

**The Pathogenicity of Ebola virus, the Treatments/Vaccines, and Social Effects through
Recent Outbreaks**

by

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University of Pittsburgh, 2022

Abstract

Ebola virus (EBOV) is a highly infectious disease that quickly spreads if not properly addressed. Over the years, the virus has claimed multiple lives on a yearly basis, and it has increased recently. During the 2014-2016 Ebola outbreak, overall, there were 28,616 patients infected and 11,310 deaths reported in Guinea, Liberia, and Sierra Leone. In Democratic Republic of the Congo (DRC), among 3481 total cases there were 2299 deaths and 1162 survivors. This outbreak had a fatality rate of 66% throughout the two years and considered the second largest in Ebola's history.

These epidemics caused morbidity and mortality far greater than any previous Ebola epidemic. Since then, there is an increased amount of information regarding the treatment, vaccination, and control of the Ebola virus that is vital to public health. This essay aims to review the literature and identify the methods used to treat and control Ebola virus spreading in Africa during the 2014 through 2021 outbreaks in Guinea, Liberia, Sierra Leone, and DRC, while analyzing the social aspects and effect of the epidemic. This assessment was based on literature and survey reviews via PubMed, The World Health Organization, and the US Center for Disease Control. The health care system in the countries where the Ebola epidemics occurred, suffer from "inadequate resources" which are worsened by poor sanitary conditions and difficult access to rural areas. These combined realities in Guinea, Liberia, Sierra Leone, and DRC, makes them vulnerable to an epidemic. Furthermore, through the published literature review, there was no

evidence of an effective treatment against the EBOV disease that leads to survival without sequelae. However, the most efficient way to prevent the EBOV is via the vaccine rVSVΔG-ZEBOV-GP. Although the vaccine has not been licensed, it is distributed based on ring vaccination system effectively protecting patients at high-risk areas. Although a vaccine exists, public health concern regarding social-economic aspects of Africa shows that the zone of conflicts presents a challenge in distributing the vaccine and ensuring that EBOV does not spread further. Trust should be built between government and humanitarian entities to prevent a future EBOV disease global epidemic.

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1.0 Introduction

Ebola virus (EBOV) is a highly infectious, and potentially lethal, disease that can spread quickly if not controlled by proper methods and care given to infected patients. It was first identified in 1976 in Zaire, Africa. Fewer than 500 cases were reported yearly, and no cases between 1979 and 1994. In 1995, what was initially identified as yellow fever was reclassified as Ebola hemorrhagic fever. From 1995 to today, Ebola’s subtype viruses have claimed a small number of deaths yearly. Unfortunately, these numbers jumped substantially from December 2013 to today. Ebola virus outbreaks went from claiming 100 victims per year to claiming 10,730 victims in 2014 alone.

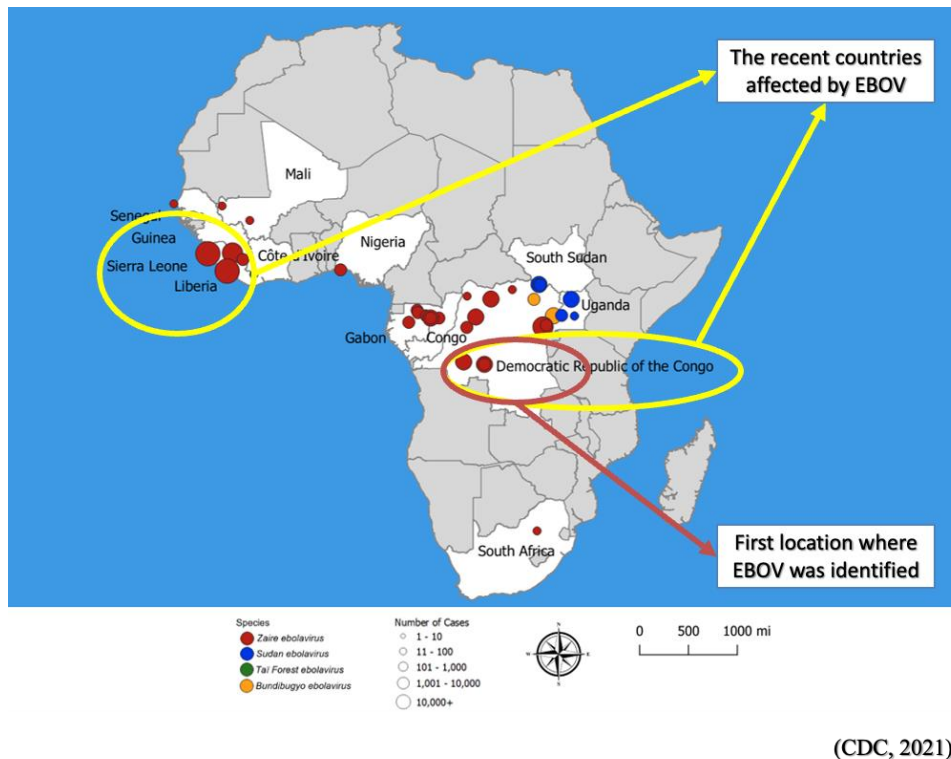


Figure 1 Map of Africa Continent highlighting the countries affected by Ebola List of Figures

During the 2014 outbreak, the World Health Organization (WHO) was initially alerted in March about the Ebola emergency. By April, Medecins Sans Frontieres (MSF) warned WHO that “the outbreak was out of control, although this was disputed by the WHO at that time.” (BBC News, 2014) In August 2014, the WHO declared Ebola outbreak a problem and slowly started responding. According to Isabelle Nuttall, who is a medical doctor with disease outbreaks experience and is the director of Global Capacities at the Alert and Response for WHO, the failure of WHO to recognize the outbreak would be later investigated after focusing on the outbreak response. Nonetheless, it was not until the end of 2014 that international adequately responded with a more aggressive approach. In a news media report at the time, Dr Nuttall called for an investigation to identify why the response to the outbreak was too slow. (BBC News, 2014).

The outbreak ended up lasting two years, and from 2014-2016, 28,616 people were infected, resulting in 11,310 deaths reported in Guinea, Liberia, and Sierra Leone (Center for Disease Control and Prevention, 2019). The 2014-2016 EBOV epidemic caused morbidity and mortality that was far greater than any previous epidemic (WHO Ebola Response Team, 2014). The case fatality rate (CFR) was much higher than previous outbreaks, based on a data collected by the World Health Organization team response. The team reported an unusually high case fatality rate in Liberia, compared to Guinea and Sierra Leone. Respectively, CFR values were 58%, 13% and 35%. (WHO Ebola Response Team, 2014)

Although the WHO declared the outbreak over in Guinea, Liberia, and Sierra Leone in 2016, there were 16 confirmed cases detected in Guinea in 2020 but no major outbreaks. However, in the Democratic Republic of the Congo (DRC) another outbreak had surfaced between 2017 to 2021. As of July 2020, a total of 3481 total cases have been reported, resulting in 2299 deaths,

with 1162 survivors. This outbreak had a fatality rate of 66% throughout the three years in DRC, and it is considered the second largest Ebola outbreak in recent history.

The Democratic Republic of Congo (DRC) is an active area of political and civil conflict. Multiple attacks on health facilities during the Ebola outbreak made it difficult to contain transmission of the disease. During the Ebola outbreak in 2011, increased civil war violence and the lack of trust in government institutions contributed to problems in controlling the EBV spread. However, contact tracing and the vaccination of more than 300,000 people living in close contact were completed (WHO, 2019). On May 3rd, 2011, the outbreak was finally declared over. (WHO, 2011)

1.1 Transmission & Symptoms

The Ebola Virus is highly contagious, and disease is spread among humans via bodily fluids, such as blood, saliva, urine, and other secretions of the actively infected people. The symptoms of the disease include “muscle weakness, muscle pain, headaches, sore throat, and later progress to vomiting, diarrhea, impaired kidney, and liver function.” (Cullinane, 2014) During outbreaks, the treatment consists of “supporting organ function and maintaining bodily fluids, such as blood and water.” For survival, the patient’s immune system must fight off the disease on its own and can be treated by fluid replenishment, if diagnosed early on. (Cullinane, 2014) Furthermore, for recovery, patients need a supportive clinic where they can be isolated and properly given supportive care (rehydration with oral or intravenous fluids) while the patient’s immune system fights off the virus and recover.

In addition to the slow response from international agencies such as the WHO during the 2014-2016 outbreak, the lack of an effective vaccine also hampered effective response. The response actions to the outbreak consisted mainly of supporting clinical staff in caring for patients and containing the disease spread by isolating patients into temporary Ebola Treatment Centers temporarily built where the outbreak was located. During this time, researchers rushed to find an effective treatment including three pharmaceutical categories: antiarrhythmic drugs, antiviral drugs, and monoclonal antibodies, and any potential vaccine in progress: the ChAd3-EBO-Z provided by GlaxoSmithKline and the rVSVΔG-ZEBOV-GP provided by Merck.

During the more recent DRC outbreak, vaccines helped contain the spread of the virus and have proven successful, but only were given on a compassionate basis- any potentially EBOV exposed person received the promising vaccine undergoing clinical trial. A study published in the Journal of Autoimmunity, Rojas (who is a medical researcher based in Bogota, Columbia) provides an extensive overview of EBOV's biology, clinical manifestation and treatments during the DRC outbreak and further recognized "a new condition known as "post-Ebola virus disease syndrome." The syndrome mimics current diseases that induce "inflammatory and autoimmune conditions, such as rheumatoid arthritis, systemic lupus erythematosus and spondylarthritis." (Rojas, et al., 2020)

2.0 Materials and Methods

Between the outbreak of 2014-2016 in western Africa and the 2017-2021 outbreak in the DRC, an increased amount of information became available regarding the treatment, vaccination, and post-Ebola syndrome, and contributed to control of the epidemic. The goal of this essay is to review the published literature and describe the pathogenicity of Ebola and the methods that were used to treat and prevent Ebola virus disease throughout these two recent major outbreaks: the first in western Africa, in Guinea, Sierra Leone and Liberia, and the second in DRC. This review is based on a literature and survey review via PubMed, The World Health Organization, and the Center for Disease Control. For the PubMed search, the publications were narrowed using the search terms “Ebola vaccine”, “Ebola vaccine trials”, “Ebola virus”, “Ebola vaccine virus” and “Ebola outbreak.” The search was narrowed to focus on publications in journals with impact factor higher than 5 and published between 2015 to 2021. The PubMed search covered the EBOV’s biology, treatment, and clinical trials. The World Health Organization and the Center for Disease Control sites were mainly consulted to search for the current methods of outbreak containment measurements and social economic characteristics.

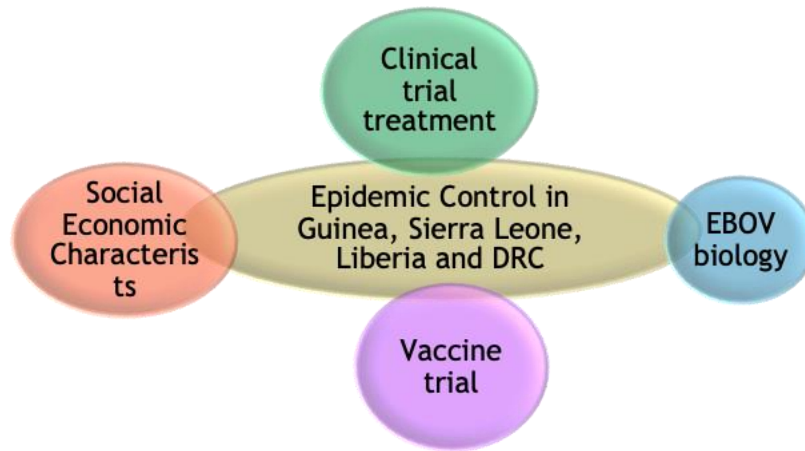
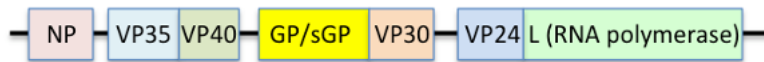


Figure 2 Overview of Essay's Goal

3.0 Overall Findings

3.1 EBOV structure, genome, and molecular infection

First, this section will further describe the virus pathogenicity and the patients' clinical symptoms. In sights of the recent outbreaks during the 2014-2016, the EBOV's biology was better defined. The Ebola virus belongs to the Filoviridae family, which includes five different species. The main causative agent of the 2014-2016 and DRC outbreaks was *Zaire ebolavirus* (EBOV). It is "an enveloped, negative-stranded RNA virus characterized by a virion of approximately 80nm diameter." (Salata, et al., 2019) Its genome encodes for seven structural proteins including nucleoprotein, virion protein, glycoprotein, and the RNA-dependent RNA polymerase.

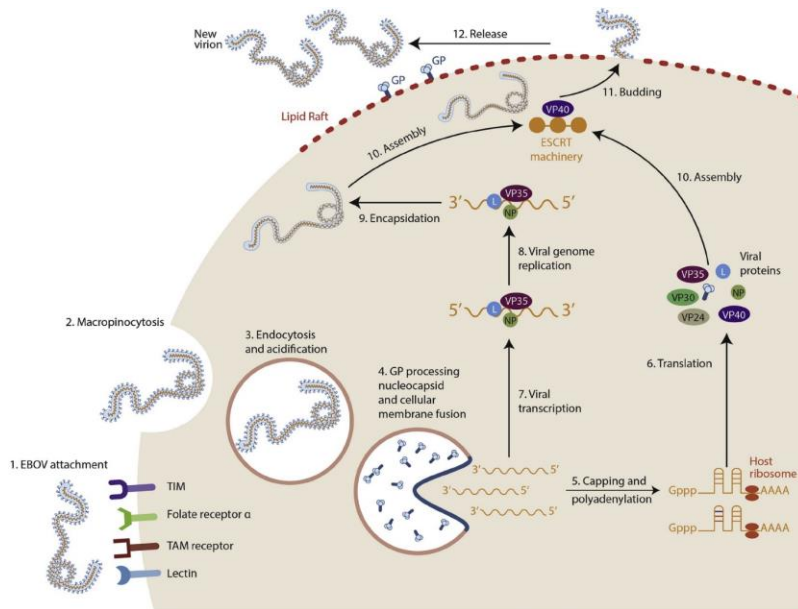


(Salata, et al., 2019)

Figure 3 Molecular Structure of EBOV

EBOV infects multiple cell types such as "monocytes, macrophages, dendritic cells, endothelial cells, fibroblasts, hepatocytes and adrenal cortical cells." Once the virus attaches itself to the cells of the host, it internalizes via macropinocytosis and goes on to replicate.

In the next figure, Rojas illustrates in detail how the virus enters cells and replicates



(Rojas, et al., 2020)

Figure 4 EBOV Host Cell Molecular Invasion and Replication

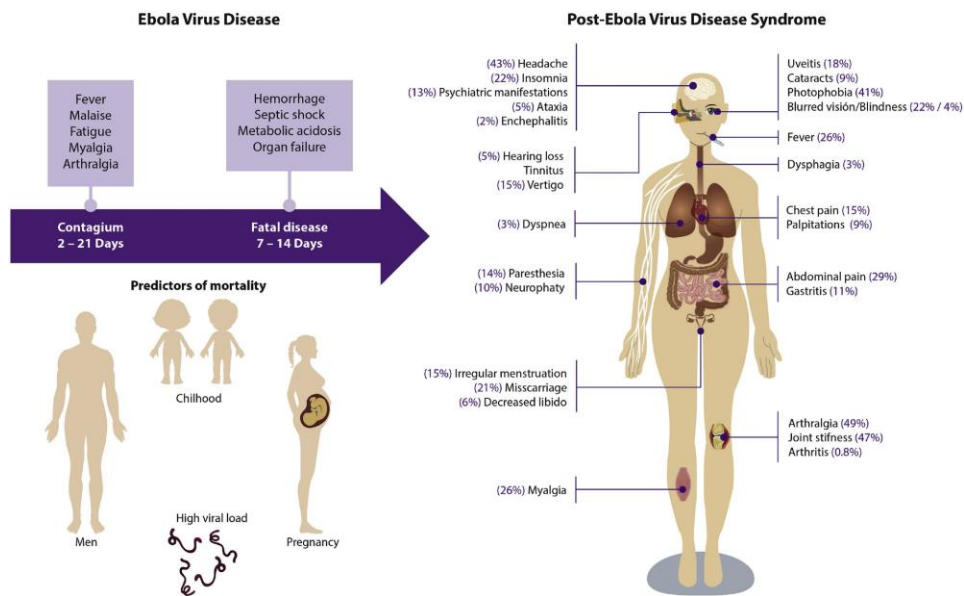
Briefly, the virus attaches to different receptors and enters the cytoplasm via macropinocytosis. Once inside the cell, the viral genome is released, and the RNA is transcribed into viral proteins and genome. Once replicated and assembled, the newly formed virus is encapsulated and released via the “budding” system. (Rojas, et al., 2020)

While EBOV has a high mortality case rate, its main path of transmission is “contact with blood or body fluids from infected humans or animals.” (Salata, et al., 2019) Patient symptoms after infection include “severe condition associated with vomiting, diarrhea, infrequent hemorrhaging and mental disorder (that could lead to a comatose state and death).” Furthermore, survivors were found to carry the viral RNA in specific organs for more than a year after the symptoms have resolved (Salata, et al., 2019).

Another study by Rojas found that patients who survived acute EBOV could develop “Post-Ebola Virus Syndrome,” therefore leading to significant morbidity. The most common sequelae

seen were “arthralgia, joint stiff-ness, and photophobia” in 40% of cases. Further, in 25% of cases, long-term symptoms were reported including “headaches, weakness, anorexia, and chest pain.” (Rojas, et al., 2020) Other symptoms were ocular manifestations, such as uveitis and cataracts found to be present in 18% and 8% of cases. Furthermore, pregnant women were at high-risk for mortality and “miscarriage and stillbirth with a frequency of 21.3% and 13%, respectively”. (Rojas, et al., 2020)

In the following figure, Rojas illustrates the symptoms throughout the infection’s stages:



(Rojas, et al., 2020)

Figure 5 Patient Symptoms During and Post Infection

In addition to being a highly infectious disease that can spread quickly, with high case fatality rates, EBOV presents significant risk of long-term morbidity.

3.2 Drug Clinical Trials

Because EBOV is highly contagious, potentially fatal, and often results in significant long-term morbidity, it is important to identify treatment and/or multiple methods of controlling the disease from spreading further out. This assessment of possible treatments will first review the studies for clinical treatments.

In the systematic review by Salat, the potential treatments for EBOV were evaluated. The study the EBOV requires laboratories with a BSL-4 containment to safely perform research studies; therefore, only a few institutions worldwide can do so. However, multiple EBV viral models have been used in BSL-2 facilities to identify possible treatments (Salata, et al., 2019). From multiple settings and based on EBOV's interaction with host entry, Salat reports on multiple studies published by other researchers.

Potential treatments studied include pharmaceuticals that interfere with the Ebola virus' entry into the host cell. The first are antiarrhythmic drugs that interfere with the glycoprotein and "with the fusion of viral envelope with the endosomal membrane," which showed promising results *in vitro* and in a mouse model. However, in a larger *in vivo* model, the antiarrhythmic drug failed to protect guinea pigs but had some anti-EBOV activity. A more promising approach used an ion channel blocker, Bepridil, which acts by inhibiting the virion from entering the host. In a mouse model, Bepridil showed 100% survival for mice exposed to EBOV. A third ion channel inhibitor, tetrandrine, currently traditional Chinese medicine, has shown therapeutic potential in mouse models, with 50% rate survival rate (Salata, et al., 2019).

Also, Salat has reported studies with antimicrobial drugs that interfere with EBOV entry, such as antimalarial drugs that affect the pH dependent step of the viral infusion. However due to its side effects, antimalarial drugs can only be taken into consideration for "highly deadly viral

infections.” Other drugs were repurposed as potential EBOV treatment, such as protein kinase inhibitors, to identify their effects as antivirals. Most of these drugs were tested either *in vitro* or animal models. While these “broad range drugs” may be useful for addressing and EBOV outbreak, further research is needed to verify clinical efficacy for human treatment (Salata, et al., 2019). Basic research often leads clinical research, but when the findings are applied on animal studies, they do not always translate to human clinical trials. A closer look to the specific treatments and vaccines to treat EBOV will be more resourceful when dealing with an outbreak.

During the West Africa 2013-2016 outbreak, an antiviral drug Favipiravir, an RNA polymerase inhibitor that was approved in Japan to treat non-severe influenza, was used as a treatment on a “compassionate-use” basis in Guinea. Previous studies done *in-vivo* and *in-vitro* had promising results. Therefore, to test its efficacy in patients with EBOV, A JIKI trial was conducted in Guinea, during the outbreak to verify the efficacy of Favipiravir in Humans. The JIKI trial was a controlled experimental trial, single arm. In this trial, there were 126 EBOV patients treated with Farapivir. Although no proven “significant correlation between the drug exposure and the virological response” was found, the results suggested a delay in mortality of treated patients and that further research was needed to evaluate if a higher dosage was applicable (Nguyen, et al., 2017).

From the JIKI trials, in a retrospective observational study, the blood chemistry was analyzed to verify potential risk factors. The study confirmed the previous Nguyen study insights into the Favipiravir drug and identified it as possible supportive treatment. However, “The kinetics of blood chemistry” reported a “key manifestation ... of renal failure.” (Kerber, et al., 2018) While finding a suitable treatment is vital for EBOV, an antiviral drug has not been successful in treating human patients with EBOV.

The figure below illustrates where in the genome the Farivipir would block and prevent viral replication:

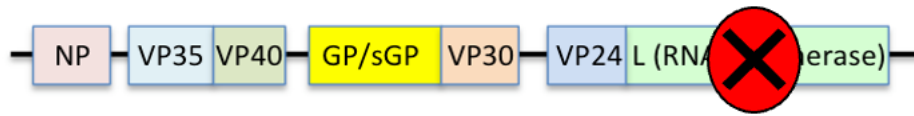


Figure 6 Farivipir Blocking Viral Function

However, in the DRC outbreak, two treatments were licensed to treat EBOV infected patients: regeneron (REGN-EB3) and mAb114. The REGN-EB3 is composed of three human IgG1 monoclonal antibodies obtained by immunized mice, and its antibodies binds to epitopes on the glycoprotein of the virus. In comparison, the mAb114 is a monoclonal antibody agent produced by memory B cells in Ebola patient survivor from the Kikwit, a province in DRC epidemic, and this drug works by strongly binding to the region of the “conserved amino acids on the receptor-binding domain of the” EBOV’s glycoprotein even in low intracellular pH environment acidic. Thus mAb114 prevents the virus from engaging with the host cell, even in the late endosome stage. Furthermore, it also “reduces the risk of escape mutants.”

In a clinical trial published in the New England Journal of Medicine, early into the outbreak of DRC in 2019, these two treatments are compared to Remdesivir and ZMapp. Both drugs, REGN-EB3 and mAb114 showed a faster rate of viral clearance and a higher survival rate in 620 total patients that were enrolled in the study (Mulangu et al. 2019). However, the full extent of, and if, the two treatments continued to be successful, remains unpublished. Further, a recent study published in 2020 indicates that neonates, born to mothers that contracted the virus while pregnant who were treated with either drug, were able to survive without a trace of EBOV in their system. However, more research is needed to distinguish if the mother’s antibodies or the drugs allowed for survival. (Ottoni, et al, 2020)

3.3 Vaccination Clinical Trial

Another alternative for addressing EBOV epidemics would be to identify an effective vaccine as a preventive method to contain EBOV spread. In a previous study in the *New England Journal of Medicine*, a phase-two clinical trial was performed with two vaccines to prevent Ebola in Liberia from April 2015 and followed up to one year. The study was designed as a double-blind trial that analyzed the “safety and immunogenicity” of two vaccines: the ChAd3-EBO-Z provided by GlaxoSmithKline and the rVSVΔG-ZEBOV-GP provided by Merck. The vaccines were randomly assigned to a cohort of 1500 adults that excluded children and pregnant/breastfeeding women. These patients were followed for 12 months, and blood collected to identify their “IgG antibody levels against Ebola surface glycoprotein” with a high rate of attendance. Although some participants reported symptoms such as headache, muscle pain, fever and fatigue, no severe side effects were identified. High antibody titers were found in patients that were vaccinated (Kennedy, et al., 2017). The study provided insight into the promising high safety of these vaccines within the Liberian population. However, given the long-term study and that it occurred during 2015, the vaccine efficacy was obscured by the high importance of containing the outbreak during that same time in West Africa.

The World Health Organization (WHO) convened an urgent meeting in 2014 to address the epidemic of Ebola spreading through West Africa. There, the WHO identified the two potential vaccines to be the best to address the epidemic: the ChAd3-EBO-Z provided by GlaxoSmithKline with National Institute of Allergy and Infectious Diseases (NIAID) and the rVSVΔG-ZEBOV-GP provided by NewLink Genetics and the Public Health Agency of Canada (Kanopathipillai, et al., 2014). As the EBOV outbreak had to be addressed aggressively, the efficacy and effectiveness of

the rVSVΔG-ZEBOV-GP vaccine was calculated based on a cluster-randomized trial ring in the population of Guinea. The study began focused on adults' population, however as the vaccine showed 100% protection, and it was safe for population use early in the study, the vaccine was expanded to all groups including children aged 6-17 years. The rVSVΔG-ZEBOV showed “high protective efficacy and effectiveness to prevent Ebola virus.” (Henao-Restrepo, et al., 2017)

Although the rVSVΔG-ZEBOV vaccine was shown to be highly efficient in protecting the population at high risk for EBOV infection, it is still not fully able to be commercialized and “more scientific research was needed before it could be licensed.” Therefore, the rVSVΔG-ZEBOV vaccine is specifically used as “compassionate use” only at the highest risk of the Ebola outbreak as a “ring vaccination strategy” where participation of patients is recruited based on a volunteer basis and their connection to a patient confirmed with the virus (WHO, 2018).

During the most recent outbreak in the DRC, more than 300,000 individuals were vaccinated with the rVSVΔG-ZEBOV vaccine between May 1st, 2018, and March 25th, 2019. The preliminary results from WHO vaccination have been promising. Although not a fully assessed study, during that period, the health facilities vaccinated more than 100,000 people including medical staff and exposed civil individuals. The vaccine was estimated to have 91% efficacy achievement in the ring-vaccination method. Further, no deaths were reported to date, and only 2 EBOV cases were noted. (WHO, 2019)

3.4 Socioeconomic Effects and The Role of Conflict on Ebola Spread

In controlling the EBOV spread in the countries of Guinea, Sierra Leone, Liberia and DRC in Africa, the economic status and infrastructure of those countries also played a role. The public health conditions are not ideal, although there have been significant improvements. Life expectancy in Africa has increased since the 1920s, when it 26.4 years, and by the early 2000s life expectancy had increased to 50.5 years. Despite improvements in overall health, however, when compared to wealthier regions, sub-Saharan Africa's life expectancy estimation is significantly lower. In the beginning of 2000s, the North America's life expectancy was 76.7, Asia 67.1, and Europe was 76.8. (Riley, 2005) The high life expectancy is related to the countries' wealth and economic system and living conditions.

According to the United Nations Development Program (UNDP), numerous civil conflicts have been reported for years in the parts of Africa where the most recent epidemic occurred, including west Africa and the DRC areas. During these past few years, these countries' "health facilities had been destroyed, food insecurity was rampant, poverty rates were high, and huge numbers of people had been displaced." (United Nations Development Programme, 2014) In Guinea, Liberia, Sierra Leone and DRC, while part of these countries attempted to re-establish their economies and improve assistance to their population, the majority of these areas are still in poverty. For example, due to its long rainy season in DRC, the country does not have easy access to the roads that lead to growth and employment. (United Nations Development Programme, 2014) Supplies tend to be scarce.

Despite these limitations that existed before the 2013-2016 Ebola epidemic in West Africa, Guinea, Liberia, and Sierra Leone's economy was slowly growing. (United Nations Development Programme, 2014) With the economy still recovering from the civil war between Sierra Leone and

Liberia from 1991 to 2002 that strongly affected Guinea, these countries' health sector was unprepared for the outbreak. Drug supplies were scarce and ambulances often commute long distances to pick up patients, adding to the cost of fuel and maintenance. The health care systems in countries in West Africa also suffers from "inadequate resources." Such resources are defined as the "low salaries for health workers, outdated technologies, poor infrastructure, inadequate medical facilities and equipment, and limited supplies." These conditions are worsened by poor sanitary conditions and difficult access to rural areas. (United Nations Development Programme, 2014) These facts made these four countries, Liberia, Sierra Leone, Guinea, and DRC, vulnerable to an epidemic.

The reasons the 2013-2016 epidemic spread so quickly are mostly likely related to the socioeconomic conditions, the social inequality and difficult access to health care systems in Guinea, Sierra Leone and Liberia. The conditions of health facilities and living environments were not ideal. Lack of proper sanitation with inadequate running water and sewage establishments aids to the spread of EBOV by increasing chances of contamination through improper hand washing and sterilization. (Annan, 2015) In 2014, the evidence-based recommendations for water, sanitation, hygiene and health (WASH) best practices were published by WHO and originally developed during the west Africa EBOV outbreak. (WHO/UNICEF, 2021) The governments in Guinea, Sierra Leone, and Liberia, along with international health organizations, started investing in WASH interventions, especially in the health centers, shortly after WHO intervened and established protocol.

Another ailment that aided the EBOV spread, hospitals in the region were not equipped with enough supplies to ensure patients had the appropriate supportive care while in quarantine containment units, and laboratories were not equipped to handle the large outbreak. Further, there

were non-border screening procedures for travelers that could have been affected. Since October 2014, CDC helped implement an exit screening at airports to prevent EBOV from spreading to other countries which consisted of temperature and illness symptoms checks. (CDC, 2015).

The spread of EBOV was also facilitated by the funeral practices and burial sites for the infected patients that died. Contact with the deceased bodies is often common in preparation for the funerals in many Western African cultures. Further, cemetery and burial spaces were inadequate, and burial teams had no proper training, nor supplies, to safely manage the infected patients being buried. In 2014, The ministry of Health in Sierra Leone along with the CDC investigated the burial sites and handling to improve the practices. This resulted in standardizing the burial protocols by increasing the level of proper personal protective equipment (PPE) to burial team workers and using leak/puncture resistance body bags to bury the bodies at least 2 meters deep. Further the Ministry of Health provided additional resources to support the waste management for those sites. (Nielsen, C.F., 2015)

Due to their poor infrastructure, Guinea, Liberia, and Sierra Leone, relied on international help to control the disease from spreading. When the WHO acknowledged the 2013-2016 Ebola epidemic in August of 2014, it was declared a global health issue and effective methods and protocols were placed to control the Ebola epidemic (United Nations Development Programme, 2014).

In 2018, DRC minister of health declared an outbreak of Ebola in North Kivu Province (Centers for Disease Control and Prevention, 2019). During the early stages of this outbreak, by November 24th , 2019, 3303 EBOV cases have been reported and 2199 deaths reported in an external situation report. Out of these confirmed cases, approximately 56% were female and 28% were children less than 18 years old. These cases appear to be concentrated in the regions of

Malabako and Beni, provinces of North Kivu, and in Mandina, in the province of Ituri (WHO Health Emergencies Programme, 2019). Unfortunately, this outbreak had occurred in an area of ongoing violent civil conflicts for over two decades. These conflicts lead to “thousands of deaths and injured people.” Furthermore, ongoing violent conflict challenges the movement of population and health workers. The DRC population’s trust in the government and humanitarian workers has lowered. A survey population identified that “mistrust and misinformation for outbreak control” exploited by the local politicians leads to increased risks of spread of EBOV created by reluctance of the population to seek medical attention and accept vaccination (Vinck , N Pham, K Bindu, Bedford, & J Nilles, 2019).

According to the WHO report on DRC’s situation, challenges remain in overcoming the communities’ reluctance where EBOV is steadily spreading, but community outreach has improved. Also, strategies for prevention have been put in place, similar to the steps previously described for the western African regions, such as the decontamination of multiple health facilities and households, placement of eight laboratories in DRC with EBOV diagnostic capability, active screening at borders, and establishment of community emergency harm reduction burial teams in areas with difficult access. Further steps that have been implemented include the use of the ring vaccination in the regions of Katwa, Beni and Butembo, in the province of North Kivu, DRC. (WHO Health Emergencies Programme, 2019)

4.0 Discussion

When sanitary conditions are inadequate and health sectors lack palliative supportive systems, EBOV is susceptible to spread. Although DRC's situation has improved, conflict there continues, creating an on-going public health problem related to prevention or management of potential Ebola outbreaks. Other African countries, Guinea, Sierra Leone and Liberia, present similar serious public health problem. If humanitarian workers and international aid are not allowed to enter the region safely to control the EBOV outbreak, it leads to a larger epidemic. Also, the system/infrastructure should be considered as they directly impact how EBOV can be addressed. Poor roads and difficult access to remote regions are a challenge to attend patients with EBOV with proper care but also to implement vaccination where applicable.

Despite their civil conflicts, strategies for prevention have been put in place, such as placement of the ring vaccination in Katwa, Beni and Butembo, decontamination of multiple health facilities and households. Eight laboratories have been placed in DRC with EBOV diagnostic capability, and active screening at borders has been initiated. Additionally, community emergency harm reduction burial teams were placed in areas with difficult access (WHO Health Emergencies Programme, 2019). These measures, along with treatment and vaccination, have been shown to be effective in containing the spread. On May 3rd, 2021, the DRC's Ebola epidemic was declared over by the WHO.

Currently, the information is lacking on how the rVSVΔG-ZEBOV vaccine affects young children (less than seven years old) and pregnant women long term, and the immunogenicity it offers. These vulnerable populations and the immunogenicity should be properly addressed in future study. Also, future and careful investigation into re-vaccination is needed, since based on

the IgG antibody level titer against EBOV response from patients vaccinated showed highest peak at 1 month from vaccination and the lower at 12 months (Kennedy, et al., 2017). Although antibody levels were still significantly present at 12 months, the long-term immunity of these patients should be analyzed for future re-vaccination, therefore possibly preventing further outbreaks. Since this vaccine has mainly addressed the epidemics for now, the vaccine's ability to cause long term immunity should be studied. Currently, there are no publications on these subjects.

Another future area for vaccine studies is the weakness in addressing host diversity. Although a wide range has been addressed in small clinical trial, the main patients receiving the vaccine, in the most recent outbreaks, were Africans at high-risk exposure areas. Other cultures such as European, Asian, Latin, and American populations would also need to be addressed as the genetic diversity could affect the vaccine's efficacy and effectiveness. (Linnik, J. E., 2016)

This review has presented recently published information on Ebola's recent outbreak in Guinea, Liberia, Sierra Leone and DRC. The information was narrowed to EBOV biology, Clinical Treatment and Trials, and socioeconomic influences. However, this review is limited by a lack of post-outbreak research available for inclusion. Published articles and health organizations do not offer vast post outbreak information. The aftermath information collected from outbreaks could inform about the sequelae of patients that survived EBOV and potential disease burden. These patients could be useful information as learning tools on how their immune systems surpassed the EBOV and how the mechanism in which the virus leads to sequelae. The "Post-Ebola Syndrome" should be further studied, especially when the sequelae can lead to a public health morbidity. Furthermore, studying the EBOV survivor's immune system could lead to more effective vaccine production and/or treatment with monoclonal antibodies.

Although humanitarian aid alleviates the affected countries' situation and prevents infectious diseases from spreading globally, areas of conflict and health settings with poor infrastructure are still at high risk for another EBOV epidemic and civil conflicts make epidemic challenging to control.

5.0 Conclusion

Currently, treatment with the antiarrhythmic drugs, antiviral drugs, and monoclonal antibodies offers small significant support to EBOV patients. The most efficient way to prevent the EBOV is via the vaccine rVSVΔG-ZEBOV-GP. Although the vaccine has not been fully licensed, it is distributed based on ring vaccination system that, so far, has been effective in protecting patients and medical staff in high-risk areas. Public health concerns remain regarding social-economic aspects of Guinea, Sierra Leone, Liberia, and DRC where zones of conflicts still present a challenge in distributing the vaccine and ensuring that EBOV does not spread further. Although it has been improved, trust should be built between government and humanitarian relief entities to continue to prevent EBOV disease global epidemic and stop any future epidemics.

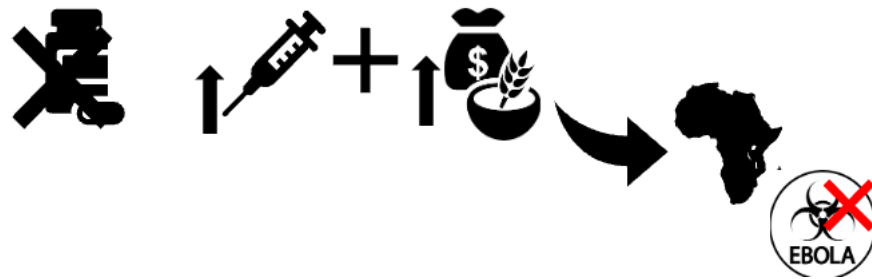


Figure 7 Overall Conclusion Findings Illustration

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