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Ebola Vaccine Trials: The Unethicality of Current Approaches

In 2014, the World Health Organization declared a Public Health Emergency of International Concern with regard to the Ebolavirus outbreak in West Africa. The world was shaken by the news, and various international health committees immediately took action and traveled to affected nations in an effort to prevent further disease transmission and control the outbreak. The World Health Organization (WHO), the US Center for Disease Control (CDC), Doctors Without Borders (MSF), and other large international health agencies were involved in providing treatments and trying to prevent the virus from spreading further. After almost 11,500 deaths and just over two years of working vigorously to control the disease, the WHO finally lifted the Public Health Emergency of International Concern status in March of 2016. Since this time, there has been very little news about the disease, and the virus seems to have mostly left American’s minds. However, a very recent outbreak in the Democratic Republic of the Congo (DRC) in August of 2018 is beginning to create international concern once again (2018 Eastern Democratic Republic of the Congo). As of November 2, 2018, there were almost three hundred confirmed Ebola cases in the DRC with 147 confirmed deaths from the disease (Ebola situation reports: Democratic Republic of the Congo). The CDC and Democratic Republic of the Congo’s Ministry of Health are collaborating, along with other international partners, to address and respond to this new outbreak (2018 Eastern Democratic Republic of the Congo). International medical establishments were criticized four years ago for their inadequate response to the 2014-2016 Ebola crisis. With criticism from previous crises and the current situation looming over the DRC, such organizations are taking steps to improve their approach to prevention and treatment of the Ebolavirus. According to physicians, clinical researchers, and public health officials, the implementation of a vaccine seems to be one of the most promising approaches.

In 2015, the World Health Organization, Guinea’s Ministry of Health, Doctors Without Borders, and the Norwegian Institute of Public Health began collaborating to develop a vaccine and implement clinical trials against the deadly Ebolavirus. A ring-vaccination strategy was used: the vaccine, specifically the rVSV vaccine, was given to high-risk individuals to prevent the spread of the virus before an outbreak could occur. According to Henao-Restrepo et al., a group of researchers involved in the 2015 Ebola ring-vaccination trials, high-risk individuals were those who “within the [previous] 21 days, [had] lived in the same household, were visited by the index case after the onset of symptoms, or were in close physical contact with [an Ebola] patient's body or body fluids, linen, or clothes” (859). These individuals were then randomly assigned to two distinct groups: an immediate group or a delayed group (Henao-Restrepo et al. 858). Individuals in the immediate group were vaccinated immediately after contact with a newly-diagnosed case of Ebola. Individuals in the delayed group received the vaccine twenty-one days after contact. Rid and Miller, other physicians involved in the vaccine trials, explained that the “[twenty-one day] delay reflected Ebola’s incubation period and created a control for the intervention clusters receiving immediate vaccination” (432). Trial results suggested that the rVSV vaccine was potentially highly effective, but more trials need to be completed to ensure the efficacy of the Ebola vaccine.

While the development of a vaccine is essential to prevent future Ebola outbreaks, the current clinical trial methods and strategies violate the Belmont Report’s ethical guidelines, ultimately making the vaccine trials unethical. The Belmont Report was designed for the protection of human subjects in biomedical research, and it provides researchers with ethical guidelines to protect research participants. When applied to the rVSV Ebola vaccine trials, one can see the researchers took an ethnocentric approach to fulfilling the Belmont principles. Rather than considering the cultural values of the African population, the researchers took a Westernized approach to perform the trials, making them unethical to implement in the African communities. It is necessary to examine and analyze the current strategy to figure out which aspects are unethical. After analyzing the unethical components of the trials, it will be possible to determine the plausibility of implementing an alternative approach.

The unethical nature of the vaccine implementation strategy is seen in various aspects of the trials. The ring vaccination strategy chose to specifically vaccinate public health workers, which is a clear violation of the principle of justice. The researchers further infringed upon the Belmont standard of justice because they employed the strategy in such a way that it may have intensified social inequalities within the African communities. The Belmont Report’s principle of beneficence was also violated because the “control” group was denied potential vaccine benefits during the twenty-one-day delay period. Furthermore, the requirement for a cold chain system to maintain vaccine potency promoted reliance on Western aid which disobeyed the Belmont Report’s principle of autonomy. Finally, research shows that members of the African communities in which the trials were being performed had a lack of knowledge about the virus itself, as well as the vaccine. Because of this, the principle of autonomy was at risk of being violated.

**Ebolavirus Composition and Vaccine Development**

It is useful to understand the specific scientific basis of the Ebolavirus to determine whether a vaccine is in fact a good approach to prevent future outbreaks. Ebolavirus is part of the *Filoviridae* family of viruses, which commonly causes disease in humans. The virus is composed of an RNA core and an outer envelope coated in glycoprotein surface projections. These surface projections allow the pathogen to incorporate itself into the cells of its host. In doing so, the virus can essentially hide within the body of its target and evade the immune system. The presence of such surface projections is a defining characteristic of Ebolavirus and, according to Sridhar, the central role of the surface projections “makes it a key antigenic target for development of Ebola vaccines” (126).

 Because the unique glycoprotein projection component of the virus makes it a good candidate for vaccine development, scientists worldwide have devoted time and energy towards developing an effective vaccine. Since 2014, the World Health Organization has been collaborating with other international health agencies, like the CDC, to develop clinical trials in African nations to test the feasibility and effectiveness of administering an Ebolavirus vaccine (CDC 2016). Various different approaches have been taken, and according to Sridhar, “since June 2014, […] an unprecedented 7 different vaccines (ChAd3, MVA-BNFilo, Ad26, MVA-EBOZ, rAd5, rVSV and a VLP-vaccine) have been expedited into clinical development” (134). Specifically, researchers have performed phase III clinical trials which show high efficacy and effectiveness for the rVSV vaccine. Essentially, the rVSV vaccine takes advantage of the unique surface projections present on the Ebolavirus. The vaccine virus contains similar surface projections, which can enter host cells instead of the pathogen, thus weakening the effect of Ebolavirus. The WHO, along with other health agencies, are taking advantage of the distinctive surface characteristics of the Ebolavirus to develop a vaccine and implement trials to determine the efficacy of such vaccines. However, despite the promise of the rVSV vaccine, there are still extreme ethical implications with the current ring-vaccination trial methods.

**Violation of the Belmont Report’s Principle of Justice**

The ring-vaccination strategy used to test the rVSV vaccine prioritized vaccination of healthcare personnel over other individuals in contact with the Ebolavirus, violating the principle of justice. The principle of justice, as outlined in the 1979 Belmont Report, asserts that there must be an even distribution of benefits and harms for research efforts to be considered ethical (The National Commission). With the ring-vaccination strategy, healthcare professionals in direct contact with Ebola patients were prioritized in receiving the vaccine (Folayan et al. 2). In the African nations, in which these vaccine trials have been implemented, all healthcare professionals are at an incredibly high risk for contracting the disease because they are in direct contact with Ebola-infected patients. While many researchers, such as Folayan et al. who studied the ethics of the rVSV trials, argue that healthcare personnel *should* be the first ones to receive the vaccine because they are providing care and benefits to many patients, prioritizing these individuals blatantly violates the principle of justice as it does not provide an *even* distribution of benefits. This exemplifies an ethnocentric approach to satisfying the Belmont Report’s standards because the researchers did not consider the fact in the African population, other people may have been at an equally high risk of contracting the virus. There are many other individuals involved in the treatment and care of Ebola patients, aside from strictly healthcare providers. For example, there are individuals who provide care to Ebola patients in non-clinical settings (such as care homes) or those who perform burials for Ebola patients, who also have direct contact with the Ebolavirus. Withholding the vaccine from these individuals and instead solely offering the vaccine to healthcare providers violates the principle of justice because it does not assure a truly even distribution of research benefits to everyone being impacted by the disease. Instead, the trials should be implemented in such a way that ensures equal access to the vaccine for all professionals working in direct contact with Ebola patients.

The ring-vaccination strategy may have exacerbated pre-existing social inequalities within the African communities in which the trials were being performed, which further violates the principle of justice. Oftentimes, the healthcare personnel providing treatment and care to patients in Ebola clinics are from developed nations, like the United States, and are sponsored by powerful international agencies, such as the WHO. On the other hand, the healthcare personnel working in non-clinical settings or managing the corpses during burial services tend to be locals from the African communities in which the trials were being performed. These differences in social and economic standing establishes a social hierarchy between the different types of healthcare personnel within Ebola-affected communities. Although there is little research explicitlylooking at the effect of the vaccine on the social structure, it is likely that introducing the Ebola vaccine through a ring-vaccination strategy further intensified this pre-existing social hierarchy. The ring-vaccination strategy offered the vaccine to clinical healthcare providers over non-clinical healthcare providers. Therefore, clinical healthcare personnel could not only enjoy economic benefits from international organizations, but through the vaccine trials, these professionals also had access to the ultimate opportunity: protection from the deadly Ebolavirus. Biomedical ethicists Folayan, Yakubu, Hiare, and Peterson suggest “there are fairer ways to prioritize people at high risk of infection […] than giving only one group of people privileged access to experimental products based on occupational status” (2). Instead, the ring-vaccination approach reinforced social inequalities and is unethical because it further violates the principle of justice by providing benefits to one group of individuals over another.

**Violation of the Belmont Report’s Principle of Beneficence and Nonmaleficence**

The specific research strategies implemented during the clinical trials for the rVSV vaccine also infringed upon the Belmont Report’s principles of beneficence and nonmaleficence. These principles state that research can only be considered ethical if researchers “do no harm” and “maximize possible benefits and minimize possible harms” (The National Commission). Through adopting a study design in which individuals were randomly assigned to be in an immediate or a delayed vaccination group, the ring-vaccination strategy ultimately denied potential vaccine benefits to a particular subset of trial participants. The delayed group was denied the vaccine for twenty-one days: the length of Ebola’s incubation period. A disease’s incubation period is the amount of time it takes for any significant disease progression to occur within humans, so the participants who did not receive the vaccine until the end of the incubation period were at a considerably high risk for disease progression. Therefore, as Rid and Miller explain, “if the vaccine was effective, participants in [… the delayed] clusters would have been at increased risk for contracting Ebola” (433). Denying the vaccine to this group of individuals for the duration of the incubation period could ultimately cause significant physical harm and even death due to virus development and progression. Thus, the principle of beneficence was violated during the trials because individuals in the delayed group were not offered the greatest balance of benefits over harms and were at considerable risk for contracting Ebola.

Many researchers have argued that the ring-vaccination strategy was ethically superior and more favorable than a randomized control trial (RCT) because it did not use a placebo vaccine. Randomized controlled trials using a placebo treatment withhold medical prevention and treatment from control groups *entirely*, meaning research subjects in this subset of the study are not offered medical benefits from the study. Although placebo studies are beneficial in determining whether a particular treatment is effective, withholding the auspicious preventative treatment from the control group is problematic when alternative treatments exist. While the ring-vaccination strategy appeared to be superior because it ultimately *did* allow all subjects to receive the vaccine, the methods still posed an ethical dilemma because some participants did not have access to the treatment until it may have been too late. The CDC states that, “when used early, [even] basic interventions [such as providing fluids and offering oxygen therapy] can significantly improve the chances of survival” (Ebola (Ebola Virus Disease): Treatment). Therefore, the researchers should have provided the delayed group with interventions like these to ensure they were receiving the best available treatment, while still maintaining a control group to test for vaccine efficacy. Therefore, even though it was ethically superior to the implementation of a placebo trial, the ring-vaccination strategy was immoral. Refusing to give the delayed group the vaccine until the end of the incubation period could be detrimental to the participant’s health, violating the principle of beneficence and nonmaleficence.

**The Feasibility of Cold Chain System in Middle and Low-Income Nations**

Many modern-day vaccines require a cold-chain: a network of healthcare facilities and corporations that collaborate to maintain drug potency and effectiveness. Specifically, cold-chain systems ensure that vaccines remain within a particular temperature range during drug assembly, transportation, and storage (The Vaccine Cold Chain (2)3). Ashvin Ashok and other research analysts have been studying the feasibility of employing cold-chain systems in middle and low-income countries. They have found that in many African nations, such systems are difficult to implement and maintain, resulting in “risks of reduced potency of vaccines, [… and] poor availability of immunization supplies” (Ashok et al. 2218). Ultimately, reduced vaccine potency can result in low immune responses and can have overall negative health impacts on patients. The risk of a compromised immune response is incredibly problematic and outweighs the immunological benefits of receiving the vaccine. Therefore, cold chains are essential in protecting human lives.

**Violation of the Belmont Report’s Principle of Autonomy: Cold Chain System**

The deployment strategy for the rVSV vaccine required a cold-chain system for implementation; however, this system promotes dependence on Western infrastructure, which violates the principle of autonomy. Research practices can fulfill the principle of autonomy if the community in which the research is being performed is empowered and can use the results to their advantage to improve public health. However, it can be argued that the rVSV trials did not empower the African communities in which the vaccine was being tested because the trials promoted a reliance on international health agencies for vaccine implementation. As Ashok et al. mentioned, due to geographical challenges and a lack of transportation infrastructure, African nations often find it difficult to implement and maintain cold chains (2218). Therefore, such communities rely on support from organizations, like the WHO, to sustain cold chain systems. Because the African communities in which the rVSV vaccine was tested were unable to maintain such a system without foreign support, they could not continue to deploy and sustain the vaccine independently. Ultimately, this reliance on external institutions removed power from the African communities because they could not use the research results in an autonomous manner. The assumption that the communities could employ and maintain a cold chain system autonomously further exemplifies how the researchers took an ethnocentric approach to fulfilling the Belmont standards. While the implementation of a cold chain system is feasible in developed nations, it is not a simple system to employ and sustain in developing nations. Therefore, the vaccine trials failed to fulfill the Belmont Report’s principle of autonomy because the communities could not use the results of the study independently and were not fully empowered by the research findings.

Because the cold chain system has been shown to be the most effective way to maintain drug quality, many biomedical professionals argue that it is required for vaccine development and use. However, the researchers implementing the rVSV vaccine in Africa must work to develop a research strategy that can both satisfy the ethical guidelines of the Belmont Report, as well as maintain vaccine quality. The principle of autonomy can be fulfilled if the researchers collaborate with the local communities to establish a cold chain system that is more sustainable. Collaboration between researchers and local community members would allow for the development of a cold chain that the locals could use and sustain, so the vaccine could be used without continual intervention from wealthy international organizations. This would allow the community to be empowered and have true ownership of the research results. Therefore, cooperation between research investigators and local community members in the rVSV vaccine trials is essential to ensure the principle of autonomy is satisfied.

**Violation of the Belmont Report’s Principle of Autonomy: Lack of Knowledge about Ebola**

The Belmont Report’s principle of autonomy was at risk of being further violated because there is a generalized lack of knowledge about Ebolavirus among residents of the African communities in which the vaccines were being tested. The Belmont Report’s principle of autonomy asserts that research participants must have the capability to make their own decisions with regard to study participation and cooperation. Specifically, the report emphasizes the importance of *informed* decision-making. In late 2017, Kathleen L. Irwin and a group of other researchers working for the World Health Organization conducted a study to determine knowledge about Ebola and attitudes towards a potential Ebola vaccine in a Guinean population of 6699 people (6917). The results found that, in general, the communities had a lack of knowledge about the virus’s transmission, as well as recovery. For example, according to Irwin et al., when asked about virus transmission “less than 5% spontaneously cited burial or funeral activities […] even though these were common modes of transmission during the epidemic,” and “more than a third of participants who responded reported that Ebola was transmitted by ambient air or mosquito bites” (6917). Additionally, 86.8% of survey respondents believed Ebola was curable, which is incorrect (Irwin et al., 6197). Ultimately, the findings of this large-scale study found that African communities were generally uninformed about the facts and details of the Ebolavirus.

Because the population in which the rVSV vaccine trials were being carried out generally had an overall lack of knowledge about Ebolavirus, obtaining informed consent may have been incredibly challenging. In fact, it is difficult to determine whether research participants were *truly* informed and fully knowledgeable, not only about the virus, but also about the specific details of the vaccine itself and the implementation strategies. Although Irwin et al.’s study did not explicitly investigate the connection between the communities’ knowledge of Ebola and the ethicality of the vaccine trials, their findings raise considerable doubt with regard to the vaccine trials. The conclusions of the study suggest that trial participants did not fully understand the basis of the virus or the trials, so their autonomy was at risk of being violated because they could not give trulyinformed consent.

**Violation of the Belmont Report’s Principle of Autonomy: Undue Influence**

 The Belmont Report explains that the principle of autonomy also includes the notion that informed consent must be obtained in a manner free of undue influence. The National Commission defines undue influence as an “offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance” and that “inducements that would ordinarily be acceptable may become undue influences if the subject[s] [are] especially vulnerable” (7). The rVSV vaccine trials were funded by wealthy health organizations and committees, like the WHO and CDC. Although these powerful associations did not offer excessive rewards for participation in the studies, the research subjects may have felt pressured into participating in the trials in hopes of establishing stronger relationships with such global institutions. Forming strong relationships with these organizations is important for these communities because it means they can then rely on them for help in future crises, such as if there were another disease epidemic.

Paul Appelbaum, who studies research ethics, collaborated with a group of other academics to study the “voluntariness of consent” in research. They found that many factors, other than solely monetary rewards, can establish undue influence. Among these factors, they assert that voluntariness in research is compromised if “patients who otherwise lack access to medical care are invited to participate in studies that promise treatment for their conditions” (Appelbaum et al. 31). The African communities in which the rVSV vaccine trials were executed traditionally have limited access to advanced medical care, so they are more susceptible to disease outbreaks. Therefore, the promise of a potential Ebola treatment by powerful, authoritative institutions, such as the WHO, may have influenced the communities’ willingness to participate in the trials. Such communities may have felt pressured into participating in hopes of entirely eliminating the Ebolavirus. This situation encapsulates the notion that Appelbaum et al. asserts would likely cause undue influence. The presence of undue influence in the rVSV vaccine trials is concerning, as it threatens the research subjects’ right of autonomy.

**Necessity for a New Approach**

The recent Ebolavirus outbreaks in various regions of Africa are having a devastating impact on individuals, families, communities, and nations. Thousands of people have died from the virus in the past several years, and unfortunately, the disease continues to be relentless. The recent outbreak in the Democratic Republic of the Congo illustrates the dire need for disease prevention, and due to the unique biological characteristics of the virus, it seems as though vaccine development is the best option. However, to determine the effectiveness of particular vaccines, international health agencies have been performing trials in a manner which is unethical and should not be continued. Therefore, a different approach must be taken to determine the efficacy of such vaccines. Authoritative organizations such as the WHO and CDC, who are performing the clinical trials, must reconsider the methods and strategies of vaccine trials to ensure that African individuals and communities benefit from the trials now, as well as in the future, to prevent further disease outbreaks. Unfortunately, there is little research suggesting superior methods of trial implementation. However, if the WHO and other international health organizations are going to continue to perform the trials in the manner they are now, they must begin to take a more culturally sensitive approach to fulfilling the Belmont Report’s ethical principles. These authorities must be more cognizant of the problems with applying the Belmont Report in an ethnocentric manner and work more proactively to protect the research subjects in the African communities. They must also work in collaboration with the local communities to ensure they are empowered by the research and can use all of the results to their advantage to improve the health of their citizens. For example, the WHO could work with the communities and use their financial resources to help develop more advanced transportation infrastructure to allow for the implementation of a cold-chain system that the population can use without continual external support. Collaboration between the researchers and the local communities will allow for a deeper cultural understanding, so the Belmont principles can be fulfilled in a less ethnocentric manner.

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