has epidemic potential, and once it takes hold in highly congested, impoverished, capital cities, it can spread exponentially. The West African epidemic has provoked a public health crisis and a security threat, further weakening economically and politically fragile states. The UN Security Council should act boldly to ameliorate the crisis, with Secretary-General Ban Ki-moon framing the mobilization as “an international rescue call.”³

Compassionate Use of Investigational Drugs and Vaccines

Although a WHO ethics panel defended the compassionate use of investigational drugs with informed consent,⁴ a rigorous, ongoing evaluation of safety and effectiveness is crucial. It is widely believed that ZMapp, which had been tested only in primates, cured 2 US aid workers treated at Emory University Hospital. (The Spanish priest died after receiving ZMapp.) There is no evidence the drug was effective, and if it was, anecdotal evidence cannot substitute for scientific evaluation. Half of those infected with the current Ebola strain recover, and intensive nursing care and hydration likely sped the aid workers’ recovery.

Given the up to 50% recovery rate, it is unclear whether unproven drugs may do more harm than good. Although animal models may justify compassionate use, such use should be done in conjunction with rigorous evaluation. Ongoing research may demonstrate harm (or good), guiding continued treatment. The same may be true of repurposing already approved drugs. Although an approved drug may be safe and

effective for one disease, it may not offer equivalent benefits for other diseases. Safety monitoring boards should oversee all unproven vaccines and drugs administered to both Ebola patients and healthy volunteers.

Even though there may have been reason to give preference to foreign aid workers, the optics of giving scarce medicines to relatively well-off Caucasians proved damaging. African doctors and nurses work under extreme peril: more than 230 health workers have lost their lives to EVD,⁵ leaving countries' human resources in tatters. The decision to give the drug to US aid workers was made behind closed doors, arguably violating Liberian law by administering an unapproved drug without the health ministry's approval. A decision to use experimental drugs on domestic workers might equally have provoked controversy, given the checkered history of Western pharmaceutical research in Africa. But the affected governments and communities need to be involved in these decisions.

Unproven vaccines pose difficult ethical dilemmas because they are administered to healthy individuals who receive no benefit if they avoid EVD exposure. In these circumstances, it becomes harder to justify experimental use on impoverished and vulnerable populations; arguably, safety testing should be done on higher-income volunteers before use in local populations.

Just Allocation of Proven Drugs and Vaccines

If scarce treatments offer benefits to patients, who should have priority access? Implementing the following ethical criteria and processes would help ensure a more equitable distribution of benefits and burdens.

Domestic Health Workers

A case can be made in favor of domestic health workers who place themselves at peril, often caring for the sick without personal protective equipment and safe infection control practices. Poor states need these health workers to care for not only Ebola patients but also patients facing myriad health hazards, such as malaria, noncommunicable diseases, and childbirth. Although foreign health workers also serve in hazardous conditions, they are more likely to be trained and to possess

personal protective equipment. If they do contract EVD, their chances of survival after medical evacuation are greater than those for local workers.

Some argue that it is reasonable to give preference to foreign workers because their governments support the development of most medical interventions. Yet privileging a rich country's citizens working abroad as a quid pro quo for drug investment lacks ethical force. Using reasoning of this sort, it would be possible to discriminate in favor of citizens of rich countries in most realms. Such reasoning would not only alienate poorer countries, but also would exacerbate large health disparities based on income.

Public Health

Using drugs or vaccines as a public health measure would be ethically justified because it could amplify the benefits to a wider population. Thus, administering a drug or vaccine in a geographic hot spot of hypertransmission could curb the disease's spread within the congregate area while making travel to nonendemic areas safer.

Need

Those who have the greatest need for assistance and can least withstand the devastating health and economic effects of serious illness also deserve priority. Candidates for priority could include children, the elderly, the mentally or physically disabled, and people living in poverty.

Good Governance

Any ethical standards chosen will have to be applied in ways that are, and are seen to be, fair. This requires engagement with those most affected, including governments and local communities. Civic engagement requires genuine listening and partnerships with a say in determining the final outcome. Good governance requires transparency, monitoring, evaluation, and accountability. What rankles those living in Africa is not only the inequity of the rich not sharing public goods. It is the indignity of decisions made unilaterally without robust participation among equal partners.

References

1. Sengupta S. New Ebola cases may soon reach 10,000 a week, officials predict. *New York Times*. October 15, 2014. <http://www.nytimes.com/2014/10/15/world/africa/ebola-epidemic-who-west-africa.html>. Accessed October 20, 2014.
2. World Health Organization. Statement on the WHO consultation on potential Ebola therapies and vaccines. <http://www.who.int/mediacentre/news/statements/2014/ebola-therapies-consultation/en/>. Published September 5, 2014. Accessed September 7, 2014.
3. Fink S, Gladstone R. Two vaccines to protect against Ebola could be available within weeks. *New York Times*. September 5, 2014. http://www.nytimes.com/2014/09/06/world/africa/ebola-vaccine-could-be-ready-by-november-who-says.html?_r=0. Accessed September 7, 2014.
4. World Health Organization. Ethical considerations for use of unregistered interventions for Ebola virus disease (EVD). <http://www.who.int/mediacentre/news/statements/2014/ebola-ethical-review-summary/en/>. Published August 12, 2014. Accessed September 7, 2014.
5. Giahayue JH. Liberia health workers' strike on Monday could hurt Ebola efforts. Reuters. October 12, 2014. <http://www.reuters.com/article/2014/10/12/us-health-ebola-liberia-idUSKCN0I10SX20141012>. Accessed October 13, 2014.

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