Trials

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Leveraging an epidemic to establish vaccine clinical trial capacity in a low resource setting: the Ugandan experience

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Abstract

Background Pandemics have increasingly become more frequent. Globally, between 1970 and 2016, a total of over 1770 disease outbreaks of 38 known and two unknown causes were reported. Vaccines are a key medical countermeasure for most of these outbreaks, however, most of these are developed and tested outside Sub-Saharan Africa. There is underrepresentation of Africa in vaccine clinical trials. This is attributed to poor visibility of existing sites, limited infrastructure and unpredictable regulatory timelines, and lack of capacity and infrastructure for basic science research.

Main text We draw on lessons from an Ebola outbreak in Uganda to suggest key factors to establishing a vaccine trial site in a low resource setting. The factors are trained clinical trial staff, availability and adaptation of generic trial protocols, establishment of vaccine cold chain storage facilities, south-south collaborations, in-country stewardship, and close collaboration with ethical and regulatory bodies.

Conclusion African institutions could capitalise on the epidemics and the accompanying responses to build capacity for vaccine trials and position themselves to take part in global vaccine trials.

Keywords Clinical trial, Trial capacity, Vaccine trial, Vaccine, Trial capacity in low resource settings

Background

Coronavirus disease (COVID-19) emerged at the end of 2019 [1] and found many countries unprepared. In the recent past, it has been noted that pandemics have increasingly become frequent [2]. The expectation was that prior pandemics such as Spanish flu of 1918/1919, severe acute respiratory syndrome of 2002/2003, H1N1 of 2009, Middle East respiratory syndrome of 2012 and the West African Ebola outbreak of 2014–2016 should have accorded countries an opportunity to learn and develop appropriate medical countermeasures. In 2022, while the world was still recovering from COVID-19, an outbreak of mpox (previously called monkeypox) was reported in several countries and continents [3, 4]. The disease has raged on and has created substantial morbidity and mortality across the world [3]. The circumstances

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to favour the emergence and rapid spread of pandemics are ripe and include increased travel across the globe, urbanisation, climate change, and increased human-animal contact, among others [5].

Based on the foregoing, there is a need for countries to be better prepared to respond to current and future pandemics. Integral to this preparedness is the availability of scientifically sound medical countermeasures, among which vaccines are fundamental. Since time immemorial, vaccines have been used as one of the important protective measures to control the spread of disease. Historically, some diseases have been eradicated through vaccination e.g. the smallpox vaccine was responsible for the eradication of smallpox in 1977 [6]. COVID-19 offers another recent example where vaccines were deployed to successfully manage the pandemic, and they created a substantial impact [7].

Globally, between 1970 and 2016, a total of over 1770 disease outbreaks of 38 known and two unknown causes were reported [8]. However, most of the vaccines deployed in control of these outbreaks have been developed and tested outside sub-Saharan Africa. Underrepresentation of Africa in vaccine clinical trials has been noted [9] and is attributed to poor visibility of existing sites, limited infrastructure and unpredictable regulatory timelines [10]. It is also attributed to a lack of capacity and infrastructure for basic science research [11]. Before COVID-19, only 2% of vaccine trials took place in Africa, while during the COVID-19 pandemic, only 14.5% of the COVID-19 trials were on the African continent [9]. There is every justification to conduct vaccine clinical trials in Africa as the biological, and sociopolitical factors associated with the emergence of diseases, epidemics, and pandemics are overrepresented on this continent. For this to happen, there is a need to build capacity and establish good clinical practice (GCP) compliant sites and get them ready to undertake vaccine trials during the interepidemic and epidemic periods.

Main text

In September 2022, Uganda declared an outbreak of ebolavirus disease (EVD), caused by the Sudan ebolavirus (SUDV) species. Despite vaccines being key in outbreak response, none with proven efficacy and safety against the SUDV species was available in Africa at that time. A vaccine trial; the ring vaccination trial (Solidarity against Ebola/TOKOMEZA trial) to evaluate the efficacy and safety of candidate SUDV species targeted vaccines was sanctioned by the World Health Organisation (WHO) and Uganda Ministry of Health (MoH). This contribution articulates a viewpoint from a perspective of using an epidemic to establish a clinical trial site ready to undertake a vaccine trial as soon as an epidemic occurs. We draw on lessons from the TOKOMEZA Ebola trial to suggest key factors to establishing a vaccine trial site in a low resource setting. These include:

(i) Clinical trial staff

Personnel are integral to the successful execution of clinical trials, and low number of personnel together with low morale has been highlighted as a significant pitfall of many clinical trials [12]. The TOKOMEZA Ebola trial recruited a multidisciplinary team of more than 100 trial staff that included Investigators, clinicians, safety physicians, nurses, laboratory technologists, cold chain specialists, logistics personnel, and community engagement officers, among others. These all received training in human subjects' protection (HSP) and good clinical practice (GCP). These are available and could be called on to support clinical trials as and when required.

(ii) Adaptation of generic protocols

These are important documents as they detail the background, methods and administration of the trial [13]. In our case, a protocol that had previously been used for another Ebola outbreak in West Africa was adapted [14]. This helped expedite the process of protocol development and ethical approval. Despite the outbreak being controlled, the protocol has been retained as a living protocol and will be annually reviewed so it can be readily deployed once there is an outbreak. There are efforts from WHO to have core protocols that could be rapidly used during disease outbreaks, and one such example is the multi-country, multi-site pan filovirus protocol for evaluating the safety, tolerability, immunogenicity and efficacy of vaccine and therapeutic candidates against filoviruses disease in healthy individuals at risk of filovirus disease [15].

(iii) Cold chain capacity

Investigational vaccines most often require cold chain (CC) and ultra-cold chain (UCC) facilities, and these could be missing at most African trial sites. With WHO and Ministry of Health, a vaccine storage facility with ultra-cold chain capacity was set up. This facility has an uninterrupted power supply with temperature monitoring capabilities. This could be used to support vaccine research for any outbreak.

(iv) South-South collaborations

These were leveraged to quickly set up the TOKOMEZA Ebola trial processes. The WHO helped create a south-south collaboration by linking the TOKOMEZA trial team with the Ebola ça Suffit trial team that had been involved in the ring vaccination trial during the Ebola outbreak in West Africa [16]. The

team included experts in the ring vaccination trial, cold chain specialists, logistics officer and experts in community engagement. Through this collaboration, skills transfer was effected. Picking up from this experience, the Ugandan team is working with the team at Université Catholique de Bukavu in DRC to support implementation of a randomised controlled trial to assess the effectiveness of the Small pox vaccine in preventing RT-PCR confirmed mpox infection among contacts of confirmed mpox infection (SMART trial). Such south-south collaborations should be encouraged as part of clinical trial capacity establishment in Africa.

(v) In country stewardship

This was demonstrated by the government of Uganda and the Ministry of Health which provided logistical and administrative support. Within a few days of the Ebola outbreak, the Ministry of Health assigned scientists to design and implement the ring vaccination trial. Further, the Ministry provided space to house the trial activities. A building within the country's national referral hospital was identified, renovated and made ready for the trial. The building has since been rebranded to a vaccine house, and it houses clinical trial staff and a vaccine cold chain facility.

(vi) Regulatory hurdles

The TOKOMEZA Ebola trial benefited from the joint scientific and ethical review mechanism, which optimises the turnaround time for review and approval of the application. The joint scientific and ethical review mechanism involves the Uganda National Council for Science and Technology (UNCST), Uganda National Health Research Organisation (UNHRO), National Drug Authority (NDA), and the local Research Ethics Committee (REC), to review the trial documents jointly rather than each entity reviewing separately [17]. During the WHO convened workshop held in Uganda in February 2024 that brought together scientists and regulators from 19 African countries, there was overwhelming support and adoption of such mechanisms [18].

In conclusion, establishing vaccine clinical trial capacity in Africa is possible. Having low resource settings partake in vaccine trials could potentially improve the uptake of safe and effective vaccines, in a setting where there is a lot of distrust in vaccine studies elsewhere.

Conclusion

African institutions could capitalise on the epidemics and the accompanying national and global responses to build capacity for clinical trials and position themselves to take part in global vaccine trials.

Authors' contributions
WM and BK conceived the idea; WM prepared the first draft; and AT, MW, HKB, WS, PBK, and BK reviewed and finalised the draft.

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Declarations

Ethics approval and consent to participate
No ethical approval was required.

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Competing interests
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