

Continental concerted efforts to control the seventh outbreak of Ebola Virus disease in Uganda: The first 90 days of the response

JANE RUTH ACENG¹, HENRY KYOBE BOSA¹, NEEMA KAMARA², DIANA ATWINE¹, HENRY MWEBESA¹, HOWARD NYIKA², KATUSIIME MAUREEN¹, CHARLES OLARO¹, ATEK KAGIRITA¹, MOHAMMED LARMODE³, LUL POUT RIEK⁴, ELVIS TEMFACK², STEPHANIE SALYER², DATIVA ALIDDEKI⁴, SHINGAI MACHINGAIDZE², FESTO MAZUGUNI², BRUCE KIRENGA¹, WINTERS MUTTAMBA¹, MISAKI WAYENGERA¹, MUDASHIR BBUYE¹, ARTHUR KASAMBULA¹, DANIEL EURIEN¹, AKELLO GRACE¹, INGRID AMPAIRE¹, ISABIRYE HERBERT¹, MATHEW TUT², DONEWELL BANGURE², WESSAM MANKOULA², IBRAHIMA SONKO², ALINON NOUWAME KOKOU², SIMON MAGODI², ADDIS MHIRAF⁴, DANIEL BULWADDA³, DANIEL KYABAYINZE¹, ZAINAH KABAMI¹, ALLAN MURUTA¹, RONY BAHATUNGIRE¹, UPENTHO GEORGE¹, SUSAN NABADDA¹, GLORIA BIRUNGI¹, KABANDA RICHARD¹, MERAWI ARAGAW² and AHMED OGWELL OUMA²

¹Ministry of Health, Kampala, Uganda; ²Africa Centres for Disease Control and Prevention, Addis Ababa, Ethiopia; ³Makerere University Institute of Infectious Diseases, Kampala, Uganda; ⁴Africa Centres for Disease Control and Prevention, Nairobi, Kenya

DOI: 10.4081/jphia.2023.2735

Abstract. On 20th September 2022, Uganda declared the 7th outbreak of Ebola virus disease (EVD) caused by the Sudan Ebola strain following the confirmation of a case admitted at Mubende Regional Referral Hospital. Upon confirmation, the Government of Uganda immediately activated the national incident management system to initiate response activities. Additionally, a multi-country emergency stakeholder meeting was held in Kampala; convening Ministers of Health from neighbouring Member States to undertake cross-border preparedness and response actions. The outbreak spanned 69 days and recorded 164 cases (142 confirmed, 22 probable), 87 recoveries and 77 deaths (case fatality ratio of 47%). Nine out of 136 districts were affected with transmission taking place in 5 districts but spilling over in 4 districts without secondary transmission. As part of the response, the Government galvanised robust community mobilisation and initiated assessment of medical counter measures including therapeutics, new diagnostics and vaccines. This paper highlights the response

actions that contributed to the containment of this outbreak in addition to the challenges faced with a special focus on key recommendations for better control of future outbreaks.

Introduction

Over the last decade (2012-2022) 14 Ebola virus disease (EVD) outbreaks have been reported in Africa. These have resulted in over thirty thousand cases (~30,000) and thirteen thousand (13,000) deaths, and have occurred in 8 countries (Uganda, Democratic Republic of Congo, Guinea, Mali, Liberia, Sierra Leone, Nigeria and Senegal), mainly in the Central and Western region of the continent (1-4). EVD is a highly infectious and fatal zoonotic disease with high social-economic impact. The Ebola virus belongs to the filoviridae family, genus *Ebolavirus*, comprised of six species including the *Zaire ebolavirus* (ZEBOV) and *Sudan ebolaviruses* (SUDV) which are responsible for the majority of EVD outbreaks in Africa (5).

As of 2022, Uganda has reported 7 outbreaks of EVD. The first outbreak was reported in 2000 from the Northern district of Gulu (6) with subsequent outbreaks occurring in 2007 in the Western part of the country; 2011 from Luweero District; 2012 in Luweero and Kibaale districts; and most recently in September of 2022 from Mubende District (7). Four of these outbreaks have been due to the Sudan species (SVD) of the ebolavirus, including the latest outbreak (8).

Several initiatives have been undertaken over time to strengthen EVD response capacities in Uganda. In 2011, the Prime Minister's office, developed a national disaster preparedness and management policy aimed at establishing institutions and mechanisms to reduce the vulnerability of

Correspondence to: Henry Kyobe Bosa, Ministry of Health, P.O. Box 7272, Kampala, Uganda
E-mail: hskyobe@gmail.com

Neema Kamara, Africa Centres for Disease Control and Prevention, P.O. Box 3243, Addis Ababa, Ethiopia
E-mail: kamanan@africa-union.org

Key words: Ebola, Sudan Ebola virus disease, emergency, response, Uganda

people, livestock and wildlife to disasters (9). In 2013, Uganda established a public health emergency operations centre (PHEOC) to coordinate and analyse health emergencies information in real time (10). The country also developed various public health emergency policies, plans and guidelines, including establishing rapid response teams (RRTs), improving surveillance and contact tracing management; and testing and confirming samples during the COVID-19 pandemic. Uganda continues to demonstrate its commitment to strengthen its International Health Regulations (IHR), 2005 minimum core capacities for prevention, detection and response through conducting regularly evaluations/assessment to identify gaps for improvement (6,7).

This paper highlights the immediate response actions and the major challenges faced within the first 90 days of the 2022 Uganda EVD outbreak response. The paper also outlines key recommendations for swift control of future outbreaks.

Epidemiological situation of SUDV outbreak in Uganda

On 20th September 2022, Uganda declared their 7th outbreak of EVD following the confirmation of a case at Mubende Regional Referral Hospital (MRRH). The confirmed case was a 25-year-old male farmer from Ngabano village, Mubende district who presented with fever and was initially being managed for malaria. Persistent symptoms prompted additional testing from the Uganda Viral Research Institute (UVRI), which confirmed the disease on 19th September 2022. The patient later died on 20th November 2022.

The most proximal case for this outbreak has not been identified so far; however, during an initial outbreak investigation, a cluster of community deaths ($n=19$) with epidemiological linkages to the first reported case was identified to have occurred in Mubende; and (3 community deaths), Kassanda (2) and Kampala (1) districts in August and September 2022 (Fig. 1, Table I). These probable cases were identified to have connections working in or around local mines where bats are known to live. However, in a limited response assessment, samples collected from 189 bats around great Mubende area were tested using polymerase chain reaction (PCR) and found negative for EVD. However, the ecological work still continues post the epidemic phase. Since confirmation, the outbreak spread took place in five districts, but the spill over in 4 districts did not result in secondary transmission (Table I).

By the time the outbreak was declared over (11th of January 2023), a total of 164 cases (142 confirmed, 22 probable) were reported, with 77 deaths (55 confirmed, 22 probable) (case fatality ratio of 47%) and 87 (61%) recoveries noted. We defined probable EVD case as any person who died from 'suspected' EVD and had an epidemiological link to a confirmed case but did not have laboratory confirmation of the disease; and a confirmed EVD case as any suspected or probable cases with a positive laboratory result of either RT-PCR or enzyme-linked immunoassay (ELISA). A suspected EVD case was defined as any person, alive or dead, suffering or having suffered from a sudden onset of high fever and having had contact with a suspected, probable or confirmed Ebola case, or a dead or sick animal, OR any person with sudden onset of high fever and at least three of the following symptoms: headache, vomiting, diarrhoea, anorexia/loss of appetite, lethargy,

stomach pain, aching muscles or joints, difficulty swallowing, breathing difficulties, or hiccups.

The mean age of cases was 28 ± 15.04 years. In univariate analysis, age group 20 to 39 years (34%, $P=0.008$) and Mubende District (62%, $P=0.005$) significantly survived compared to those who died (Table II). Among the confirmed cases, 19 (13.4%) were healthcare providers, of whom 7 (39%) died; and 14 (9.9%) were children between the ages of 0 and 9 years of whom 8 (57%) died. The highest case fatality ratio was among children <10 years (75.0%) and adults between 40 to 49 years (61.5%) (Table II).

Outbreak response strategy

Cross-border coordination and collaboration. The PHEOC was immediately activated upon confirmation of the first case. The Ministry of Health, and the World Health Organisation (WHO) Country office for Uganda officially declared the 7th EVD outbreak and called on the public to be vigilant and report any suspected cases for further investigation. Immediate actions taken included strengthening outbreak investigation in the Mubende district that had started on 17th September 2022, convening a high-level emergency stakeholder meeting in Kampala with neighbouring countries, Regional Economic Communities, Africa Centers for Disease Control and Prevention (Africa CDC)/Africa Union, WHO and partners to deliberate on concrete measures to enhance preparedness and readiness for EVD in the region. This emergency convening led to establishing the Africa Ebola Coordination Taskforce (AfECT) among at-risk Member States to strengthen communication, preparedness and response on 12th October 2022. The stakeholders endorsed the development of legal and regulatory processes for cross boarder deployment of rapid response teams and public health experts.

As part of giving impetus to evidence generation and science-based decision-making, stakeholders also agreed on building capacity for research and biomedical technologies for EVD. In acknowledging that timely sharing of technical expertise and other resources and assets was critical for EVD preparedness and response, continental stakeholders also committed to undertake prompt communication of epidemiological and laboratory surveillance data and other relevant reports sharing information on potential security threats and other security issues occurring in areas affected by outbreaks. To strengthen continental preparedness, benchmarking visits, joint simulation exercises, and joint trainings were to be done between Member States at risk of EVD to build workforce capacity, including strengthening capacities at primary and community levels. The meeting successfully spearheaded the development of a collaborative framework to coordinate preparedness and response to Ebola Virus Disease outbreaks and other public health emergencies and a six-month joint action plan (December 2022 to May 2023) focusing on strengthening coordination, human resources and information sharing among Member States. The Government of Uganda also instituted three rounds of 21-day targeted lockdown in the two most affected districts to limit transmission in the affected districts, specifically the city and shield the rest of the world (11).

Table I. Distribution of EVD cases and deaths by district in Uganda, as of 11th January 2023.

District	# of Sub counties affected	Confirmed cases (n=142)	Confirmed deaths (n=55)	Probable deaths (n=22)	Recoveries (n=87)
Kyegegwa	02	04	01	00	03
Kassanda	04	49	20	02	26
Mubende	11	64	29	19	38
Wakiso	03	04	00	00	03
Kampala	03	17	02	01	16
Jinja	01	01	01	00	00
Masaka	01	01	01	00	00
Bunyangabu	01	01	00	00	01
Kagadi	01	01	01	00	00

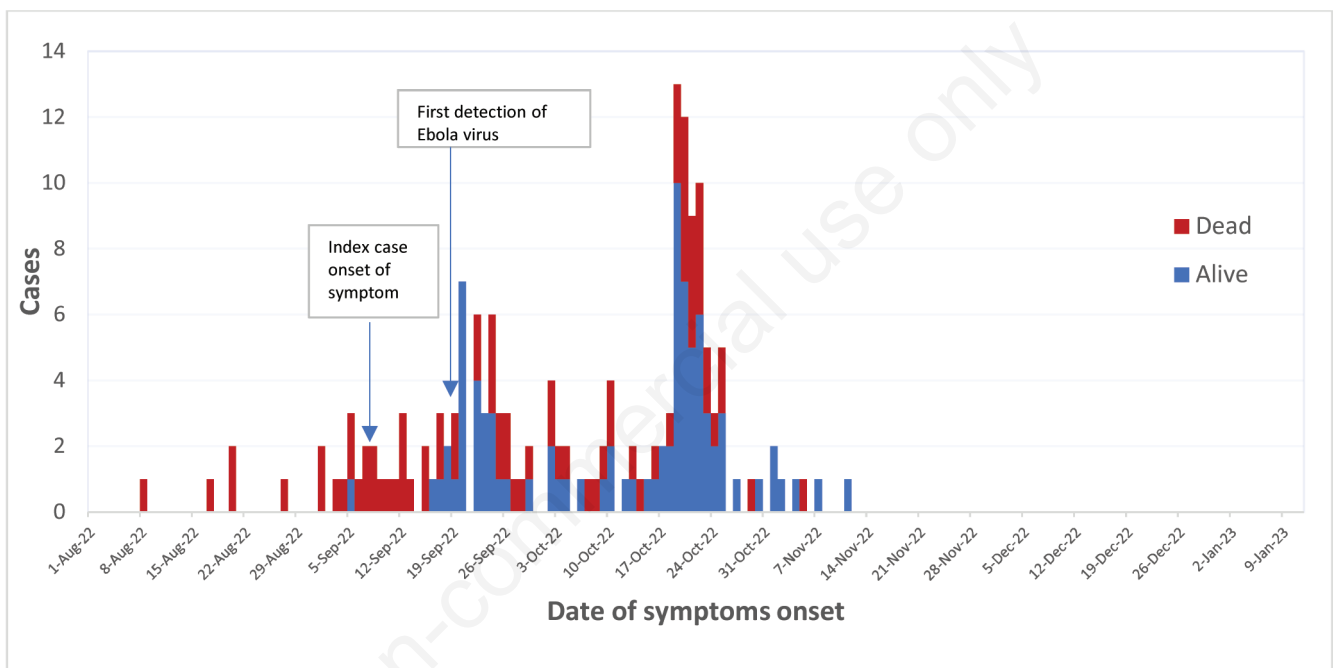


Figure 1. Epidemiological curve of probable and confirmed Ebola cases in Uganda, 1 August 2022 to 11 Jan 2023.

Country level coordination

Ministry of Health repurposed the existing COVID-19 response structures whose overall supervision was under the National Task Force. The National Task Force was chaired by the Director General of the Health Services. Above the National Task Force (NTF) was a Ministerial Strategic Committee chaired by the Minister of Health. The Strategic Committee and the NTF provided overall strategic direction to the response as well as coordination of partners in the response. The Incident Management Team (IMT) was activated within the Ministry of Health (MOH) and structured around the critical incident management system functions and their associated sub-functions with ramifications at sub-national level. The IMT reported to the Strategic Committee and NTF and was led by the Incident Commander. The IMT was responsible for day-to-day management and technical implementation of the Ebola response activities. The IMT comprised pillars headed

by pillar heads drawn from various departments within MOH and each pillar had clear roles and responsibilities. The pillars included: Coordination, Surveillance, Laboratory, Case management (including Infection Prevention and Control, safe and dignified burials, Psychosocial support sub-pillars), Water, Sanitation and Hygiene (WASH), Risk communication and social mobilization, Community engagement, Logistics, Continuity of Health services and Vaccination. Daily coordination meetings were conducted to ensure pillar functionality and inter-linkages were enhanced. The IMS structure ensured that all implementation takes place effectively and was designed to afford the response flexibility needed to address potential changes as the outbreak evolved to different district. Field incident Commanders with tactical field teams were assigned to support Mubende, kasanda, Masaka, Kampala and jinja district task Force a similar structure like the NTF. The IMT reported to the Strategic Committee and was led by the Incident Commander. Subject Matter experts developed

Table II. Demographic characteristics of confirmed and probable Ebola cases in Uganda as of 11th January 2023 (N=164).

Variables	Alive n (%)	Dead n (%)	Total n (%)	Case fatality ratio (%)	χ^2 P-value
Age, years, mean (SD)	-	-	28 (15.04)		
Age group					
0-9	6 (7)	18 (23)	24 (15)	75.0	0.008
10-19	10 (11)	8 (10)	18 (11)	44.4	
20-29	30 (34)	15 (19)	45 (27)	33.3	
30-39	27 (31)	15 (21)	42 (26)	38.1	
40-49	9 (10)	13 (17)	22 (13)	59.1	
50+	5 (6)	8 (10)	13 (8)	61.5	
Sex					
Female	31 (36)	38 (49)	69 (42)		0.076
Male	56 (64)	39 (51)	95 (58)		
District					
Bunyangabu	1 (1)	0 (0)	1 (1)		0.005 ^a
Jinja	0 (0)	1 (1)	1 (1)		
Kagadi	0 (0)	1 (1)	1 (1)		
Kampala	16 (18)	2 (3)	18 (11)		
Kassanda	28 (32)	23 (30)	51 (31)		
Kyegegwa	3 (3)	1 (1)	4 (2)		
Masaka	0 (0)	1 (1)	1 (1)		
Mubende	35 (40)	48 (62)	83 (51)		
Wakiso	4 (5)	0 (0)	4 (2)		

^aP-value for Fisher's exact test; SD, standard deviation.

Documenting the Ebola virus disease response in Uganda, 19 September, 2022 to 11 January, 2023

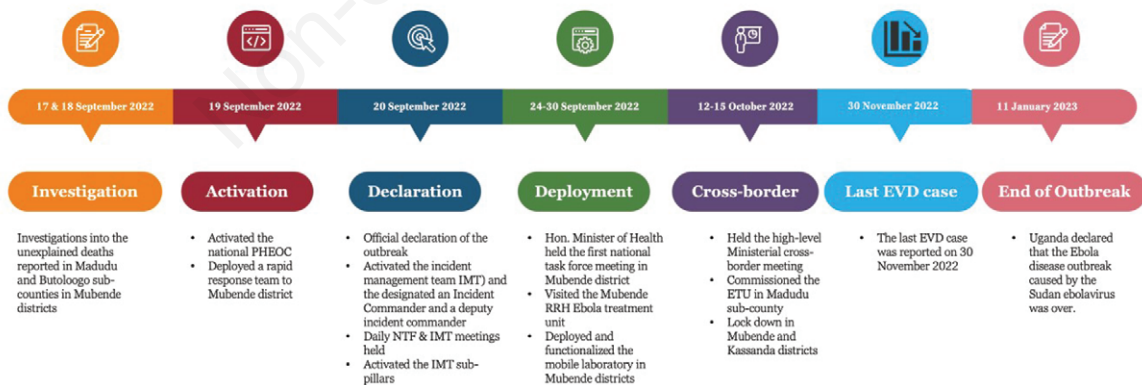


Figure 2. Timelines of events.

the National Response plan which was reviewed, approved and implemented. The NTF mobilised resources and coordinated cross-border collaborations in PHE surveillance and response.

Surveillance. The IMT conducted risk profiling and mapping of all the district neighbouring Mubende to assess the

vulnerabilities and response capacities. The Ministry of Health deployed a team that was entirely responsible to conduct case investigations and supported in adopting the case definitions through analysis of case reports and field visits to identify possible sources of exposure and aid risk categorisation and contact tracing. The surveillance system was strengthened by establishing an alert management desk to receive alerts

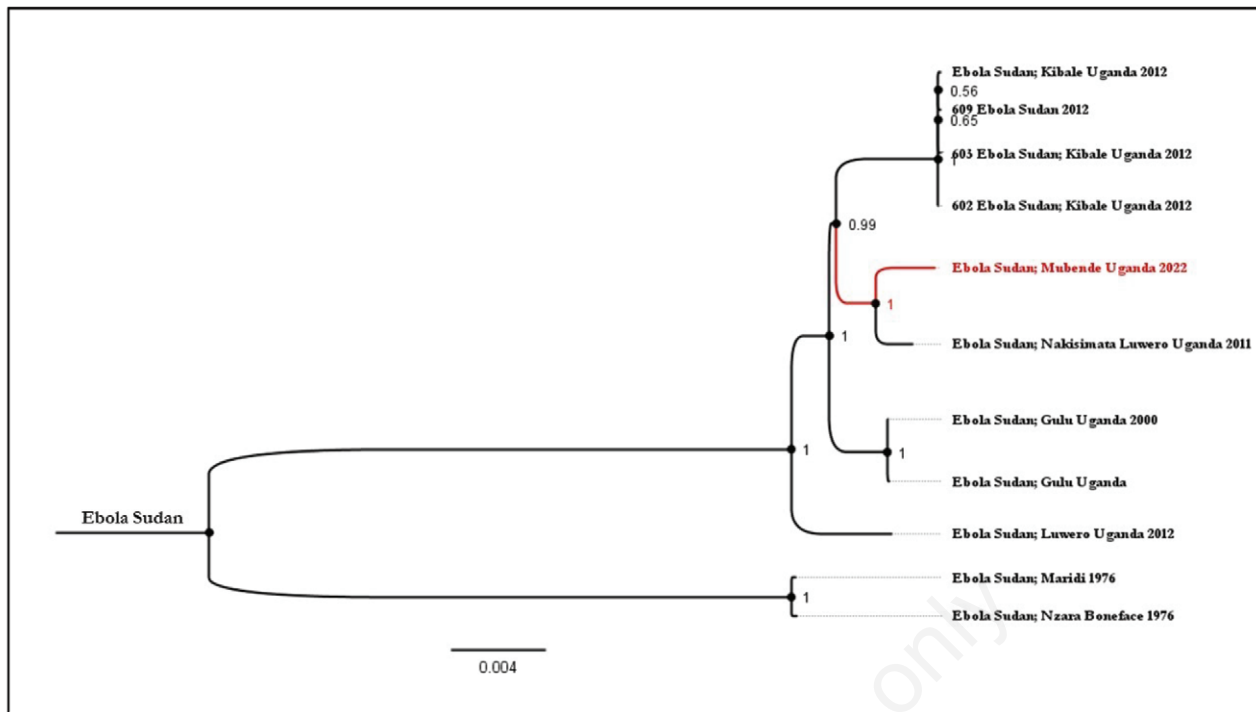


Figure 3. The phylogenetic tree with the bootstrap values showing the relationship of the Mubende SUDV strain (2022) with Nakisimata strain previously identified in Gulu and Luwero districts in Uganda. The lineages have been inferred using maximum likelihood and the General Time Reversible model.

from the health facility and community levels. This was key in identifying community infections, characterising affected communities and monitoring disease patterns and trends. In addition, management of contacts was affected. As of 11th January 2023, 4,793 contacts were listed in the district contact tracing database (Mean 29.2 contacts per case) and the contact follow-up rate was 100%.

Diagnostics. Uganda is a beneficiary of the East African Public Health Laboratory Network which facilitated deployment of a mobile laboratory within 7 working days of the outbreak. This added capability to the laboratories to reduce the long turnaround time to around 6 h. The laboratory capability included conducting high-volume diagnostic testing and genomic sequencing. Genomic sequencing was conducted to understand linkage or any differences between the current strain to previous Ebola outbreaks. Analysis of samples taken from the confirmed case showed that this outbreak was genetically linked to previous outbreaks and conservation of the genetic similarity with the original virus in the 1970s (8) Genomic sequences showed that Nakisamata strain that first appeared in Luwero district, in May 2011 had the highest percentage identity and similarity at 99.6%, followed by Gulu strain at 99.3% and Kibale at 99.2% (12). Although the Mubende outbreak genome sequence is most similar to the Nakisamata strain, phylogenetic analysis shows that it belongs to a bigger clade of Ebola viruses previously detected in Southern Uganda and documented in outbreaks in Luwero and Kibaale (Fig. 3) (13). Genomic sequencing was also used to identify linkages between the cases whose epidemiological link was not very clear after conducting case investigations. This helped close any gaps in the transmission chain of cases.

Risk communication. Teams made frequent radio talk shows for risk communication to the communities. The MOH adopted a robust community engagement work plan targeting specific population, hence a tailored community response. The MOH employed a dynamic social listening-bottom-up approach for risk communication. This involved Uganda's leadership at various levels holding community gatherings with local council chairpersons and Village Health Teams in most affected districts of Mubende, Kassanda and Kyegegwa to listen to their needs, worries and opinions on the outbreak response. This approach provided a forum for communicating correct information and dispelling rumours, hence fostering local trust in the response system. The response team adopted an interpillar community engagement strategy-eight groups with technical representation from all pillars of response were constituted; the group are led by the MOH officials who conducted daily community visits to mapped hotspot villages. The groups engaged and assessed the ongoing response activities and provided feedback to the district task force for improvement.

Patient management. In Mubende district, an Ebola treatment unit (ETU) comprised of 48 beds was set up with 24 beds each for suspected and confirmed cases at the MRRH. The emergency unit was repurposed to provide an additional 23 beds for suspected cases. A survivor's clinic was also set up for integrated mental health and psychosocial support services during recovery. Considering the distance from Mubende to UVRI, a mobile laboratory was also set up which considerably reduced the sample turnaround time from 24 to 6 h. In Madudu sub-county, the epicenter, an 8-bed transition ETU was set up. A few-confirmed cases, specifically a cluster of healthcare workers were managed a treatment unit in Fort Portal (6 bed).

Later, these healthcare workers were transferred to Entebbe isolation units (67 beds). The two facilities were prioritized for health worker management, and Kampala Metropolis confirmed cases.

Mortality surveillance. To facilitate an end-to-end case identification process during the response, a SUDV mortality surveillance system was implemented that identified all deaths irrespective of cause in all the response districts to identify silent transmission and not miss any case. A presidential directive was sent out initially to the epi-centre districts (Mubende and Kassanda) to ensure samples were collected from all dead bodies. Subsequently we rolled the directive to other response districts (Kampala, Jinja, Masaka). Teams from national level were deployed to affected districts to establish networks for death reporting at health facility and community level through trainings of health workers (laboratory officers, morticians and mortuary attendants and surveillance officers). At facility level, the in-charges were alerted to have deaths registered and captured in the mortuary register, samples collected before discharging the body outside the unit.

Community engagement. Orientation of Village Health Teams, parish coordinators, funeral homes, police and security organs, village chairpersons, media stations were conducted and toll-free lines shared to enable them easily update the alert management desk in case of any death in the community. Upon receiving a death alert, teams were dispatched from the call centre (laboratory, surveillance officers and morticians or Safe and Dignified Burial teams (SDB)) to verify, complete a case investigation form and collect samples from carderviors (arterial blood and/or buccal swab) for SUDV testing. The enhanced mortality surveillance during this response contributed to real-time detection of deaths and informed quick decisions during the response.

Safe handling and dignified burial. To ensure safe handling and dignified burial (SDB) of confirmed and suspected deaths, over 350 burial teams were trained, PPEs and supplies provided and deployed in the affected districts. We had one SDB team trained per subcounty to conduct the burials. Mubende and Kassanda districts, which recorded the highest death rates, 69 and 29% respectively had SDB teams conduct burials for all deaths. The SDB team strictly followed the safe and dignified protocol and procedures and ensured the families of the deceased were engaged in the process. These teams verified, tested and recorded all deaths that occurred in Mubende and Kassanda. SDB teams in other response districts (Masaka, Jinja, Kampala Metropolitan Area) were trained and kept on alert mode in case the need to bury a suspicious death arose as per the Ebola protocols. Using SDB approach in the epi-centre districts was essential in reducing the risk of transmission to, families and communities. However, its implementation was not without challenges such as shortage of vehicles, fuel and airtime for the teams to communicate during death verification, workload especially at the peak of the outbreak, and violence especially at the start of the outbreak. Nevertheless, the teams were dedicated in ensuring safe and dignified burials which reduced the risk of transmission of the virus. Engagement of key opinion leaders was key in reducing violence in the

community. We had partners supporting with fuel and vehicles to ease movement of SDB teams.

Therapeutics trials. Although the management of SUDV is largely supportive, the MOH, on issuance of WHO interim guidelines on SUDV therapeutics, approved two investigational therapeutics (MBP134 and remdesivir) for administration under compassionate use based on clinician discretion and patient consent (14). Significantly, in this outbreak, patients were able to access investigational therapeutics within two weeks of declaration of the outbreak through a bilateral request to the United States government. Due to limited supplies of MBP134, the initial donated amount was prioritized for special populations including children. Remdesivir is locally available, but there were sufficient therapeutics by the 5th week of the response. Health workers in various ETUs were trained onsite to build capacity to deploy these products in terms of transportation, storage, preparation, and administration, and to monitor for and report adverse events.

In the absence of proven and licensed medical countermeasures against SUDV ebolavirus, the Scientific Advisory Committee (SAC) instigated the development of Uganda's strategic agenda for EVD 2022. In addition, recommendations were made for the compassionate use of convalescent plasma from survivors of previous SUDV outbreaks in Uganda, use of remdisivir and the monoclonal antibody cocktail MBP134. Moving forward, SAC recommended a stayed approach of inter-epidemic research to generate the needed evidence for future outbreaks. A dedicated research pillar has been erected under the IMT to oversee and coordinate these research and innovation efforts.

Vaccination against SUDV. Outbreak response measures for infectious diseases like Ebola include vaccinating people who have been exposed or had contact. Whereas, there was a vaccine effective against Ebola Zaire, a vaccine for Ebola Sudan (the strain that responsible for the outbreak) was not available. Several candidate vaccines were available but these needed to be evaluated in a clinical trial setting. A rapid ring vaccination trial for 3 candidate vaccines was approved within the shortest time possible (working with the WHO Blueprint and developers). Within one week of the outbreak, the World health Organisation (WHO) and Ministry of Health-Uganda assigned a Principal Investigator (PI) to lead a trial to evaluate the efficacy and safety of a Sudan ebolavirus candidate vaccine in Uganda. The PI working with the Ministry of health assembled an Investigation team of scientists to implement the trial. The 'Ring vaccination trial to evaluate the efficacy and safety of a Sudan ebolavirus vaccine in Uganda' was implemented by Makerere University Lung Institute (MLI). South-South collaboration was demonstrated during the trial through WHO seconding a team of scientists to work with the Ugandan team. The technical team had been part of Ebola 'ça Suffit' in West Africa. The team worked with the Ugandan Investigators to finalise and adapt a generic protocol (Ebola 'ça suffit' trial protocol). The trial technical team also worked with the Ugandan team to quickly establish bases for the trial, all furnished with ultra-cold chain facilities to handle the vaccines. The investigation team leveraged the joint scientific

Table III. Period taken to achieve the different trial milestones.

	Milestone	Time taken ^a
1	Principal Investigator appointment by MoH	1 week
2	Arrival of WHO technical assistance for the trial	2.5 weeks
3	Sub-Investigator appointments by MoH	3 weeks
4	Finalisation/Adaptation of generic protocol	3 weeks + 3 days
5	Setting up an ultra-cold chain facility	6 weeks
6	IRB approval	8 weeks
7	Uganda National Council for science and technology approval	9 weeks
8	National drug Authority trial certificate	9 weeks
9	GCP and protocol training of staff	6 weeks
10	Dry runs	8 weeks
11	Wet runs	9 weeks
12	Arrival of 1st candidate vaccine in the country	11 weeks
13	Ring definition	11 weeks

and ethical review mechanism to optimize the turnaround time for the review and approval of the trial application. Under this mechanism, joint reviews are carried out jointly with other regulatory bodies and comments to the application for the attention of the Investigators availed, leading to a faster approval process. Indeed, the trial was able to get all the ethical and regulatory approvals within 9 weeks of the outbreak, a feat that had not been heard of. MLI leveraged the COVID-19 research experience and structures to support the trial processes including logistics management, trial staff recruitment, training and deployment. This together with the south-south collaboration and stewardship from the Ministry of Health were instrumental in ensuring the trial was ready to recruit the first participant by the time the vaccines arrived in the country 11 weeks after the outbreak was announced (Table III).

Challenges and key strategies to control the outbreak. Despite significant coordinated response efforts, several challenges threatened the optimal control of the outbreak. These challenges include: Malaria-Ebola co-circulation and Malaria-Ebola co-infection, lack of adequate resources, lack of approved therapeutics and vaccines for Sudan Ebola virus, community non-compliance and sub-optimal community engagement, stigma, inadequate surveillance, inadequate health infrastructure and low healthcare worker compliance to standard Infection Prevention and Control (IPC) measures.

Malaria-Ebola co-circulation. Uganda has a high malaria prevalence. In the early phases of Ebola illness, malaria and Ebola signs and symptoms do overlap. As a result, the window of suspicion for Ebola among the care providers was compromised. They instead had a higher suspicion index for malaria than for Ebola. Hence, some patients were treated for malaria first, delaying referral for Ebola testing, which contributed to the patients' delays in receiving Ebola treatment and overall poor outcomes, especially at the start of the outbreak. Whereas WHO recommends malaria mass drug administration in complex emergencies, the concept of Malaria-Ebola

co-circulation, and co-infection is poorly described (11,15,16). This also exposed the health care workers, leading to Ebola infections. However, along the response, this limitation was overcome after notifications and sensitizations of healthcare workers and communities on Ebola virus clinical manifestations and the need to report and investigate any case exhibiting Ebola-Malaria clinical signs.

Lack of centralized resource management pool. Limited capacity to manage financial, infrastructural and human resources to control the outbreak especially in the current context of the COVID-19 pandemic and other pre-existing major public health problems such as HIV/AIDS, TB and malaria. As the situation was evolving more support in the form of in-kind streamed in the country and a proper control mechanism was not in place to track what has been received and utilized. In an outbreak of this nature and magnitude, there is a need to establish a transparent, reliable and regularly updated accountability system to win the trust of all partners and stakeholders involved.

Lack of approved therapeutics and vaccines for Sudan Ebola virus. Although advances have been made in therapeutics and vaccines for Zaire EBOV, no vaccines or therapeutics are currently approved for the SUDV cause SVD outbreaks are rare, and smaller in magnitude (12). While capacity to deploy therapeutics was established in this outbreak, no randomized controlled trials were implemented during this outbreak to generate high quality data on efficacy and safety for the Sudan Ebola strain. Optimized supportive care for the patients was prioritized. Acceleration of the development and deployment of therapeutics, vaccines and diagnostics for SUDV is needed to improve outcomes for patients in future outbreaks.

Community poor-compliance and sub-optimal community engagement. Community poor-compliance to laid down interventions was a challenge, with some sick patients (n=2) escaping from EVD treatment centres and contacts (n=18)

relocating to other towns. This resulted in new foci of transmission as was seen in the Kampala city cluster of transmission around an escapee who left Mubende to Luwero to seek traditional treatment after feeling ill. Similar scenarios were observed in Entebbe and Masaka districts. This phenomena has been reported in previous EVD outbreaks in DRC and Liberia where cases fled to urban areas resulting in unprecedented case counts (17) Sub-optimal community engagement in the response was observed by continuing risky practices such as exhuming dead bodies to perform burial rituals, as was observed in Kassanda district which resulted in 23 people being infected. Upscaling risk communication and strengthening community engagement in affected districts remains critical to a successful response. Empowerment of community leaders with the right messages and collaborating with them to set up interventions that take into account their values and cultures is also of paramount importance. Clear, concise, and tailored messages translated into local languages should be emphasized. Building a trustworthy and trusted response integrated within the communities is key to success (18).

Stigma. Survivors and relatives of cases have reportedly been stigmatised and ostracised in the communities, predisposing them to mental ill-health and this may result in non-reporting of suspected cases for fear of being confirmed and consequently ostracised. EVD survivors may experience some EVD related symptoms after discharge that may last for some time (19,20). This may be perceived by the communities as continuation of sickness by survivors. Support to monitor survivors when they eventually return to their communities in order to minimize the risk of stigmatization, transmission of EVD to those not already affected, and post-EVD complications should be prioritized. Documenting health concerns of survivors and providing comprehensive supportive care will lead to better recovery. Survivors' clinics have been established in Mubende and Kassanda districts and these should be equipped with necessary supplies and logistics (human resources, vehicles, diagnostics among others) to facilitate medical and psychological support to survivors.

Inadequate surveillance. Inadequate surveillance led to late detection of the outbreak which was not suspected when clusters of deaths had occurred since August 2022 in Ngabano village; Mubende district. Moreover, at the health facility, there is low index of suspicion of EVD as seen with the first case who was initially treated for malaria, a practice which not only exposes health care practitioners but increases the risk of disease spread. Strengthening early warning systems including revitalizing event-based surveillance systems at the community and health facility levels will enable detection of small outbreaks and unusual events. There is a need to support sensitization of clinicians and healthcare workers on using the EVD standard case definitions and reporting. Early detection of cases leads to early containment of the outbreaks (12).

Inadequate health infrastructure and low healthcare worker compliance to standard Infection Prevention and Control (IPC). The health system will not adequately manage

diseases with outbreak potential if there are limited treatment centres/isolation facilities. There are currently three (3) functional ETUs located in Mubende, Entebbe and Kassanda, and two isolation units in Mulago hospital and Madudu health centre. Cases were being transported to Mubende district for treatment, posing a risk of infection to health workers (HCWs) as was seen by the infection and subsequent death of an ambulance driver. Additionally, adherence to IPC by the healthcare workers in the healthcare settings is minimal. Most healthcare workers have had to be quarantined, while others got due to poor adherence to standard IPC measures when handling patients. In some healthcare facilities, this led to suboptimal provision of healthcare services because of shortage of staff. However, it should be noted that most of the HCWs infections occurred during the initial period when the EVD cases had not been declared. This challenge could be solved by implementing comprehensive IPC programs including capacity building, mentorship and supportive supervision to sustain practice and adherence of IPC in ETUs, non-affected hospitals and the communities (21). These programs should be routine to keep the health workforce up to date and ready for the next outbreak.

Conclusion

The early and rapid escalation of measures instituted, plus the ongoing review and adjustment of interventions informed by emerging evidence in the response in this outbreak managed to slow down transmission, leading to rapid containment. Despite that, more needs to be done. The Government of Uganda exhibited high transparency in responding to the outbreak and all stakeholders were involved in planning response measures. The strategic partnership of the Government of Uganda with Africa CDC and WHO was a critical element of a coordinated regional response to public health emergencies. Several implementation challenges were identified, particularly in community engagement and inadequate human and financial resources, which calls for enhanced mobilization. These had roots in community apathy generated by the aggressive public health measures during COVID-19 (22). Community engagement, facility-based IPC, vaccine development and enhanced community surveillance will need to be prioritised in the short to medium term to control the future outbreaks.

Acknowledgement

The Ministry of Health, Uganda and Africa CDC would like to appreciate the Office of the Prime Minister for providing strategic leadership to the response. In addition, we acknowledge partners including but not limited to World Health Organization (WHO), United Nations International Children's Emergency Fund (UNICEF), United States Centres for Disease Prevention and Control (US CDC), United States Agency for International Development (USAID), Médecins Sans Frontiers (MSF), World Food Program (WFP), International Organization for Migration (IOM), United Kingdom Aid, European Union, Save the Children and African Union for their valuable contributions to the response and containment of EVD in Uganda.

Funding source

This article received no specific funds from any agency for publication.

Author's contributions

Jane Ruth Aceng, Ahmed Ogwell Ouma, Henry Mwebesa, Olaro Charles, Daniel Kyabayinze, approved the final version to be published. Kyobe Henry Bosa, Lul Pout Riek, Neema Kamara, Howard Nyika, Stephanie Salyer, Dativa Aliddeki, Elvis Temfack, Shingai Machingaidze, Festo Mazuguni, Larmode Mohammed, Bruce Kirenga, Winters Muttamba, Misaki Wayengera, Katusiime Maureen, Mudashir Bbuye, Arthur Kasambula, Daniel Eurien, Akello Grace, Ingrid Ampaire, Isabirye Herbert conceptualized, designed and drafted the article. Merawi Aragaw, Mathew Tut, Donewell Bangure, Wessam Mankoula, Ibrahimia Sonko, Alinon Nouwame Kokou, Simon Magodi, Addis Mhiraf, Zainah Kabami, Allan Muruta, Rony Bahatungire, Upenotho George, Susan Nabadda, Gloria Birungi, Kabanda Richard, Shingai Machingaidze reviewed and edited the manuscript. Kyobe Henry Bosa, Merawi Aragaw and Lul Pout Riek revised the manuscript for intellectual content.

Conflict of interest

The authors have declared that they have no financial or personal relationship that may have influenced to write this article.

References

- Rugarabamu S, Mboera L, Rweyemamu M, Mwanyika G, Lutwama J, Paweska J and Misinzio G: Forty-two years of responding to Ebola virus outbreaks in Sub-Saharan Africa: A review. *BMJ Glob Health* 5: e001955, 2020.
- Awah PK, Boock AU and Kum KA: Ebola virus diseases in Africa: A commentary on its history, local and global context. *Pan Afr Med J* 22 (Suppl 1): S18, 2015.
- Muyembe-Tamfum JJ, Mulangu S, Masumu J, Kayembe JM, Kemp A and Paweska JT: Ebola virus outbreaks in Africa: Past and present. *Onderstepoort J Vet Res* 79: 451, 2012.
- History of Ebola Virus Disease (EVD) Outbreaks|History|Ebola (Ebola Virus Disease)|CDC [Internet]. 2022 [cited 2022 Dec 2]. Available from: <https://www.cdc.gov/vhf/ebola/history/chronology.html>.
- Ebola virus disease|Nature Reviews Disease Primers [Internet]. [cited 2022 Nov 6]. Available from: <https://www.nature.com/articles/s41572-020-0147-3>.
- Kayiwa J, Kasule J, Ario A, Sendagire S, Homsy J, Lubwama B, Aliddeki D, Kagirita A, Komakech I, Brown V, *et al*: Conducting the Joint external evaluation in Uganda: The process and lessons learned. *Health Secur* 17: 174-180, 2019.
- JEE_2021 Report on the 2021 Uganda Multi-Sectoral Self-Assessment and Operational Planning [Internet]. [cited 2023 Feb 17]. Available from: https://www.cphl.go.ug/sites/default/files/2022-07/JEE_2021%20Uganda%20Mult-sectoral%20Self-Assessment%20Report_26Oct2021%20%282%29%20%281%29.pdf.
- Li YH and Chen SP: Evolutionary history of Ebola virus. *Epidemiol Infect* 142: 1138-1145, 2014.
- The National Policy for Disaster Preparedness and Management|United Nations Development Programme [Internet]. [cited 2022 Nov 17]. Available from: <https://www.undp.org/uganda/publications/national-policy-disaster-preparedness-and-management>.
- Borchert JN, Tappero JW, Downing R, Shoemaker T, Behumbiize P, Aceng J, Makumbi I, Dahlke M, Jarrar B, Lozano B, *et al*: Rapidly building global health security capacity-Uganda demonstration project, 2013. *MMWR Morb Mortal Wkly Rep* 63: 73-76, 2014.
- Alonso PL: The role of mass drug administration of Antimalarials. *Am J Trop Med Hyg* 103 (2 Suppl): 1-2, 2020.
- Shoemaker T, MacNeil A, Balinandi S, Campbell S, Wamala JF, McMullan LK, Downing R, Lutwama J, Mbidde E, Ströher U, *et al*: Reemerging Sudan Ebola virus disease in Uganda, 2011. *Emerg Infect Dis* 18(9):1480-3, 2012.
- Albariño CG, Shoemaker T, Khristova ML, Wamala JF, Wamala JF, Balinandi S, Tumusiime A, Campbell S, Cannon D, Gibbons A, *et al*: Genomic analysis of filoviruses associated with four viral hemorrhagic fever outbreaks in Uganda and the Democratic Republic of the Congo in 2012. *Virology* 442: 97-100, 2013.
- Sudan Ebolavirus-Experts deliberations. Candidate treatments prioritization and trial design discussions [Internet]. [cited 2023 May 18]. Available from: <https://www.who.int/publications/m/item/sudan-ebolavirus-experts-deliberations-candidate-treatments-prioritization-and-trial-design-discussions>.
- Edwards HM, Counihan H, Bonnington C, Achan J, Hamade P and Tibenderana JK: The impact of malaria coinfection on Ebola virus disease outcomes: A systematic review and meta-analysis. *PLoS One* 16: e0251101, 2021.
- World Health Organization. Mass drug administration for falciparum malaria: A practical field manual [Internet]. Geneva, World Health Organization, 2017. Available from: <https://apps.who.int/iris/handle/10665/259367>.
- Nyenswah T, Fahnbulleh M, Massaquoi M, Nagbe T, Bawo L, Falla JD, Kohar H, Gasasira A, Nabeth P, Yett S, *et al*: Ebola epidemic-Liberia, March-October 2014. *Morb Mortal Wkly Rep* 63: 1082-1086, 2014.
- Fallah MP, Skrip LA and Enders J: Preventing rural to urban spread of Ebola: Lessons from Liberia. *Lancet* 392: 279-280, 2018.
- de St Maurice A, Ervin E, Orone R, Choi M, Dokubo EK, Rollin PE, Nichol ST, Williams D, Brown J, Sacra R, *et al*: Care of Ebola survivors and factors associated with clinical Sequelae-Monrovia, Liberia. *Open Forum Infect Dis* 5: ofy239, 2018.
- Tiffany A, Vetter P, Mattia J, Dayer JA, Bartsch M, Kasztura M, Sterk E, Tijerino AM, Kaiser L and Ciglencski I: Ebola virus disease complications as experienced by survivors in sierra Leone. *Clin Infect Dis* 62: 1360-1366, 2016.
- Shrivastava SR, Shrivastava PS and Ramasamy J: Ebola disease: Infection prevention and control in hospital and community settings. *Iran J Nurs Midwifery Res* 20: 526-527, 2015.
- Okello G, Izudi J, Teguzirigwa S, Kakinda A and Van Hal G: Findings of a Cross-sectional survey on knowledge, attitudes, and practices about COVID-19 in Uganda: Implications for public health prevention and control measures. *Biomed Res Int* 2020: 5917378, 2020.