

Ebola confirmed in Uganda and suspected in DRC

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Prepared by the GloPID-R Research and Policy team with support from the Pandemic PACT programme

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Background

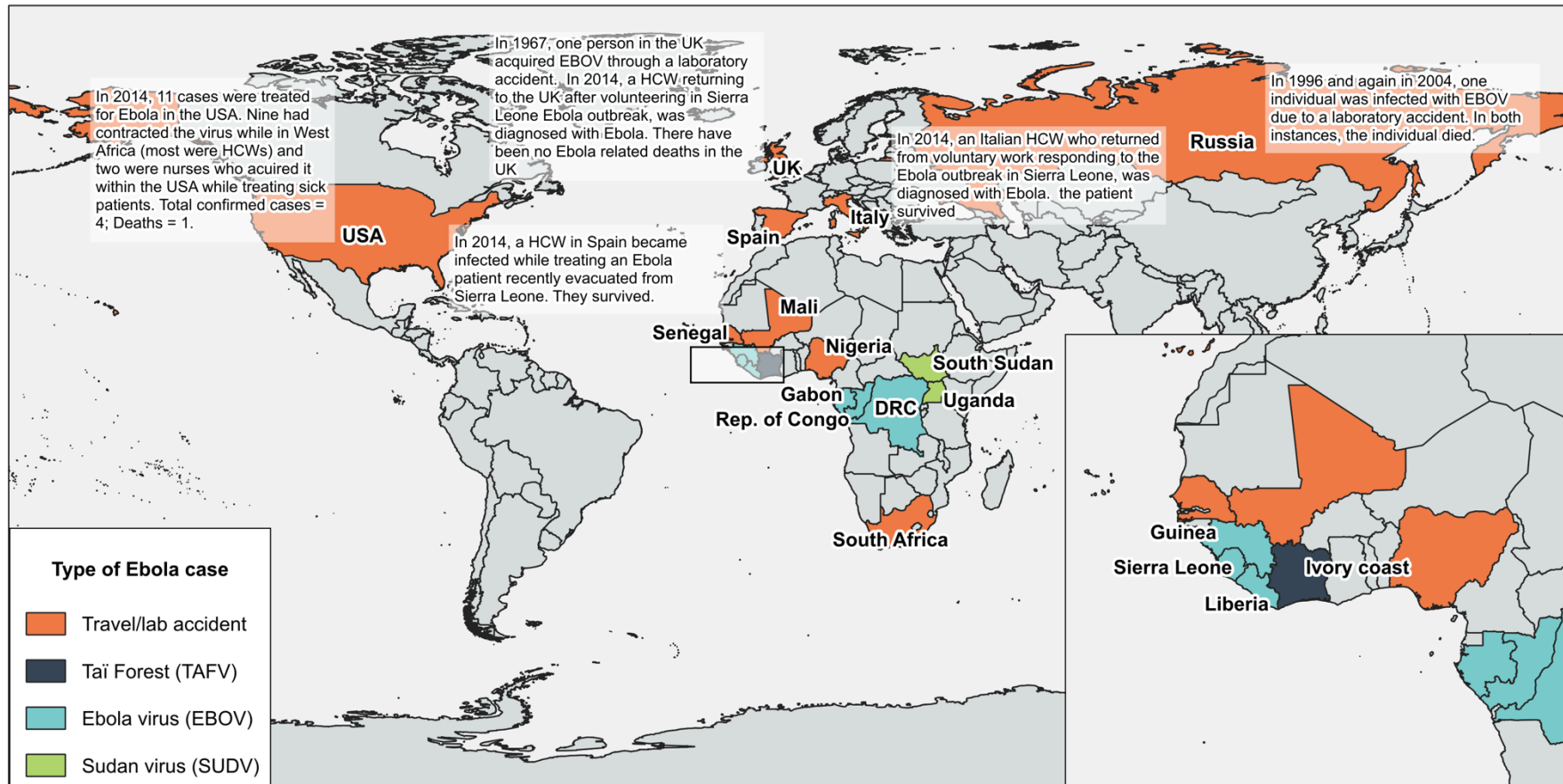
On 30 January 2025, Uganda announced one confirmed case of Sudan Virus Disease (SVD) after a nurse from the capital city, Kampala, died¹. The announcement came soon after the Democratic Republic of Congo (DRC) reported 12 suspected cases of Ebola and eight deaths in the Equateur province². SVD and Ebola Virus Disease (EVD) are highly infectious, potentially lethal zoonotic diseases caused by Sudan Virus (SUDV) and Ebola Virus (EBOV), respectively. Both are part of the Orthoebolavirus genus (formerly ebolavirus) belonging to the *Filoviridae* viral family^{3–9}. There are six Orthoebolaviruses (**Table 1**)^{6,8}. The two main viral species responsible for infecting humans are EBOV and SUDV, and the resulting disease is often referred to as Ebola. SUDV and EBOV were first discovered in 1976 after two almost simultaneous outbreaks occurred in South Sudan and the Democratic Republic of the Congo (DRC), resulting in over 500 cases^{3,5,10–12}. South Sudan, which was affected by SUDV, had a mortality rate of 53%, and the DRC, which was affected by EBOV, had a mortality rate of 88%^{10–12}. In South Sudan, the outbreak is believed to have originated in cotton factory workers in Nzara before spreading to nearby Maridi, where transmission was intensified among healthcare workers in active hospitals^{11,12}. In the DRC, cases were predominantly spread in hospitals and clinics via contaminated needles after the index case was treated at a hospital^{10,12}.

Table 1: Types of orthoebolaviruses according to the International Committee on Taxonomy of Viruses (ICTV)

Virus name	Virus name Abbreviation	Human disease caused by virus (if applicable)
Ebola Virus	EBOV	Ebola Virus Disease (EVD)
Sudan Virus	SUDV	Sudan Virus Disease (SVD)
Bundibugyo virus	BDBV	Bundibugyo virus disease
Taï Forest Virus	TAFV	There has only been one reported case of non-lethal human disease in the Ivory Coast after close contact with chimpanzees ^{8,12,13}
Reston Virus	RESTV	Not known to cause human disease
Bombali Virus	BOMV	Not known to caused human disease

Since 1976 and before the announcement of the recently confirmed SVD case in Uganda, there were eight reported outbreaks of SVD in South Sudan (n=3) and Uganda (n=5) (**Figure 1**)^{5,12}. There have been over 20 EVD outbreaks in Africa. The DRC has reported the highest frequency of outbreaks, with the most recent being in 2022^{5,12}. Between 2014 and 2016, Guinea, Sierra Leone, and Liberia suffered the largest EVD outbreak^{5,12}. It led to over 28,000 cases and over 11,000 deaths¹². Travel-imported cases that led to local transmission or cases that arose from laboratory accidents have been reported in several countries, including the United States, the United Kingdom, Spain, and Italy¹². All are attributed to EBOV, and most occurred during the 2014 to 2016 outbreak¹². Ebola outbreaks have had a case fatality ratio ranging from 25% to 90%, and healthcare workers are especially at risk^{3,12}.

The animal reservoir for orthoebolaviruses is yet to be confirmed however, fruit bats are believed to be the natural hosts for EBOV specifically⁴. Ebola viruses in general have affected non-human primates, but the source of infection remains unknown⁴.



Abbreviations: HCW (Healthcare worker);
 USA (United States of America); UK (United Kingdom); DRC (Democratic Republic of the Congo); Rep. of Congo (Republic of Congo).

Table: Ebola outbreaks in Africa

B = Bundibugyo virus outbreak
*** = 2 outbreaks in the same year**

Note: All travel/lab accident cases were affected by EBOV

	Year of outbreak (YY)																					
ptions try	76	77	79	94	95	96	00	01	03	04	05	07	08	11	12	14-16	17	18	20	21	22	
South Sudan															B			*		*	*	
Gabon						*																
Ivory coast																						
South Africa																						
Uganda																						
Rep. of Congo									*			B										
Guinea																						
Sierra Leone																						
Liberia																						
Senegal																						
Nigeria																						
Mali																						
Total cases	602	1	34	52	315	93	425	124	178	17	12	395	32	1	55	28,708	8	3,524	130	46	170	
Total deaths	431	1	22	31	254	67	224	97	157	7	10	229	15	1	20	11,371	4	2,320	55	27	61	

Figure 1: Geographical spread of Ebola

Map made in QGIS using Natural Earth data. Data on Ebola outbreaks obtained from US CDC 'Outbreak History'. Available from: <https://www.cdc.gov/ebola/outbreaks/index.html>

Transmission, Clinical Presentation, and Diagnosis of Ebola

Ebola is transmitted to humans through close contact with the blood and bodily fluids of infected animals such as fruit bats, monkeys, apes, or antelopes found in the rainforest^{3,14}. The virus enters via broken skin or mucous membranes³. Human-to-human transmission occurs through direct contact with the blood and bodily fluids of an infected, symptomatic human or objects they may have contaminated³. There is also evidence that sexual transmission can occur after recovery while the virus is still present in an individual's blood^{3,14}. The virus is also known to be present in breast milk and it is recommended that individuals with Ebola or those who recently recovered, should avoid breastfeeding¹⁵.

The incubation period ranges from 2 to 21 days however, the average time till symptom onset is 8 to 10 days after exposure to the virus^{3,16}. Common initial symptoms include fever, muscle pain, headache, and weakness (**Figure 2**)^{3,16}. Symptoms then progress to unexplained bleeding and a maculopapular rash, vomiting, diarrhoea, and abdominal pain^{7,16}. Complications include multisystem organ failure, haemorrhage, shock, and spontaneous abortion in pregnancy^{7,17}. Ebola survivors can have persistent symptoms lasting two years or longer and these include vision problems, loss of appetite, weight gain, depression and anxiety, memory loss, and fatigue^{3,16}. There is a range of diagnostic methods including reverse transcriptase polymerase chain reaction assay (RT-PCR), antibody-capture enzyme-linked immunosorbent assay (ELISA), antigen-capture detection tests, serum neutralizing tests, electron microscopy, and cell culture virus isolation³.

Laboratory detection is necessary for an accurate Ebola diagnosis due to its clinical similarities to other diseases such as malaria, yellow fever, and Lassa fever^{3,18}. However, there are several challenges to diagnostics. There is a lack of laboratories in rural settings which can lead to a delay in diagnosis and ultimately mismanagement of cases and further spread of the disease¹⁸. This highlights a need for rapid diagnostic tests but unfortunately, many rapid diagnostic tests stopped being produced at the end of the West Africa Ebola outbreak^{18,19}. They are also costly and there is a lack of clarity on approval pathways for their use in non-outbreak periods^{18,19}. This has led to a lack of rapid diagnostic tests in endemic regions¹⁸. Co-infections and the need for diagnostics to differentiate between pathogens is also a challenge¹⁸. Diagnostic tools need a high specificity however, the point-of-care tests suggested for use by the WHO in the 2014 West Africa Ebola outbreak were unable to achieve a specificity of over 90% and did not meet the 'desired' or 'acceptable' criteria listed in the WHO target product profile^{18,19}. There are other rapid diagnostic tests currently under development that may be able to address this challenge¹⁸.

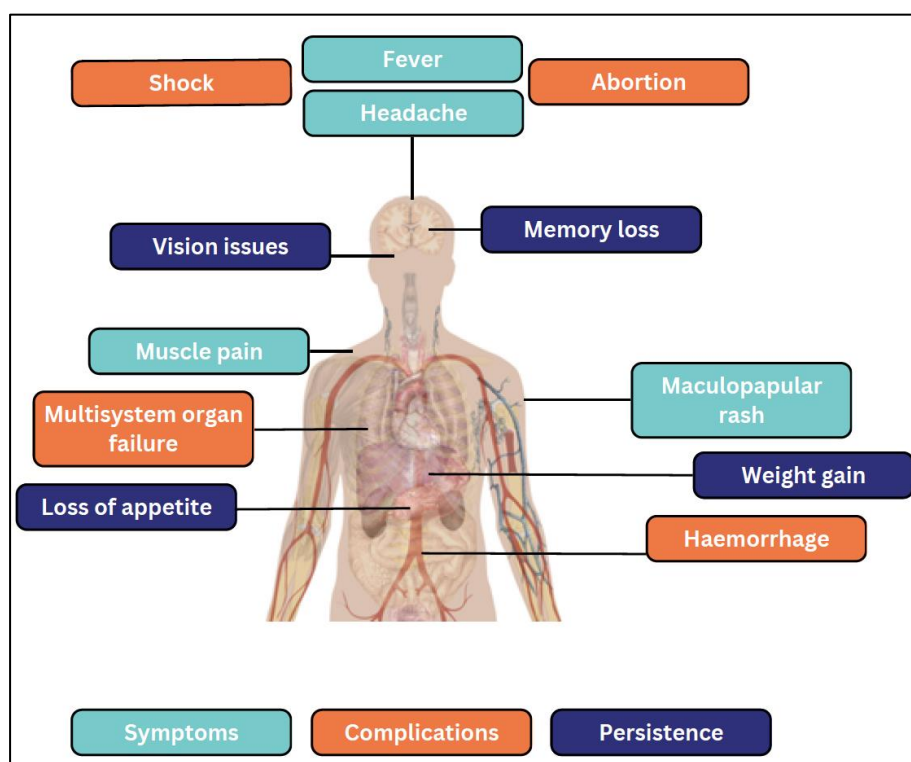


Figure 2: Clinical presentation of Ebola

Therapeutics and Prevention

Ebola is a fatal disease. The time from onset of symptoms to death is roughly 10 days²⁰. Of those who recover, they may experience persistent symptoms lasting 2 years or more after their recovery³. While there are vaccines and therapeutics available for EBOV, there are no licensed vaccines or therapeutics for SUDV^{21,22}.

Access to early optimal supportive care improves chances of survival and includes oral and intravenous fluids, blood transfusions, and medicines to treat other infections and/or pain and gastrointestinal symptoms³. Beyond vaccination, preventative measures include a) hand hygiene, b) avoiding contact with people who are sick or died from Ebola including safe burial, c) reducing the risk of wild animal to human transmission, d) preventing sexual transmission, and e) ensuring safe handling of Ebola viruses in laboratories³. Healthcare workers are particularly at risk for contracting Ebola as they care for Ebola patients and should therefore ensure that they always follow standard infection control precautions for all patients regardless of their diagnoses³.

Therapeutics and vaccines in development for Sudan Virus Disease

After a 2022 outbreak of Sudan Virus Disease in Uganda, the WHO identified two therapeutic products as top priority based on evidence from nonhuman primate studies (NHPs): MBP134 (developing organisation: MappBio) and remdesivir (developing organisation: Gilead)^{23,24}. MBP134 is a monoclonal antibody cocktail with efficacy data in NHPs and safety data from a human trial²⁴. Remdesivir is an antiviral with reported efficacy in NHPs however, in the PALM trial evaluating therapeutics for EBOV, Remdesivir did not improve mortality compared to other therapeutics and was subsequently not recommended for use by the WHO^{23,24}. In 2022, the Ugandan National Regulatory Authority authorized MBP134 and Remdesivir for compassionate use²⁴. No therapeutics have sufficient clinical data on efficacy²⁴. Therefore, the WHO started a "SOLIDARITY-trial Ebola disease therapeutics" in Uganda in 2022 to evaluate the efficacy and safety of MP134, remdesivir, and corticosteroids²³. However, the trial came to a halt as the outbreak was declared over in January 2023. The trial may resume with future SUDV Ebola outbreaks²³.

There is limited data on whether the licensed vaccines for EBOV provide any cross-protection against SUDV²⁵. A more recent study demonstrated that Ervebo can elicit an immune response in guinea pigs, but further evidence is needed from NHPs and humans²⁵. The Janssen two-dose Ebola vaccine is believed to provide cross-protection against SUDV due to the incorporation of SUDV glycoproteins in the second dose however, there is limited clinical data, and the vaccine is not suitable for an outbreak response^{25,26}. During the 2022 SUDV outbreak in Uganda, the WHO published a list of vaccine candidates in development²⁷. Most candidates were in the preclinical phase however two had reached phase I clinical trials²⁷. In November 2022, the WHO vaccine prioritization working group recommended using three vaccines in a planned ring vaccination trial in Uganda after promising results from the TokomezaPlus Ebola Phase I/II randomised control trial²⁸. These were, in order of priority: 1) VSV-SUDV from the International Aids Vaccine Initiative (IAVI), 2) ChAd3-SUDV from the Sabin Institute, and 3) biEBOV from Oxford University/Jenner Institute²⁸.

The VSV-SUDV vaccine is a live attenuated vaccine based on the licensed Ervebo vaccine used for EBOV^{23,28}. It was prioritised by the WHO mainly due to the well-documented safety of the Ervebo vaccine which is now recommended for use in children and pregnant women^{23,28}. The VSV-SUDV protected NHPs against disease and a Phase I clinical trial is underway with the possibility of a Phase II trial in Ugandan healthcare workers^{23,28}. The ChAd3-SUDV vaccine is an adenovirus 3 vector vaccine^{23,28}. Pre-clinical and Phase I trials demonstrate protection in NHPs for 12 months and safety in human adults and children^{23,28}. A Phase II trial with healthy volunteers in Uganda was launched in July 2024²⁹. The biEBOV vaccine is an attenuated adenovirus vector vaccine using the same platform used to develop the COVID-19 vaccines^{23,28}. A study on mice demonstrated an antibody response to the vaccine and a Phase I study in the UK and Tanzania demonstrated the safety and tolerability of the vaccine^{23,28}. However, a study published in March 2024, stated that the vaccine does not protect NHPs³⁰.

Therapeutics and vaccines against Ebola Virus Disease

Gao et al (2022) conducted a systematic review and network meta-analysis to evaluate the efficacy and safety of therapies for EBOV³¹. Their work was funded by the WHO³¹. Two trials (PREVAIL II and PALM) were eligible after screening³¹. These trials evaluated ZMapp, remdesivir, mAb114, and REGN-EB3 therapeutics³¹. REGN-EB3 and mAb114 were deemed to have higher certainty evidence that they reduced mortality compared with ZMapp or remdesivir³¹. It was not clear if ZMapp and remdesivir reduce mortality compared with standard care³¹. After this review, the WHO has published guidance on therapeutics for EBOV which includes strong recommendations for REGN-EB3 (commercial name: Inmazeb) and mAb114 (commercial name (Ebanga) in patients with laboratory-confirmed EBOV or infants with unconfirmed status born to individuals with confirmed Ebola³². Inmazeb and Ebanga have been FDA-approved since October 2020 in the US for the treatment of Ebola caused by EBOV^{6,7}. The WHO recommends against using remdesivir or ZMapp, given the findings from clinical trials³².

There are two vaccines licensed for use against EBOV: rVSV-ZEBOV (commercial name: Ervebo) and Ad26.ZEBOV/MVA-BN-Filo (commercial name: Zabdeno/Mvabea)^{23,33–37}. Ervebo is a single-dose vaccine developed by Merck & Co.^{23,34}. A booster vaccination is also available at 4 months for individuals at high risk of Ebola exposure³³. Ervebo is demonstrated to have an efficacy of 97.5% to 100% when administered pre-exposure to EBOV and results in a detectable antibody response at 12 months in 76% of adults and 87% of children^{7,34,38}. In a challenge study with NHPs, Ervebo was demonstrated to provide protection as rapidly as 3 to 7 days post-vaccination^{7,39}. After promising clinical trial findings, the vaccine was authorized for use by the European Medical Agency (EMA) in 2019^{26,37}. The vaccine has also been licensed for use in Burundi, the Central African Republic, the DRC, Ghana, Guinea, Rwanda, Uganda, and Zambia²⁶. More recently, the US FDA approved Ervebo for individuals over 1 year old in August 2023⁷. A global stockpile of Ervebo was established in 2021 by the International Coordinating Group on Vaccine Provision to ensure

timely and equitable distribution of the vaccine^{26,33}. The DRC was the first country to receive vaccines from this stockpile followed by Uganda, Switzerland (for international healthcare workers), and Guinea-Bissau²⁶. To guide funding and necessary research on Ervebo, a learning agenda with prioritised vaccine implementation research questions and activities is being developed by Gavi, the WHO, and UNICEF²⁶.

Zabdeno/Mvabea is a two-dose vaccine developed by Janssen Pharmaceutica. The first dose is Zabdeno and the second dose is Mvabea administered 8 weeks later^{23,33,34}. The vaccines have proved safe in Phase I, II, and III trials and 41% of adults and 78% of children had a detectable antibody response at 12 months^{7,38,39}. However, there remains a lack of evidence around the exact protection that these vaccines provide^{34–36}. For this reason, the EMA authorised the use of this vaccine in 2020 only under ‘exceptional circumstances’^{35,36}. The long time between first and second dose administration makes this vaccine unsuitable for use in outbreak response^{25,26}.

Sudan Virus Disease in Uganda

Epidemiology

As of 30 January 2025, one case of SVD has been confirmed in Kampala, Uganda¹. The case was a nurse at the Mulago National Referral Hospital who died from the disease¹. Forty-five contacts are being followed up, and these include healthcare workers and family members of the confirmed case¹.

Uganda has experienced five previous outbreaks of SVD¹². Before 30 January 2025, the most recent SVD outbreak in Uganda occurred in November 2022 and resulted in 164 cases and 55 deaths (CFR: 33.5%)¹².

Public Health Response

The identification of SVD in Uganda’s densely populated city, Kampala, is concerning¹. The World Health Organization (WHO) has rapidly deployed a team of public health experts to support Uganda in its response to this outbreak¹. The WHO has also allocated \$1 million US dollars from the Contingency Fund for Emergencies¹.

Suspected Ebola Virus Disease in DRC

There are 12 suspected cases of Ebola and eight deaths in DRC². All deaths occurred between 10 and 22 January 2025, and all cases are from the Equateur province². Samples have been sent to the National Institute of Biomedical Research in Kinshasa for confirmation².

The DRC has experienced over 10 EVD outbreaks since 1976^{2,12}. The Equateur province in DRC has experienced three outbreaks^{2,12}. The most recent EVD outbreak in Equateur, DRC, occurred between April and July 2022^{2,12}. This outbreak resulted in five cases and five deaths (CFR: 100%)¹².

Useful Resources

- The Pandemic PACT grant tracker allows users to obtain information and analyses on active Ebola research and funding globally since 2020. The tracker can be accessed on the [Pandemic PACT website](#) and it can be filtered to include only Ebola-related activities.
- The WHO Research & Development (R&D) [Ebola/Marburg Roadmap](#) (2019) prioritises research for the development of medical countermeasures against Ebola and Marburg viruses.
- Further resources including ‘Target product profiles (TPPs)’, ‘Trial Designs’, and ‘Roadmaps’ can be found on the WHO R&D [webpage](#) dedicated to Ebola and Marburg.

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