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Ebola virus disease (EVD) outbreak re-emergence regulation in East Africa: preparedness and vaccination perspective

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Dear Editor,

Sudan ebolavirus (SUDV), Bundibugyo ebolavirus, Taï Forest ebolavirus, and Zaire ebolavirus (EBOV) are the most potentially life-threatening and grievous species reported among the *Ebolavirus* genus[1]. Previously, the most common cases pointed to EBOV as the primary causative agent of Ebolavirus epidemics and fatalities. From 2013 to 2016, a devastating EBOV outbreak in West Africa resulted in 29,000 illness cases, prompting WHO global member countries to prioritise vaccine candidates in the early stages of development[2]. The impending spread of EBOV in Guinea, Uganda, and the Democratic Republic of the Congo highlighted the ongoing need for secure and effective vaccine programmes against emerging infections using the most secure deployment precautions and methodologies. The West Africa outbreak and all current outbreaks in other countries have been prevented through the effective immunisation of healthy individuals through vaccination and their interactions with identified patients, medical practitioners, and frontline emergency professionals[3,4]. Despite the fact that EBOV outbreaks previously only infected a small percentage of the global population, they have occasionally caused widespread suffering and huge economic costs in endemic countries. Reported transmission of such viruses beyond nonendemic zones[2,5] in conjunction with the bioweapon potentiality of ebolaviruses necessitates the discovery and production of EBOV vaccines globally.

In 2012, the Sudan Ebola virus outbreak's emergence was previously documented. Recently, Uganda may have been deeply saddened by the Sudan-originated Ebola virus disease (EVD) infection pandemic, which originated on 20 September 2022. The Ministry of Public Health has published and approved a total of 146 cases, 55 recorded fatalities and 87 occurrences for the WHO through 5 December 2022. In Sudan, EVD was introduced due to the EBOV from the DRC. The present globalised EVD incidences in different areas of Sudan, Yuganda and Western Africa have demonstrated the limitations and deficiencies of predesigned vaccines to counteract the ailment, validating the prompt demand to produce standardised guidelines to develop Ebola vaccines in advance of the pandemic. The DRC recently updated the nation about the epidemics on 23 April 2022, and 4 July 2022, which were accompanied by the third outbreak in 2018.

Following cases of EVD in July 2022, the Uganda Ministry of Public Health, from 20 September to 5 December 2022, has already reported 142 incidents of SVD, among which 55 are dead (case fatality rate/risk: 39%) and 87 have started to recover, according to the WHO. Twenty-two other mortalities within significant patients have also been documented in the population who died just before a sample was taken. Since the updated Disease Outbreak News statement, 19 documented cases have been reported among all healthcare workers, which include seven individual deaths. Fortunately, the rapid transmission of the Ebola virus was effectively inhibited through serious precautions, strict surveillance, and monitoring by actively participating national authorities. In order to enhance the prompt and successful response to Ebola-mediated serious infectious diseases in the context of the threat to the health of the public, the Centers for Disease Control and Prevention and WHO function collaboratively with a significant range of communities from different nations on a worldwide platform. According to the current situation reported by the WHO, the situation of EVD indicates that preparedness and vaccines for EVD with enhanced efficacy are urgent global requirements in the future[6].

From a technological perspective, it is necessary to be completely prepared for this slowly emerging infectious and incurable EVD, and epidemic crisis through immediate and judicious vaccine development approaches. The authorisation of clinical research, vaccine safety, monitoring of viral strains for vaccine development, convenient synthesis, and distribution of vaccines are complex, time-consuming approaches that require approval and permission from the biggest pharmaceutical corporations.

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The re-emergence of viral infectious diseases and their spread through zoonoses[7,8] is affected by a number of social factors, such as the growth of cities, the international movements of individuals, the balance between the environment and ecology, and people's immune systems.

Implementing a combination of intervention strategies such as case management, community integration, screening, contact tracing, developing laboratory capabilities, and safe and dignified burials are essential for managing SUDV disease outbreaks. Irrespective of the patient's presumptive diagnosis, primary healthcare professionals should always follow standard conventional protocols when providing healthcare treatments. To decrease the risks of healthcare services amplifying the outbreak, infection prevention and control measures must be adopted with prolonged supervision and monitoring of healthcare (e.g. training of the healthcare workforce, hand hygiene, environmental cleaning, appropriate personal protection equipment supplies, waste management, disinfection, etc.). Although there are potential medications that will be used in randomised controlled trials, there are currently no approved treatments for SUDV. The treatment and management of SUDV patients should take place in centres with adequate safe quarantine, treatment and care practices, and skilled medical professionals. Because of the large number of people travelling cross-border between Uganda and its neighbouring countries, primary surveillance at ports and checkpoints is an essential aspect of the pandemic action plan to minimise the chances of global spread. Although there are potential vaccinations that are being tested in trials, there are currently no approved SUDV vaccines. By considering the evidence-based information currently accessible about the ongoing outbreak, WHO suggests against imposing any limitations on travel to or exchange with Uganda.

Although the initial emergence of the Ebola vaccine focused on initiatives to denature the virus, in vivo animal experimental model research or preclinical trials provide a broad range of tools for the genomic, protein or viral vaccine design.[9] In pre-exposure and post-exposure therapeutics, RNA interference, DNA immunisation, virus-like particles, polymeric delivery systems, Venezuelan equine encephalitis virus replicons, attenuation, serotypes, and replication-competent viral platforms such as human parainfluenzavirus 3 and recombinant vesicular stomatitis virus (rVSV)

Currently, a variety of vaccines are available, including rVSV-ZEBOV-GP; V920; rVSVAG-ZEBOV-GP (ERVEBO); Ad26. ZEBOVMVA-BN-Filo boost (Zabdeno/Mvabea); ChAd3-EBO-Z (+/−) Mvabea (cAd3-ZEBOV/ChAd3-EBO-Z); and GamEvac-Combi. The classes of vaccines consist of vaccines that are analogous to viral particles, DNA-based vaccines, complete virus recombinant vaccines, incompetent replication-originating vaccines, and competent replication vaccines. The adoption of immunogens, fast responsiveness, and cross-protective immunity-based vaccination with a commitment to persistent protection are the challenges and difficulties raised in the progressive development of Ebola vaccines. Another such challenge with vaccine generation and distribution is postauthorization, postlicensing and post-surveillance to safeguard the efficacy and efficiency of the vaccine in curbing the Ebola outbreak. The preclinical and clinical procedures for the production of an Ebola vaccine have demonstrated and proven their outstanding advancement. In their advanced forms, these vaccines showed promising potential as candidates for countless targeting strategies. Moreover, there is still a requirement for improved performance in relation to the challenges and complexities associated with the potency, efficacy, longevity, and cost-effective approaches in the generation of Ebola vaccines. On the other hand, current immunisations require some relatability of an individual's immunological responses, epidemiological data studies and clinical trial findings in the population in order to consider the vaccine's efficacy. Based on these findings, novel potential vaccines can be developed and used to control re-emerging infectious diseases that could lead to an increase in Ebola infections in the near future. This strategic plan essentially requires substantial observations, monitoring, analysis and willingness among epidemiologists, researchers, vaccine-developing pharmaceuticals, stakeholders, and funders on a worldwide platform.

The requirement for a safe and reliable vaccine to stop additional outbreaks increased when the Ebola virus pandemic returned to Guinea[10]. The most recent EVD vaccine approaches focused on EBOV, the predominant Ebola virus form, which has recently been the subject of various phase 1 through phase 4 human research clinical trials[11]. In phase 1 studies, a small number of healthy people are analysed to examine the adverse effects of the vaccination inclusion. In phase 2 studies, a larger population is used to examine the safety and immunogenicity of the developed vaccines. Phase 3 studies assess a vaccine's efficiency during an epidemic, while phase 4 trial studies are used to track the safety of the vaccine after it has been made available for purchase[12]. Out of 70 or more research studies for the EBOV vaccine, only 2–3 of them have received FDA approval as of 2020. Recombinant VSV-based vaccine (VSV-EBOV), Ad26-ZEBOV/MVA-BN-Filo vaccine and GamEvac-Combi vaccine are the vaccines worthy of note that have effectively prevented the illness from spreading further. Replicative vectored vaccines, nonreplicative vectored vaccinations, polypeptide vaccines, protein nanoparticle vaccines, and DNA vaccines are some of the vaccine options against the EBOV virus that are nowadays available on the market[13].

It is essential for administrative authorisation of vaccines to identify processes that ensure the security and effectiveness of proposed vaccinations. The WHO deserves admiration for the development of resources for EBOV pathology, sero-testing and molecular analysis (https://www.who.int/biologicals/expert_committee/BS2316_AntiEBOV_Antibodies_WHO_1st_IS_and_WHO_1st_International_Ref_Panel.pdf). Since bioassays are often used in these processes, the ability to compare the outputs of the tests or analyses across time or even between laboratories depends on the availability of reference components for effective diagnosis and data augmentation.

The preclinical and clinical phases of the development of an Ebola vaccine have proven to be outstanding achievements. In their advanced stages, these vaccines appeared to be promising candidates for multiple targets. However, there is still room for improvement with regard to the hurdles and difficulties associated with the efficiency, intensity, longevity and cost-effective techniques in the development of Ebola vaccines. Contrarily, the present vaccinations require a comparison of an individual's immunological reaction, epidemiological data and clinical trial results in the population regarding the vaccine's effectiveness. Based on these findings, new vaccines can be designed and used for the treatment of re-emerging infectious illnesses that could result in Ebola infections in the future. Strong monitoring, observation, analysis and readiness are essential for this strategy among researchers, epidemiologists, vaccine-developing pharmaceuticals, stakeholders and funders on a worldwide basis. The current report mainly focuses on an innovative outlook for the

development of the Ebola vaccine and combating the eventual emergence of this infectious disease.

Ethical approval

The authors declare no involvement of animal studies or human participants in the study as it is a compiled letter article.

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Author contribution

S.M., A.D. and K.D.: designed the study; S.M., J.B. and P.U.: made the first draft; P.S., S.P., H.C. and K.D.: updated the manuscript; S.M., H.C., M.A.I. and K.D.: reviewed the final draft. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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There are no conflicts of interest.

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Data availability

Data not available/not applicable.

References

[1] Feldmann H, Sprecher A, Geisbert TW. Ebola N Engl J Med 2020;382:1832–42.
[2] Centers for Disease Control and Prevention. Ebola (Ebola virus disease): History of Ebola Virus Disease (EVD) Outbreaks; June 2021. Accessed 4 October 2021. http://www.cdc.gov/vhf/ ebola/history/chronology.html
[3] Henao-Restrepo AM, Camacho A, Longini IM, *et al*. Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised trial (Ebola Ça Suffit!). Lancet 2017;389:505–18; Erratum in: Lancet 2017;389(10068):504.
[4] World Health Organization. Preliminary results on the efficacy of rVSV-ZEBOV-GP Ebola vaccine using the ring vaccination strategy in the control of an Ebola outbreak in the Democratic Republic of the Congo: an example of integration of research into epidemic response; 10 April 2019 meeting report. Accessed 4 October 2021. https://www.who.int/csr/resources/publications/ebola/ebola-ringvaccination-results-12-april-2019.pdf
[5] Masterson SG, Lobel L, Carroll MW, *et al*. Herd immunity to ebola-viruses is not a realistic target for current vaccination strategies. Front Immunol 2018;9:1025.
[6] WHO. Ebola. Uganda 2022. Accessed 21 November 2022. https://www.who.int/emergencies/situations/ebola-uganda-2022
[7] Excler JL, Saville M, Berkley S, *et al*. Vaccine development for emerging infectious diseases. Nat Med 2021;27:591–600.
[8] Sridhar S. Clinical development of Ebola vaccines. Ther Adv Vaccines 2015;3:125–38.
[9] Fausther-Bovendo H, Kobinger G. The road to effective and accessible antibody therapies against Ebola virus. Curr Opin Virol 2022;54:101210.
[10] Agnandji ST, Loembe MM. Ebola vaccines for mass immunisation in affected regions. Lancet Infect Dis 2022;22:8–10.
[11] Matz KM, Marzi A, Feldmann H. Ebola vaccine trials: progress in vaccine safety and immunogenicity. Expert Rev Vaccines 2019;18:1229–42.
[12] Williamson ED, Westlake GE. Vaccines for emerging pathogens: prospects for licensure. Clin Exp Immunol 2019;198:170–83.
[13] Sharma AR, Lee YH, Nath S, Lee SS. Recent developments and strategies of Ebola virus vaccines. Curr Opin Pharmacol 2021;60:46–53.