

# Reconsidering the Ethical Permissibility of the use of Unregistered Interventions against Ebola Virus Disease



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# Background – Ebola Virus Disease



- ☞ EVD first appeared in remote villages in Central Africa (Zaire) in 1976 – 318 cases, 280 deaths. (88% mortality)
- ☞ 1995: Outbreak in Congo – 315 cases, 250 deaths. (79% mortality)
- ☞ 2000-2001: Outbreak in Uganda – 425 cases, 224 deaths. (53% mortality)
- ☞ 2007: Outbreak in Congo – 264 cases, 187 deaths. (71% mortality)
- ☞ “Prior to 2014, Ebola was considered a rare disease. The only control tools available date back to the Middle Ages: early detection, isolation, infection control, and quarantine.” [1]

# Current State



- ☞ The current outbreak was believed to have started in March 2014 (but was later identified by retrospective study as beginning on 26<sup>th</sup> December 2013), is the largest and most complex since EVD was discovered. [1]
- ☞ Outbreak mainly contained to West African countries of Guinea, Liberia, and Sierra Leone.
- ☞ As of April 2015, the average case fatality rate was approximately 50%.
- ☞ There are currently no licensed Ebola vaccines or curative treatments, but two potential vaccine candidates are undergoing evaluation. [2]
- ☞ Current standard of care is “Supportive Care,” i.e. hydration, balancing electrolytes, treating infections as they occur, etc.

# Timeline



- ☞ 26<sup>th</sup> December, 2013 – Retrospective-study identified outbreak start date in Guinea. [1]
- ☞ 23<sup>rd</sup> March 2014 – WHO's African Regional office reports EVD outbreak in Guinea. By 29<sup>th</sup> March it had spread to Liberia.
- ☞ 1<sup>st</sup> April – WHO supplies arrive in Guinea to support outbreak.
- ☞ 25<sup>th</sup> May – Ministry of Health in Sierra Leone confirms first case of EVD.
- ☞ 6<sup>th</sup> August - The first meeting of the Emergency Committee convened by the Director-General under the International Health Regulations regarding the Ebola virus disease outbreak in West Africa was held by teleconference.
- ☞ 8<sup>th</sup> August – WHO declares EVD a public health emergency of international concern.

# Timeline



- ☞ 11<sup>th</sup> August – WHO convenes expert ethics panel to discuss the ethical appropriateness of providing unregistered interventions to infected populations as one of 5 questions; declares an ethical imperative to do so.
- ☞ 29<sup>th</sup> August – Total probable, confirmed and suspected cases of EVD in current outbreak: 3052, with 1546 deaths.
- ☞ 31<sup>st</sup> December – Total probable, confirmed and suspected cases of EVD in current outbreak: 20,206 with 7905 deaths.
  - ☞ An increase of 17,154 new cases and 6359 more deaths in just 4 months.
- ☞ 19<sup>th</sup> May, 2015 – Total Cases in Guinea, Sierra Leone, and Liberia: 26,933, with 11,120 deaths.[7-9]

# Response to Current Crisis: WHO Ethics Expert Panel



- ❧ 11<sup>th</sup> August – WHO convenes expert ethics panel to discuss the ethical appropriateness of providing unregistered interventions to infected populations.
- ❧ 12 delegates were invited to advise WHO Director-General during 3 hour meeting held by teleconference.
- ❧ Position is inconsistent – Panel claims it would be ethically appropriate in some readings, but ethically imperative in others, to pursue such interventions.

# Ethics Expert Panel



- ☞ “[The panel members] concluded unanimously that it would be acceptable on both ethical and evidential grounds to use as potential treatments or for prevention unregistered interventions...”

Versus:

- ☞ “The panel strongly recommended that these investigational drugs...be urgently tested in humans...”

Different still:

- ☞ “...the panel agreed unanimously that, in the exceptional situation of the current outbreak, there is an ethical imperative to offer the available experimental interventions...” [3]
- ☞ Addressing the issue “on the ground” was acted on based on an imperative and not simply the acceptability of a practice which gave groups (Governments, Pharmaceutical companies, etc...) a carte blanche to act outside of accepted practice, standards and processes.

# Response to Current Crisis: Ethics Expert Panel



Panel presents that the ethical acceptability / obligatoriness is dependent on numerous criteria:

1. Transparency about all aspects of care
2. Fair distribution
3. Promotion of cosmopolitan solidarity
4. Informed Consent
5. Freedom of Choice
6. Confidentiality
7. Respect for persons
8. Preservation of dignity
9. Involvement of the community

# The Problem



- ❧ “Before the outbreak, there was no commercial incentive to develop treatments or vaccines for filovirus diseases, and the lack of any such intervention has left public health authorities and clinicians in the affected countries with no specific prevention or treatment options, despite the fact that outbreaks have been occurring for nearly four decades.” [3]
- ❧ Neither the World Health Organization, governments, nor pharmaceutical companies prioritized EVD over the last 40 years.
- ❧ The current outbreak was not declared as a ‘Global Health Emergency’ by the WHO until 8<sup>th</sup> August, 2014 – 4 ½ months into the outbreak (initial start date).
- ❧ The WHO Africa Office, which oversees the region, initially did not welcome assistance by the U.S. CDC in response to the outbreak. [4]
- ❧ The WHO pins blame for ‘botching response to Ebola outbreak’ on incompetent, politically motivated appointments in African Office. [5, 6]

# The Problem



∞ *Imperative*: noun [...]

2: something that is imperative: as

*a*: command, order

*b*: rule, guide

*c*: an obligatory act or duty [10]

∞ Is it an imperative *a priori*? Or only if the aforementioned criteria can be met? Must the WHO be able to confirm that the criteria can be met in order to declare the imperative dependent upon them? Must there be a verification mechanism in place for the imperative to exist?

# The Problem



- WHO Assistant Director-General of Health Systems claims that WHO role in the review of research (and presumably treatments), is that of facilitator and convener only. However, the *Ebola Response Roadmap* presents the planned WHO activities seemingly as being outside of this scope, for example:
  - Guidance on safety, efficacy, quality, regulatory standards and ethical use of therapies in the R&D pipeline (As governed by the Declaration of Helsinki?).
  - Coordination and facilitation of the ethical deployment of existing experimental treatments and vaccines. [11]

# Questions Arising



- ⌘ Might an imperative be justified even though the WHO claimed that “Ethical criteria based on traditional research ethics [...] should guide the use of such interventions”?
  - ⌘ Evidence-based medicine.
  - ⌘ Established human research processes.
  - ⌘ Can provided criteria actually be met?
  
- ⌘ Declaration of Helsinki:

35. In the treatment of a patient, where proven interventions do not exist or have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician’s judgment it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, this intervention should be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information should be recorded and, where appropriate, made publicly available. [12]
  
- ⌘ Should/does the current EVD outbreak qualify as meeting this provision?

# For Consideration



- ⌘ What does the future of public health crisis management look like for emerging diseases, especially communicable diseases, given the WHO response *vis-a-vis* the most recent EVD outbreak?
- ⌘ Is the process, as laid out in the declaration of Helsinki for human subject research, still relevant?
- ⌘ Will we simply revert to the last clause of the Declaration of Helsinki in future cases?
- ⌘ Have we set a precedent for public health crisis management for emerging diseases?
- ⌘ How is it being justified that this is an exception or exceptional case, as distinct from other cases? E.g. AIDS, SARS, etc...



Questions?

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