Ethical Implications of Experimental Ebola Treatment

Alexander S Chen

Background

The current outbreak of the Ebola virus in West Africa has resulted in over 6,200 infections and 2,909 deaths[i], making it the most severe and largest ever documented outbreak[ii]. Compounding this problem is the fact that the outbreak has primarily taken place in least developed countries (LDC)[iii]. These two facts taken together make disease treatment an extremely complex issue, especially when considering the case of experimental drugs.

The severe nature of the outbreak, as well as the difficulty inherent in experimental drug distribution, raises three important concerns: how to ethically distribute a scarce drug supply, the criteria with which recipients should be selected, and the parties that should bear the cost of such treatments.

Drug Distribution within a Parallel Track Framework

To satisfactorily address the ethical implications of experimental drug distribution, it is instructive to consider historical examples.

In the early years of the HIV/AIDS epidemic, frustration over the length of time required to approve novel antiretroviral treatments resulted in the FDA announcing revised regulations to cut the time for drug approval[iv]. Not only was this a precedent for using experimental drugs to treat life-threatening diseases, but it also led to development of the parallel track for clinical trials[v]. In essence, the parallel track concept is a method of clinical testing that includes the standard, highly controlled admission criteria for clinical trials of an experimental drug along with an additional track where the drug is made available to those who do not meet the clinical trial criteria, but who are still in dire need of any potentially effective treatments[vi]. Consequently, this FDA supported[vii] method provides a valuable tool with which to ethically distribute experimental Ebola treatments.

Using the parallel track, healthcare workers would provide experimental drugs to two populations. One population is optimized to contribute beneficial clinical data, e.g. is provided appropriate care, experimental and placebo treatments, monitored for side effects, etc.[viii] The other population would be optimized for maximum disease prevention, e.g. the population consists of serious patients who would not be admitted to a clinical trial due to severe Ebola symptoms possibly being confused with drug side-effects[ix]. And although the WHO suggests that experimental drugs only be used in clinical trials[x], one of the values of the parallel track is its flexibility: the proportion of patients in either the “clinical” or “compassionate” track can be changed depending on the circumstance. If little is known about whether or not a drug has detrimental side effects, the parallel track might only include a clinical track until more data is gathered. If evidence is gathered suggesting experimental efficacy, the parallel track would be altered to allow a larger number of patients into the compassionate track.

Ethical Considerations of Population Selection

Within this general parallel track framework, we must further determine how to select the

patient populations that will become recipients of treatment.

In this regard, there are two branches of thought – to select a random population from which there would be the most benefit in terms of clinical data production[xi], or to select a population who, if saved by the treatment, would provide the highest instrumental value[xii], i.e. prioritizing healthcare workers[xiii]. We can inform our discussion by examining motives behind both thought processes.

In terms of prioritizing experimental data, the motive would be that risks and benefits of experimental drugs are largely unknown – it would be morally irresponsible to expand drug usage and potentially cause more harm than good[xiv]. Alternatively, the motive behind instrumental value allocation would be to prioritize certain patients such as healthcare workers in order to ultimately provide benefit to other patients as well[xv]. For both cases, the goal is to maximize the number of lives saved – one by minimizing detrimental side effects, the other by maximizing the lives that could be further benefited once a treated patient recovers[xvi].

In other words, the two schools of thought both attempt to maximize number of lives saved. And if we agree that this is a worthwhile criterion to base our population selection upon, the nature of the current Ebola outbreak suggests we prioritize healthcare workers by instrumental value allocation for the following reasons.

Ending the Ebola epidemic is largely a matter of logistics. In LDC's such as Liberia, there is a lack of healthcare workers – fewer than 250 doctors for a population of over four million[xvii]. And despite an influx of applicants, including foreign health workers[xviii], every single healthcare worker in the country will be required to treat patients and provide training. Furthermore, because the epidemic can't be contained until 70% of the sick are isolated in treatment centers (which are run by healthcare workers)[xix] we find that the workers are essential to ending the epidemic itself.

Although it would be ideal to treat both healthcare workers and patients, the scarcity of these experimental drugs, even with current efforts to increase production, suggests that there would be little impact if provided to a general population of several thousand infected individuals[xx]. But within a physician population of less than 300, there could be a much larger impact that would, in the long run, also save lives in the general population.

Therefore, by prioritizing healthcare workers for selection into a parallel track framework, we achieve three goals: we maximize clinical data production, minimize the impact of disease among our affected population, and maximize an instrumental value essential to ending the epidemic itself.

Burden of Cost

When considering the costs associated with potential Ebola treatments, it would be unethical to place the financial burden of drugs still in trial phase upon subjects. Doing so would favor the lives of financially privileged individuals over the general population[xxi].

So where would the money come from? Let us fist turn to how the global community has responded to the Ebola outbreak as a whole. The WHO predicts the epidemic to cost $570 million over the next 6 months[xxii]. Such a figure is a quarter of Liberia's GDP[xxiii], and it would be unrealistic to expect similar LDC's to shoulder the costs alone. Fortunately, the international community has realized that this is not a West African epidemic, but a potentially global one. Consequently, containment and eradication

is a responsibility of NGO's and governments around the world – a realization reflected in the $22 million of aid from Japan and the UK[xxiv], $50 million pledged by the Gates Foundation[xxv], and the $750 million budgeted by the US military[xxvi].

In the case of experimental treatments, we must take a similar approach. The governments and health systems of afflicted countries are already stressed to their breaking points[xxvii]; therefore, the costs of drug distribution would have to fall upon the international community, which has a shared interest in seeing the epidemic end as soon as possible.

And there are indications that this shared-burden approach is already being implemented. Drugs are planned to be provided at cost by manufacturers to patients[xxviii], various international NGO's are already paying for experimental treatments[xxix], and the US Government has plans to work with private pharmaceutical companies to increase drug productions[xxx].

It is clear that the international community is recognizing the threat posed by the Ebola epidemic. And while experimental drugs are only a small part of the eradication equation, it is important to consider the ethical implications in order to better understand how we might tackle the epidemic – whether it is now, or a crisis we must face in the future.

References:

[i] WHO. Experimental therapies: growing interest in the use of whole blood or plasma from recovered Ebola patients (convalescent therapies). http://www.who.int/mediacentre/news/ebola/26-september-2014/en/ (accessed Oct. 17, 2014). http://www.afro.who.int/en/clusters-a-programmes/dpc/epidemic-a-pandemic-alert-and-response/outbreak-news/4256-ebola-virus-disease-west-africa-15-august-2014.html (accessed Oct 15, 2014).

[ii] Cumming-Bruce, N. W.H.O. Chief Calls Ebola Outbreak a 'Crisis for International Peace'. http://www.nytimes.com/2014/10/14/world/africa/ebola-virus-outbreak.html (accessed Oct 16, 2014).

[iii] UNCTAD. UN list of Least Developed Countries. http://unctad.org/en/pages/aldc/Least%20Developed%20Countries/UN-list-of-Least-Developed-Countries.aspx (accessed Oct 15, 2014).

[iv] Food and Drug Administration (FDA) (1988) 'Making drugs available for life-threatening diseases'. October 19th. http://www.avert.org/history-hiv-aids-us.htm#footnote44_6ozk8ne (accessed Oct. 17, 2014).

[v] AIDSinfo. First AIDS Drug Tested Under Parallel Track Policy; other d4T related press releases. (1992). http://aidsinfo.nih.gov/news/93/first-aids-drug-tested-under-parallel-track-policy;-other-d4t-related-press-releases (accessed Oct 17, 2014).

[vi] FDA US Food and Drugs Administration. Drug Development and Review Definitions. http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm176522.htm (accessed Oct. 17, 2014).

[vii] Fauci AS (2012) Preface: evolving ethical issues over the course of the AIDS pandemic. Public Health Reviews. 2012;34.

[viii] Rid A, Ezekial E. (2014). Ethical considerations of experimental interventions in the Ebola outbreak. The Lancet.

[ix] Rid A, Ezekial E. (2014). Ethical considerations of experimental interventions in the Ebola outbreak. The Lancet.

[x] WHO. Ethical considerations for use of unregistered interventions for Ebola virus disease (EVD). (2014) http://www.who.int/mediacentre/news/statements/2014/ebola-ethical-review-summary/en/ (accessed Oct. 17, 2014)

[xi] Rid A, Ezekial E. (2014). Ethical considerations of experimental interventions in the Ebola outbreak. The Lancet.

[xii] Arie S. Ebola: an opportunity for a clinical trial? BMJ 2014; 349: g4997.

[xiii] Pollack A. Ebola drug could save a few lives. But whose? New York, NY: The New York Times, Aug 8, 2014. http://www.nytimes. com/2014/08/09/health/in-ebola-outbreak-who-should-get- experimental-drug.html (accessed Oct 18, 2014).

[xiv] Rid A, Ezekial E. (2014). Ethical considerations of experimental interventions in the Ebola outbreak. The Lancet.

[xv] Persad G, Wertheimer A, Emmanuel E. (2009). Principles for allocation of scarce medical interventions. The Lancet.

[xvi] Persad G, Wertheimer A, Emmanuel E. (2009). Principles for allocation of scarce medical interventions. The Lancet.

[xvii] Fink S (2014). With Aid Doctors Gone, Ebola Fight Grows Harder. http://www.nytimes.com/2014/08/17/world/africa/with-aid-doctors-gone-ebola-fight-grows-harder.html (accessed Oct. 17, 2014). NY Times

[xviii] Mckay B. (2014). Lack of Qualified Staff Hurts Ebola Fight in Africa. http://online.wsj.com/articles/lack-of-qualified-staff-hurts-ebola-fight-in-africa-1412293011 (accessed Oct. 17, 2014). The Wall Street Journal.

[xix] Mckay B. (2014). Lack of Qualified Staff Hurts Ebola Fight in Africa. http://online.wsj.com/articles/lack-of-qualified-staff-hurts-ebola-fight-in-africa-1412293011 (accessed Oct. 17, 2014). The Wall Street Journal.

[xx] Loftus P (2014). Ebola Drug Race Ramps Up in Earnest. The Wall Street General.

[xxi] Rid A, Ezekial E. (2014). Ethical considerations of experimental interventions in the Ebola outbreak. The Lancet.

[xxii] Smeltz A. (2014). Taming Ebola virus threatens to cost $1 billion, cripple medical systems. http://triblive.com/home/photos/6933146-74/ebola-health-africa#axzz3GY78l4lO (accessed Oct. 18, 2018)

[xxiii] The World Bank. GDP in current US $. http://data.worldbank.org/indicator/NY.GDP.MKTP.CD (accessed Oct. 18, 2014).

[xxiv] Smeltz A. (2014). Taming Ebola virus threatens to cost $1 billion, cripple medical systems. http://triblive.com/home/photos/6933146-74/ebola-health-africa#axzz3GY78l4lO (accessed Oct. 18, 2018)

[xxv] Bill and Melinda Gates Foundation. (2014). Bill & Melinda Gates Foundation Commits $50 Million to Support Emergency Response to Ebola. http://www.gatesfoundation.org/Media-Center/Press-Releases/2014/09/Gates-Foundation-Commits-$50%20Million-to-Support-Emergency-Response-to-Ebola (accessed Oct. 18, 2014).

[xxvi] Schwartz F. (2014). U.S. Military Effort to Combat Ebola in Africa to Enter New Phase. http://online.wsj.com/articles/u-s-military-effort-to-combat-ebola-in-africa-to-enter-new-phase-1413406781 (accessed Oct. 18, 2014). The Wall Street Journal.

[xxvii] Martinze A, Bax P, Giokos E. (2014) Guinea Says Ebola Pushing Affected Economies to Breaking Point. http://www.bloomberg.com/news/2014-10-14/guinea-says-ebola-pushing-affected-economies-to-breaking-point.html

[xxviii] Ashton J. (2014). Ebola virus: What price for a miracle cure? http://www.independent.co.uk/life-style/health-and-families/health-news/ebola-virus-what-price-for-a-miracle-cure-9785917.html (accessed Oct. 18, 2014).The Independent.

[xxix] Akpan N. (2014). Ebola Evacuees: Who Are They, Where'd They Go, How'd They Fare? http://www.npr.org/blogs/goatsandsoda/2014/10/15/353268622/ebola-evacuees-who-are-they-whered-they-go-howd-they-fare (accessed Oct. 18, 2014). NPR.

[xxx] The Guardian. (2014). US labs asked for proposals to produce experimental Ebola drug ZMapp. http://www.theguardian.com/world/2014/oct/17/us-labs-proposals-produce-ebola-drug-zmapp (accessed Oct. 18, 2014).