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A review of Bundibugyo ebolavirus and the 2026 outbreak: lessons for epidemic preparedness

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Word Count: 5,042

Funding: JD contributes as part of the UK Public Health Rapid Support Team, which is funded by the UK Government's National Institute for Health and Care Research **(**NIHR512896)

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Summary

The ongoing 2026 outbreak of Ebola disease caused by Bundibugyo ebolavirus (BDBV) in the Democratic Republic of the Congo and Uganda has renewed attention to one of the least studied human-pathogenic *orthoebolaviruses*. Since its discovery in western Uganda in 2007, only two recognised outbreaks had been reported, limiting opportunities to define the epidemiology, pathogenesis, diagnosis, clinical spectrum, and optimal management of BDBV or to develop species-specific countermeasures.

The current outbreak, declared a Public Health Emergency of International Concern by WHO on 17 May 2026, has also exposed the gap between scientific innovation and operational readiness. Although pan-filovirus diagnostics, investigational vaccines, therapeutics, and adaptive clinical trial platforms are now available, their deployment has been constrained by delayed diagnosis, limited access to species-inclusive diagnostics, insecurity, population displacement, and fragile health systems.

In this Review, we synthesize current evidence on BDBV from its discovery to the current 2026 outbreak, highlighting advances in epidemiology, clinical management, diagnostics, vaccines, therapeutics, and preparedness. More broadly, the outbreak demonstrates that scientific innovation alone is insufficient: its public health impact depends on integrated, species-inclusive systems capable of rapidly detecting, evaluating, and responding to outbreaks caused by any human-pathogenic *orthoebolavirus.*

Search Strategy

We searched PubMed, Embase, Web of Science, Scopus, Google Scholar, WHO Disease Outbreak News, Africa CDC materials, national Ministry of Health updates, ClinicalTrials.gov, the Pan African Clinical Trials Registry, ISRCTN, and relevant outbreak-response partner websites for articles and reports published from 01 Jan 2007 to 12 July 2026. Search terms included “Bundibugyo”, “Bundibugyo ebolavirus”, “Bundibugyo virus disease”, “BDBV”, “Ebola disease”, “Ebolavirus”, “*Orthoebolavirus*”, “filovirus”, “diagnostic”, “vaccine”, “therapeutic”, “monoclonal antibody”, “remdesivir”, “obeldesivir”, “post-exposure prophylaxis”, “survivor”, “viral persistence”, “surveillance”, “genomic epidemiology”, “infection prevention and control”, and “preparedness”. We prioritized primary outbreak investigations, peer-reviewed clinical and preclinical studies, systematic or authoritative reviews, WHO and Africa CDC guidance, trial registry entries, and contemporaneous outbreak situation reports. Because the 2026 outbreak was ongoing at the time of writing, we also reviewed selected official and partner updates when peer-reviewed data were not yet available. We included English-language sources and relevant reports available in English translation. Evidence was synthesized narratively because available BDBV-specific clinical data are limited and heterogeneous.

Key Messages

- *Bundibugyo orthoebolavirus* is a human-pathogenic *orthoebolavirus* capable of sustained human-to-human transmission, cross-border spread, and large, complex outbreaks.
- The 2026 outbreak has demonstrated that scientific advances—including pan-filovirus diagnostics, investigational vaccines and therapeutics, and adaptive trial platforms—must be matched by operational readiness to achieve public health impact.
- Despite nearly two decades since its discovery, BDBV-specific evidence on pathogenesis, clinical disease, immune responses, and long-term outcomes remains limited, with much current knowledge extrapolated from *Zaire orthoebolavirus* and *Sudan orthoebolavirus*.
- Evaluation of suspected Bundibugyo virus disease should be integrated into acute febrile illness algorithms and supported by species-inclusive molecular diagnostics, genomic sequencing, and resilient laboratory networks.
- No vaccine or therapeutic has demonstrated clinical efficacy against *Bundibugyo ebolavirus*, but the rapid launch of therapeutic and post-exposure prophylaxis trials during the 2026 outbreak illustrates the value of outbreak-ready clinical research platforms.
- Future filovirus preparedness will require integrated, species-inclusive systems that combine surveillance, diagnostics, clinical research, countermeasure development, infection prevention and control, community engagement, sustainable financing, and locally led scientific leadership.

Introduction

Since the description of Ebola virus in 1976, six *orthoebolavirus* species have been identified, but only *Zaire orthoebolavirus* (EBOV), *Sudan orthoebolavirus* (SUDV), and *Bundibugyo orthoebolavirus* (BDBV) have caused recognized outbreaks with sustained human-to-human transmission.[1] Preparedness should therefore prioritise pathogens with demonstrated human epidemic potential while maintaining surveillance for species whose ecology and spillover risks remain uncertain.

The 2026 outbreak of Bundibugyo virus disease (BVD) in eastern and northeastern Democratic Republic of the Congo and Uganda has exposed the operational consequences of these evidence gaps. With more than 1,900 confirmed cases and over 700 deaths reported as of 14 July 2026, the outbreak is the largest recorded BVD outbreak and, based on reported cases at the time of writing, one of the largest Ebola disease outbreaks ever documented.[2–4] The epidemic has highlighted limitations of preparedness strategies built largely around EBOV—diagnostic platforms initially failed to detect BDBV, no licensed vaccine or therapeutic has established clinical efficacy against BVD, and critical evidence is being generated as the outbreak expands.[5–7]

The current outbreak is unfolding in a markedly different scientific and geopolitical landscape than when BDBV was first identified. Advances in genomics,[8] vaccine platforms,[9] and clinical trial networks,[10] have expanded opportunities for research, but these gains coincide with reductions in global health funding and increasing pressure on the systems that underpin outbreak preparedness.[11,12]

The 2026 BDBV outbreak is more than a resurgence of a less-studied ebolavirus—it is a test of whether decades of scientific advances can be translated into timely, equitable, and species-inclusive preparedness. Using the current outbreak as a case study, we synthesize the evolution of knowledge from the virus's discovery to present, highlight persistent gaps in diagnostics, vaccines, therapeutics, clinical care, and operational readiness, and outline priorities to strengthen preparedness for future filovirus outbreaks.

Discovery and Emergence of *Bundibugyo Ebolavirus*

Prior outbreaks

BDBV was first identified during an outbreak of Ebola disease in Bundibugyo District, western Uganda, in 2007.[13–15] Prior to the 2026 outbreak, only two recognised outbreaks have been attributed to BDBV **(Table 1)**.[13–19]

The first recognized BDBV outbreak occurred in western Uganda between 2007 and 2008, resulting in 149 confirmed and probable cases, including 56 laboratory-confirmed cases, and 37 deaths (overall case-fatality ratio, 24.8%).[18] Among the 43 patients with acute laboratory-confirmed infection, 17 died (case-fatality ratio, 40%), highlighting differences between overall outbreak case-fatality estimates and outcomes among laboratory-confirmed clinical cases.[17] The outbreak was initially detected following a cluster of severe illnesses and deaths in Kabango village, including a 26-year-old woman who developed fatal disease shortly after childbirth.[15] Subsequent investigations identified a filovirus genetically distinct from EBOV, SUDV, and other known *orthoebolaviruses*, leading to the designation of *Bundibugyo orthoebolavirus* as a new species.[14,15,18]

Clinical manifestations were broadly consistent with those of other forms of Ebola disease, with fever, headache, asthenia, abdominal pain, and gastrointestinal symptoms predominating. Haemorrhagic manifestations were reported in a substantial proportion of patients in some cohorts, but they were neither universal nor required for diagnosis.[14,17,18]

The second documented outbreak occurred in Isiro, DR Congo, in 2012 and comprised 62 confirmed, probable and suspect cases, including 36 laboratory-confirmed infections, and 34 deaths (overall case fatality ratio, 54.8%).[19,20] Genomic and epidemiological investigations suggested the outbreak resulted from an independent zoonotic introduction rather than direct continuation of the 2007 Uganda outbreak.[20,21] Although considerably smaller than the current epidemic, it confirmed that BDBV could re-emerge in distinct geographic settings and cause clinically severe disease. The outbreak also provided important insights into transmission dynamics, clinical presentation, and outbreak control.[19]

Although substantially smaller than major epidemics caused by EBOV, these outbreaks established BDBV as a human-pathogenic ebolavirus capable of sustained human-to-human transmission while providing relatively limited opportunities for prospective clinical trials, vaccine evaluation, and therapeutic development.

The 2026 Bundibugyo ebolavirus outbreak

On 15 May 2026, DR Congo declared an outbreak of Ebola disease caused by BDBV after laboratory confirmation of cases in Ituri Province.[22,23] At the time of declaration, authorities had identified eight laboratory-confirmed cases, 246 suspected cases, and 80 suspected deaths, with epidemiologically linked cases already detected across the border in Uganda.[22] Two days later, the World Health Organization (WHO) declared the outbreak a Public Health Emergency of International Concern (PHEIC), followed by Africa CDC's declaration of a Public Health Emergency of Continental Security, reflecting concern about the trajectory of the outbreak.[24,25]

Since its declaration, the 2026 BVD outbreak has expanded rapidly. As of 14 July 2026, more than 1,900 confirmed cases and over 700 reported deaths have been reported in DR Congo, with an additional 20 confirmed cases and two deaths reported in Uganda.[2,3] This epidemic is already among the largest recorded Ebola disease outbreaks, although comparisons to the 2014-2016 West Africa epidemic and the 2018-2020 DR Congo outbreak remain provisional while transmission continues.[4]

Real-time genomic analyses support a single zoonotic spillover followed by sustained human-to-human transmission and demonstrate the value of genomic surveillance during filovirus outbreaks.[8]

Outbreak response challenges

The outbreak is unfolding against a backdrop of chronic insecurity, population displacement, fragile health systems, and longstanding mistrust, all of which impeded surveillance, contact tracing, laboratory diagnosis, clinical care and infection prevention and control (IPC).[26–29] Healthcare worker infections, diagnostic delays, cross-border transmission, attacks on health facilities, delayed salary payments, healthcare worker strikes, and workforce shortages illustrate how operational constraints shape the trajectory of the response.[28,29]

Community trust is equally central to outbreak control.[26] Reluctance to report symptoms, accept isolation, or participate in contact tracing reflects not only misinformation, but also fear, stigma, memories of previous Ebola outbreaks, perceived inequities in care, and distrust of government or external responders. These social and historical factors influence care-seeking, acceptance of safe and dignified burial practices, and adherence to public health measures.[30] Key challenges affecting the current response are summarized in **Panel 1**.

Epidemiology and lessons learned

Although the evidence base remains limited, several important epidemiologic lessons have emerged. First, BDBV is capable of sustained human-to-human transmission, cross-border spread, and large outbreaks.[28] Second, early disease presents as a non-specific febrile illness with gastrointestinal symptoms, complicating recognition in settings where malaria, sepsis, arboviral infections, and other acute febrile illnesses are common.[16,19] Third, recurrent diagnostic challenges highlight the need for

species-inclusive assays that detect all pathogenic *orthoebolaviruses* rather than relying solely on epidemiologic risk factors.[6] Finally, reported case-fatality ratios should be interpreted cautiously because surveillance intensity, case ascertainment, healthcare access, supportive care, and security conditions differed across outbreaks, and the 2026 epidemic remains ongoing.[28] The limited size of previous outbreaks also constrained the generation of BDBV-specific clinical, virological, immunological, and implementation evidence, leaving important knowledge gaps that are now being addressed during the 2026 outbreak.

Virology and Pathogenesis

Virus characteristics

Bundibugyo orthoebolavirus (*Orthoebolavirus bundibugyoense*; BDBV) is a member of the genus *Orthoebolavirus* and is genetically and antigenically distinct from EBOV and SUDV.[1] These differences are especially important in the glycoprotein (GP), the principal antigenic target of several vaccines and monoclonal antibodies.[14,17] Divergence in GP may affect vaccine antigen matching, antibody binding, and cross-protection, while differences in genomic target regions can reduce molecular diagnostic performance unless assays include conserved or BDBV-specific targets. These genetic and antigenic differences also mean that evidence supporting EBOV-directed vaccines or monoclonal antibodies cannot be extrapolated to BDBV, requiring species-specific evidence for regulatory approval.

Pathogenesis

Current understanding of BDBV pathogenesis is derived largely from studies of EBOV and SUDV, with relatively few data from BDBV infection itself. As with other pathogenic ebolaviruses, infection is thought to begin after mucosal or cutaneous exposure, with early infection of monocytes, macrophages, and dendritic cells facilitating systemic dissemination.[31] Disease severity is thought to reflect both direct viral injury and dysregulated host immune responses, resulting in endothelial dysfunction, coagulopathy, capillary leak, and multiorgan failure.[31,32] BDBV-specific data on tissue tropism, replication kinetics, host immune responses, and correlates of severe disease remain limited.

Preclinical studies therefore provide critical evidence to guide BDBV countermeasure development. In vitro and animal models suggest that pathogenic ebolaviruses differ in replication kinetics, susceptibility to therapeutics, and therapeutic windows.[1,33] In non-human primates, both species-matched and multivalent vaccine strategies protect against lethal BDBV challenge, whereas protection cannot be assumed with EBOV-directed approaches alone.[34–36] These findings support the development of both BDBV-specific and pan-ebolavirus countermeasures but also highlight the need for robust human clinical efficacy data.

Knowledge gaps

Despite nearly two decades since its discovery, important knowledge gaps remain regarding BDBV biology, transmission, immunity, and long-term outcomes. Tissue tropism and viral persistence in immune-privileged sites—including the eye, central

nervous system, and reproductive tract—remain poorly characterized.[37] Correlates of protective immunity and key aspects of transmission biology, including shedding kinetics, determinants of infectiousness, environmental contamination, and ecological drivers of zoonotic spillover, also remain poorly understood. Although bats are presumed to be the natural reservoir for ebolaviruses, direct ecological evidence for BDBV is limited.[38] These gaps continue to constrain countermeasure development and underscore the need for sustained BDBV-specific research during both epidemic and inter-epidemic periods.

Clinical Presentation and Disease Phenotype

Clinical manifestations

The clinical presentation of BVD is broadly similar to other forms of Ebola disease, although species-specific clinical characterisation remains limited. Following an incubation period of 2 -21 days, patients typically present with fever, fatigue, headache, myalgia, and gastrointestinal symptoms—including nausea, vomiting, abdominal pain, and diarrhoea —which can result in substantial fluid and electrolyte losses.[1,18,39] Data from the ongoing 2026 outbreak—the largest clinical description of BDBV to date —confirms that fever and gastrointestinal symptoms predominate, with vomiting and diarrhoea occurring in approximately two-thirds of patients.[40] Difficulty breathing, difficulty swallowing, headache, anorexia, and abdominal pain are also common, whereas haemorrhagic manifestations occur in only about 10% of laboratory-confirmed cases, reinforcing that bleeding is neither universal nor required for diagnosis.[40]

Severe disease may progress to shock, altered mental status, acute kidney injury, hepatic dysfunction, coagulopathy, respiratory compromise, and multiorgan failure.[1,32,41] Laboratory abnormalities include thrombocytopenia, leukopenia followed by leucocytosis, elevated liver aminotransferases, metabolic acidosis, renal impairment, and coagulation abnormalities.[1,39]

Data from the 2026 outbreak suggest that higher viral loads (lower PCR cycle-threshold values) are associated with mortality, although prognostic biomarkers require further study.[40]

Challenges in clinical recognition

The non-specific presentation of early BVD remains a major challenge for clinical recognition and timely diagnosis because its initial manifestations overlap with those of common endemic infections including malaria, typhoid fever, viral hepatitis, leptospirosis, rickettsial infections, arboviral infections, and bacterial sepsis.[41,42] Accordingly, patients with suspected BVD should be evaluated within integrated acute febrile illness algorithms that assess simultaneously for filovirus infection and other common infectious aetiologies. Delayed recognition can postpone isolation, IPC measures, contact tracing, and early supportive care. Patients may initially be managed in general wards or outpatient settings before viral haemorrhagic fever is suspected, increasing the risk of healthcare-associated transmission.[43] These challenges underscore the importance of effective triage and IPC systems for rapid identification and safe management of suspected viral haemorrhagic fever.

Long-term sequelae and survivorship

Long-term outcomes following BVD remain poorly characterized. Evidence from other Ebola outbreaks suggests that survivors may experience persistent physical, neurological, ocular, musculoskeletal, and psychological sequelae.[44–46] BVD survivors likely experience a similar spectrum of complications, but their incidence, severity, duration, and mechanisms remain undefined.

Key unanswered questions include the frequency of BDBV viral persistence in immune-privileged sites such as the testes, eyes, and central nervous system, the risk of delayed relapse or transmission, the durability of protective immunity, and the burden of long-term reproductive, ocular, neurological, musculoskeletal, and mental-health sequelae. Addressing these questions will require multidisciplinary survivor cohorts integrating clinical, virological, ophthalmological, neurological, reproductive health, and patient-reported outcome assessments to define long-term disease burden and guide survivor care.

Diagnostics

The 2026 outbreak exposed a critical diagnostic vulnerability: many frontline molecular platforms deployed for Ebola outbreak response were designed primarily to detect EBOV and initially failed to identify BDBV. Accurate and timely diagnosis is central to outbreak control, informing case identification, isolation, contact tracing, IPC, clinical management, and eligibility for investigational countermeasures. Effective diagnostic pathways include four complementary components: clinical screening, confirmatory molecular testing, genomic sequencing, and laboratory systems capable of delivering these services rapidly during outbreaks.

Initial screening

The 2026 outbreak reinforced the importance of maintaining a broad diagnostic approach when evaluating patients with acute febrile illness. During outbreaks, screening should combine standardized clinical assessment with epidemiologic risk factors while recognizing that reliance on exposure history alone may delay diagnosis. Integrating pan-filovirus testing into broader acute febrile illness algorithms may improve early case detection, particularly before transmission chains are recognized.

Confirmatory molecular testing

Given that much of the deployed Ebola diagnostic infrastructure was developed for EBOV, several patients with clinically suspected Ebola disease initially tested negative, delaying outbreak recognition.[6] Widely deployed GeneXpert assays used in previous Ebola responses did not detect BDBV, necessitating additional molecular testing and sequencing for confirmation.[47] Pan-filovirus assays, including the Altona RealStar Filovirus Screen and KH Medical RADIONE Ebola Detection kit, detect BDBV, but limited reagent availability, specimen transport, decentralised testing capacity, and laboratory surge capacity delayed early deployment.[7] Evaluation of the RADIONE assay during the ongoing outbreak demonstrated 95% overall agreement

with the WHO-approved RealStar Filovirus Screen assay, supporting the feasibility of rapid point-of-care molecular diagnosis in resource-limited outbreak settings.[48]

The outbreak has accelerated diagnostic development and regulatory evaluation while highlighting the gap between innovation and field implementation. On 2 July 2026, WHO added the first molecular diagnostic for BDBV to its Emergency Use Listing (EUL), providing an expedited pathway for procurement and deployment during the ongoing response.[49] The Cepheid Xpert Hemorrhagic Fever panel, which includes BDBV targets and can be deployed on existing GeneXpert instruments, offers an important opportunity to expand species-inclusive testing.[50] In parallel, WHO, Africa CDC, and partner organizations are establishing a joint validation platform to generate the clinical performance data needed for laboratory-based, near point-of-care, and rapid diagnostic tests under outbreak conditions.[7,49,51]

Genomic sequencing

Genomic sequencing complements molecular diagnosis by confirming species identity, defining transmission chains, supporting molecular epidemiology, and monitoring viral evolution. It can also identify genetic changes that may affect diagnostic performance or influence vaccine and therapeutic effectiveness.[8,52] Current outbreak viruses are genetically distinct from those identified in the 2007 and 2012 outbreaks, confirming that the 2026 epidemic resulted from an independent zoonotic introduction rather than continued circulation of earlier BDBV lineages.[8,53] Sequencing of 139 genomes from 16 health zones further demonstrates the value of real-time genomic surveillance for defining transmission networks, tracking geographic spread, and informing public health decision-making.[8]

Operational implementation

Diagnostic performance depends not only on assay characteristics but also on laboratory systems capable of delivering accurate results with rapid turnaround times. During the current outbreak, laboratory capacity expanded from a limited number of reference laboratories performing approximately 200–400 tests daily to ten laboratories capable of performing more than 2,000 tests per day.[49] Despite this progress, implementation remains constrained by reagent shortages, laboratory interruptions, delays in specimen transport from remote areas, limited decentralized testing capacity, and workforce limitations, all of which continue to delay diagnosis and outbreak response.[7,51] These experiences demonstrate that species-inclusive assays alone are insufficient and must be supported by sustained investment in laboratory infrastructure, supply chains, workforce capacity, and operational preparedness to ensure rapid and equitable deployment during outbreaks.

Vaccines

Current evidence

Most licensed and advanced Ebola vaccine candidates target EBOV. Although the rVSV-ΔG-ZEBOV-GP vaccine is highly effective against EBOV disease, its efficacy against BDBV remains unknown, and WHO advised against its use outside clinical trials during the current outbreak.[5] As the vaccine is based on the EBOV glycoprotein, cross-protection against BDBV cannot be assumed. Moreover,

deployment outside research protocols could complicate interpretation of vaccine-effectiveness while diverting resources and attention from the evaluation of BDBV-specific or multivalent vaccine candidates.

Preclinical and clinical evidence

Preclinical studies indicate that vaccine-induced protection against BDBV is achievable with BDBV-specific, multivalent filovirus, and next-generation vaccine platforms.[34–36] In non-human primates BDBV-specific rVSV-vectored vaccines protect against lethal BDBV challenge, whereas EBOV-directed rVSV vaccines have provided incomplete, regimen-dependent protection.[35,54] Multivalent vaccine candidates have induced BDBV glycoprotein-specific immune responses and conferred protection against lethal challenge in animal models.[34–36] These findings support continued vaccine development, but require confirmation in human studies.[55]

Regulatory pathways and outbreak evaluation

Establishing regulatory pathways for BDBV vaccines remains challenging because outbreaks are infrequent, geographically heterogeneous, and often decline before conventional phase 3 efficacy trials can be completed. Evaluation will likely require complementary evidence integrating efficacy data from well-characterized animal models under regulatory frameworks such as the US Food and Drug Administration (FDA) Animal Rule with immunobridging, human safety and immunogenicity data, and emergency regulatory mechanisms, including Emergency Use Authorization and, where applicable, WHO Emergency Use Listing. Although these approaches cannot replace human efficacy data, they provide scientifically rigorous pathways for evaluating vaccines when conventional efficacy trials are not feasible.

The 2026 outbreak has accelerated evaluation of several investigational candidates, including rVSV-vectored, ChAdOx1-vectored, and mRNA-based vaccines (Table 2).[9,56] The Oxford Vaccine Group has also launched the first phase 1 clinical trial of a BDBV-specific ChAdOx1 vaccine candidate (BD-Ebov), representing the first human evaluation of a vaccine specifically developed against Bundibugyo ebolavirus.[56]

Operational implementation

Scientific advances are insufficient if vaccines cannot be deployed rapidly when and where outbreaks occur. WHO has indicated that the most advanced rVSV-vectored BDBV candidate is unlikely to have trial doses available for several months, whereas the Oxford-Serum Institute of India candidate may enter clinical evaluation sooner, subject to completion of animal efficacy studies and regulatory review.[57,58] These timelines highlight that manufacturing capacity, advance regulatory planning, stockpiling, and equitable access are as important as vaccine design for enabling timely clinical trials and emergency vaccination strategies.

Future directions

The emergence of multiple pathogenic *orthoebolavirus* species underscores the need for vaccine strategies that provide broad and durable protection across EBOV, SUDV, BDBV, and other medically important filoviruses. Continued investment in species-

inclusive and pan-filovirus vaccines, together with mechanisms to evaluate and deploy them rapidly, will be essential for future outbreak preparedness.

Therapeutics

Current evidence

No therapeutics have been approved specifically for Bundibugyo virus disease, and current treatment recommendations are informed largely by evidence generated during EBOV outbreaks. Randomised clinical trials conducted during EBOV outbreaks demonstrated survival benefits from glycoprotein-directed monoclonal antibody therapies, leading to regulatory approval of ansuvimab and REGN-EB3 for treatment of EBOV disease.[59] The PALM trial also established that randomized therapeutic trials can be successfully conducted during Ebola outbreaks.[59,60] However, because these products target the EBOV glycoprotein, their effectiveness cannot be assumed for antigenically distinct species such as BDBV, underscoring the need for broadly active countermeasures and BDBV-specific clinical evaluation.[61]

Candidate therapeutics

Broad-spectrum antivirals and pan-ebolavirus monoclonal antibodies are the most promising therapeutic strategies for BVD. Remdesivir inhibits the filovirus RNA-dependent RNA polymerase and demonstrates in vitro activity against EBOV, SUDV, MARV, and BDBV, with efficacy in EBOV-infected rhesus macaques and extensive human safety experience from COVID-19 and the PALM trial.[59,62–64] Although differences in BDBV viral kinetics and treatment windows warrant prospective evaluation, these data support its investigation during the current outbreak

MBP134 is a broadly neutralizing two-monoclonal-antibody cocktail targeting conserved ebolavirus glycoprotein epitopes. In vitro and animal studies demonstrate activity against multiple *orthoebolaviruses*, including protection against EBOV, SUDV, and BDBV.[61] In a lethal BDBV macaque model, five of six treated animals survived after a single late-treatment dose, whereas all untreated controls died.[61] These findings have made MBP134 a higher priority candidate for clinical evaluation.[5]

Maftivimab, one component of the FDA-approved Inmazeb combination, recognizes a conserved glycoprotein epitope and demonstrates cross-neutralizing activity against multiple *orthoebolavirus* species, including BDBV, although comparable BDBV animal efficacy data are lacking.[65]

Clinical evaluation and adaptive platform trials

Following recommendations from the WHO Therapeutics Technical Advisory Group, remdesivir and MBP134 were selected for evaluation in the WHO SOLIDARITY PARTNERS treatment trial. Patient enrolment began on 2 July 2026, in DR Congo.[10] The adaptive platform trial will compare remdesivir, MBP134, combination therapy, and optimised supportive care, with 28-day survival as the primary endpoint.[5,10] The design preserves clinical equipoise while enabling rigorous evaluation of promising therapeutic candidates identified through preclinical studies.

Adaptive platform trials are particularly valuable for rare pathogens because opportunities to generate high-quality evidence often disappear as outbreaks come

under control. When approved therapies are unavailable and conventional trials cannot be implemented immediately, complementary mechanisms such as the WHO Monitored Emergency Use of Unregistered and Investigational Interventions (MEURI) framework can support prospective collection of clinical, safety, and virological data under appropriate ethical oversight.[66]

Post-exposure prophylaxis

Post-exposure prophylaxis (PEP) represents an important complementary strategy because household contacts, healthcare workers, burial teams, and other high-risk contacts can often be identified before symptom onset. On 14 July, 2026, the EBO-PEP trial was launched in Ituri Province, DR Congo, with the goal of enrolling 1,000 participants to evaluate obeldesivir, an oral antiviral prodrug of remdesivir, as PEP among contacts of confirmed BVD cases (NCT06841614; PACTR202502853321394).[67] Publicly available preclinical data indicate that obeldesivir provides protection in non-human primate models of ebolavirus infection when administered shortly after exposure.[68] If effective, an oral PEP strategy could complement contact tracing by preventing disease among high-risk contacts. Its success, however, will depend on rapid case confirmation, timely contact identification, prompt treatment initiation, adherence, safety monitoring, and successful implementation under outbreak conditions.

Future therapeutic development

Future therapeutic development should prioritise broadly neutralising monoclonal antibodies, antibody combinations that reduce viral escape, direct-acting antivirals, and host-directed or combination therapies with activity across multiple *orthoebolaviruses*.[61,69] Combination therapy may be particularly promising; in an advanced SUDV macaque model, remdesivir combined with MBP431 - an optimised derivative and newer-generation version of MBP134 - achieved 80% survival compared with 20% survival with monotherapy.[70] These findings support continued evaluation of combination therapy together with sustained investment in manufacturing, regulatory pathways, and deployment strategies to ensure promising therapeutics can be evaluated and accessed early during future outbreaks.

Supportive Care

Supportive care remains the foundation of clinical management for BDBV. Evidence from EBOV outbreaks indicates that prompt recognition of shock, intravenous fluid resuscitation, electrolyte correction, nutritional support, treatment of coinfections, and close monitoring of organ function improve survival.[39,42,71] Laboratory-guided management of renal dysfunction, hepatic injury, coagulopathy, and metabolic derangements is increasingly important, while severe disease may require oxygen therapy, vasopressors, blood products, renal replacement therapy, and other critical care interventions, although these capabilities remain limited in DR Congo and Uganda.[39,42]

Recent filovirus outbreaks have also demonstrated the value of protocolised care, point-of-care diagnostics, multidisciplinary teams, and treatment-unit innovations such as CUBE isolation units that facilitate safe bedside assessment.[72–74] Strengthening workforce capacity, laboratory systems, supply chains, oxygen

infrastructure, referral networks, and clinical protocols are essential to improving outcomes in outbreaks. [75]

Research Priorities and Future Directions

The limited evidence base for BDBV reflects the rarity, unpredictability, and often short duration of previous outbreaks, which have constrained prospective clinical investigation and left much of current knowledge dependent on extrapolation from EBOV and SUDV.[72] The 2026 outbreak has therefore reframed the central challenge from identifying what should be studied to ensuring that research systems are sufficiently prepared to generate evidence whenever outbreaks occur. Future progress will depend on maintaining outbreak-ready research infrastructure during both epidemic and inter-epidemic periods rather than rebuilding capacity after transmission is established. Key research priorities for the current outbreak are summarized in **Panel 2**.

Generating evidence during outbreaks

Future outbreaks should function as learning health systems in which clinical care, laboratory diagnostics, genomic surveillance, and prospective research are integrated into routine response. Standardized clinical datasets linked with virological, immunological, genomic, and clinical metadata, together with rapid genomic sequencing, biobanking, and timely deposition of sequence data into openly accessible platforms, are essential to define determinants of severe disease, viral persistence, transmission dynamics, correlates of protection, diagnostic performance, therapeutic effectiveness, and long-term outcomes. Equitable data-sharing frameworks that respect national ownership while promoting locally led scientific leadership will accelerate evidence generation and improve outbreak response.

Optimising clinical care

Supportive care remains the cornerstone of Ebola disease management, yet many components of optimal supportive care remain incompletely defined for BDBV. Future research should identify scalable approaches to fluid and electrolyte management, organ support, and delivery of advanced supportive care in resource-constrained settings.[73] Emerging innovations—including point-of-care diagnostics, telemedicine, and outbreak-adapted treatment units such as CUBE-style isolators—should also be evaluated for their effectiveness, feasibility, and scalability during outbreaks.[74]

Accelerating countermeasure development

Current and future outbreaks provide rare opportunities to generate clinical evidence for BDBV-specific and pan-ebolavirus countermeasures. Priorities extend beyond demonstrating efficacy to ensuring diagnostics, vaccines, therapeutics, and PEP can be manufactured, regulated, stockpiled where appropriate, and rapidly deployed. Equally important will be implementation research evaluating how these interventions can be delivered safely, equitably, and at scale in resource-constrained settings. During the 2026 outbreak, the International Pandemic Preparedness Secretariat applied the principles of the 100 Day Mission, issuing progress updates for diagnostics, therapeutics, and vaccines on Days 15 and 30 of the Ebola Clock,

providing one model for accelerating coordinated countermeasure development and evaluation.[7]

Building outbreak-ready research systems

Outbreak-ready research systems are essential to ensure that opportunities for evidence generation are not lost. Pre-positioned master protocols, harmonized ethics and regulatory approvals, standing contractual agreements, trained research networks, standardized data collection, and sustained community partnerships should enable rapid activation of adaptive platform trials whenever outbreaks arise. The launch of the WHO SOLIDARITY PARTNERS treatment trial on 02 July 2026 demonstrates what can be achieved when these systems are established before outbreaks begin.[10] Similar adaptive approaches should be extended to vaccine and PEP studies to maximize opportunities for generating outbreak-derived evidence. Where randomized trials cannot be initiated immediately, complementary mechanisms such as the WHO MEURI framework can support prospective collection of standardized clinical, safety, and virological data under appropriate ethical oversight.[66] At the same time, insecurity, population displacement, community mistrust, and disruptions to healthcare delivery continue to threaten trial implementation, highlighting the need for sustained investment in regional clinical research capacity.

Preparedness systems

The 2026 outbreak has highlighted that effective preparedness depends on interconnected surveillance, laboratory, clinical, research, community, and financing systems rather than any single intervention. Maintaining these capacities between epidemics is essential if future outbreaks are to be detected, investigated, and controlled before transmission becomes widespread. The key components of the species-inclusive filovirus preparedness framework are summarized in **Figure 1**.

Surveillance

Preparedness begins with surveillance systems capable of rapidly detecting and investigating unusual clusters of severe illness and linking community, clinical, laboratory, and cross-border reporting. Early detection depends on interoperable surveillance platforms, timely data sharing, and workforce capacity to investigate suspected cases. The availability of near-real-time genomic data during the 2026 outbreak illustrates how sequencing has evolved from a retrospective research tool into a core component of epidemic intelligence, informing surveillance, transmission mapping, and public health response.[8]

Laboratory Systems

Laboratory preparedness extends beyond diagnostic assays. Countries at risk of filovirus spillover require molecular diagnostic capacity, laboratory surge capability, reliable specimen transport networks, genomic surveillance, quality assurance, biosafety infrastructure, and reporting systems that minimize diagnostic turnaround times.

Infection Prevention and Control

Recurrent healthcare-associated transmission across successive Ebola outbreaks demonstrates that IPC remains a systems challenge rather than simply a technical one. Sustained implementation depends on reliable water, sanitation and hygiene infrastructure, consistent supplies of personal protective equipment, routine training, healthcare worker staffing, surveillance for healthcare-associated infections, and institutional safety cultures that are maintained between outbreaks.[76] The current outbreak again illustrated how delayed diagnosis, resource constraints, and disruptions to routine healthcare can rapidly amplify transmission within healthcare facilities.

Medical countermeasures

Operational readiness should be measured not only by the availability of candidate products but by whether they can be delivered, evaluated, and equitably accessed early in an outbreak.This depends not only on product development but also on manufacturing capacity, regulatory preparedness, procurement mechanisms, stockpiling where appropriate, and operational plans that enable equitable access during the earliest phases of an outbreak.

Community partnerships

Community engagement should be viewed as core preparedness infrastructure rather than an emergency response activity. Long-term partnerships with community leaders, survivors, civil society organizations, and frontline healthcare workers can strengthen trust before outbreaks occur, improving acceptance of public health interventions when emergencies arise. Experiences across successive Ebola outbreaks have shown that fear, stigma, misinformation, inadequate risk communication, and longstanding mistrust of health authorities can delay care seeking, reduce reporting of suspected cases and contacts, discourage acceptance of isolation and treatment, and undermine public health interventions. Social memory of previous outbreaks and perceptions of inequitable access to care may further influence community willingness to engage with response activities.

One Health

Preparedness also requires a One Health approach that integrates wildlife surveillance, ecological surveillance, environmental sampling, reservoir studies, risk mapping, and community-based reporting with human surveillance, laboratory networks, and local public health systems. Understanding how land-use change, climate variability, biodiversity, and human–animal interactions influence spillover risk will be essential for identifying areas at highest risk, informing interventions to reduce zoonotic spillover, and strengthening early detection. Integrating these systems can improve understanding of spillover risk while supporting earlier detection and more coordinated responses.

Sustainable financing and research infrastructure

Regional centres of excellence can strengthen laboratory, clinical, and research capacity while promoting locally led scientific leadership. However, these systems

require predictable long-term financing. Sustained domestic investment, regional financing mechanisms, and continued international partnerships are essential to preserve expertise, infrastructure, and operational readiness between epidemics rather than rebuilding capacity during each outbreak. As countries strengthen preparedness, financing strategies should also support a planned transition from externally funded emergency programmes to sustainable, nationally owned systems while preserving international surge capacity for large epidemics.

The rapid mobilisation of CEPI-supported vaccine programmes together with the launch of therapeutic and PEP trials during the 2026 BVD outbreak demonstrates what coordinated global investment can achieve.[9] At the same time, the outbreak exposed persistent vulnerability: countermeasure development, clinical research, and operational preparedness continue to accelerate only after outbreaks are underway. Preparedness should therefore be judged not by the existence of promising technologies, but by whether surveillance systems, laboratories, research networks, financing mechanisms, regulatory pathways and countermeasures are operationally ready before the next spillover occurs.

Ultimately, preparedness is only as strong as its weakest component. Surveillance, diagnostics, clinical care, research, community engagement, governance, and financing function as an integrated system; failure of any one element can delay case detection, impede countermeasure deployment, weaken community trust, and compromise outbreak control despite advances in science and technology.

Conclusion

The 2026 BVD outbreak should mark a turning point in filovirus preparedness. Its legacy should not be defined solely by the countermeasures evaluated or the evidence generated during this epidemic, but by whether it catalyses sustained investment in integrated, species-inclusive systems capable of rapidly detecting, studying, and responding to future outbreaks of any human-pathogenic *orthoebolavirus*.

Acknowledgements

We thank Rachel Friedman and Hannah Melchinger for their assistance with manuscript preparation process.

Declaration of generative AI and AI-assisted technologies in the manuscript preparedness process

During the preparation of this work, the author(s) used Claude for editing and improving readability of the manuscript. The authors(s) reviewed and edited the output as needed and take full responsibility for the content of the published article.

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Table

Table 1. Epidemiologic characteristics of documented Bundibugyo ebolavirus outbreaks

	2007 - 2008	2012	2026 - present
Country	Uganda	DR Congo	DR Congo & Uganda
Dates	August 2007 – February 2008	August – November 2012	May 2026 – ongoing
Duration	6 months	3 months	2 months
Confirmed cases	56	36	**DR Congo:** 1926 confirmed (14 July 2026)[16] **Uganda:** 20 confirmed (14 July 2026)[16]
Probable cases	93	21	---
Suspect cases	--	5	225 (11 July 2026)
Confirmed deaths	37[12]	34[13]	**DR Congo:** 702 (14 July 2026)[16] **Uganda:** 2 (14 July 2026)[16]
Case fatality rate	24.8%[10,12*]	54.8%[13]	~34.9%
Geographic extent	Bundibugyo District, Uganda	Province Orientale, DR Congo	**DR Congo:** Ituri, North Kivu, South Kivu, Tshopo, Haut-Uélé **Uganda:** Kampala, Wakiso
Cross-border spread	No	No	Yes (first documented for BVD)
Diagnostics	Limited RT-PCR	RT-PCR	Pan-filovirus/species-inclusive molecular diagnostics
Medical countermeasures	None	None	Investigational vaccines, therapeutics, & clinical trials
WHO PHEIC declared	No	No	Yes (17 May 2026)

CFR = case fatality rate; PHEIC = public health emergency of international concern.
** For the 2007 outbreak, the overall outbreak CFR was 37/149 (24.8%); among 43 patients with acute laboratory-confirmed infection, 17 died (40%.)*

Comparison of outbreak size, mortality, geographic spread, and available countermeasures across the three known BVD outbreaks. Figures are from contemporaneous WHO, national, and published reports. Differences in reporting categories limit direct comparisons, particularly for the ongoing 2026 outbreak which is ongoing.

Table

Panel 1: Key Challenges to Containing the 2026 Bundibugyo Ebolavirus Outbreak

Diagnostics and laboratory capacity

- Initial reliance on EBOV-focused assays delayed recognition of BDBV
- Limited availability of species-inclusive molecular diagnostics
- Laboratory capacity, reagent shortages, and specimen transport delays
- Need for decentralized molecular testing, sequencing, and laboratory networks

Medical Countermeasures

- No licensed BDBV-specific vaccine
- No proven BDBV-specific therapeutic
- Need to evaluate candidate vaccines, monoclonal antibodies, antivirals, and post-exposure prophylaxis during an ongoing outbreak

Conflict, insecurity, and population mobility

- Ongoing armed conflict limits access to affected communities
- Population displacement and mobility complicate surveillance, contact tracing and follow-up
- Security concerns restrict movement of personnel and supplies
- Cross-border transmission and population movement between DR Congo and neighboring countries

Community trust and risk communication

- Mistrust of authorities and outbreak responders
- Fear, stigma, misinformation and rumors regarding Ebola
- Challenges implementing safe and dignified burials
- Delayed care-seeking and resistance to public health interventions

Fragile health systems

- Concurrent burdens of malaria, tuberculosis, HIV, measles, cholera, and malnutrition
- Limited healthcare workforce and treatment capacity
- Delayed salary payments and healthcare worker strikes disrupted service delivery and outbreak response
- Competing priorities for laboratory and surveillance resources

Infection prevention and control (IPC)

- Healthcare worker infections
- Shortages of personal protective equipment and IPC supplies
- Overcrowded treatment facilities and healthcare settings
- Persistent IPC gaps due to delayed case recognition, workforce shortages, and limited infrastructure

Surveillance and contact tracing

- Weak surveillance systems and delayed case detection
- Undetected transmission chains
- Limited genomic surveillance and sequencing capacity
- Difficulty reaching contacts in insecure or remote settings

Global health financing and preparedness

- Reductions in global health funding
- Strain on multilateral response mechanisms
- Risk that diminished preparedness investments weaken surveillance, laboratory capacity, workforce development and outbreak response
-

Control efforts have been hindered by limitations in diagnostics and medical countermeasures, fragile health systems, insecurity, population mobility, community mistrust, recurrent IPC failures, surveillance constraints, and reductions in global health financing. Together, these factors have complicated surveillance, case detection, clinical care, and outbreak response.

Table

Table 2. Candidate medical countermeasures for Bundibugyo ebolavirus: vaccines and therapeutics

Category	Candidate	Developer	Mechanism / Platform	BDBV evidence	Stage / Trial	Notes
Vaccine	**rVSV-BDBV-GP**	IAVI / UTMB	Recombinant VSV vector Single dose	Survival benefit in NHP models Postexposure protection demonstrated	Preclinical Phase 1 planned	*WHO-identified most promising single-dose candidate* *~7–9 months to clinical-grade production*
Vaccine	**ChAdOx1-BDBV**	Oxford / Serum Institute of India	Chimpanzee adenovirus vector Two doses	Preclinical data with related filoviruses BDBV- specific preclinical studies ongoing	Preclinical Phase 1 planned	*May be first to reach clinical-grade availability (~2–3 months)*
Vaccine	**mRNA-BDBV**	Moderna	Lipid nanoparticle mRNA	Platform validated for related filoviruses BDBV-specific data in development	Preclinical	*Largest CEPI investment (up to US$50 million)*
Therapeutic	**MBP134**	Mapp Biopharmaceutical	Two-mAb cocktail targeting glycoprotein (GP)	Protective in NHP models including BDBV Evaluated during the 2022 Sudan virus outbreak	Prioritized for evaluation in the PARTNERS adaptive platform trial[1]	*WHO Priority 1* *No licensed indication*
Therapeutic	**Maftivimab**	Regeneron	Monoclonal antibody Binds EBOV GP	Broad neutralizing activity across multiple Ebola species including BVD	Candidate for evaluation in the PARTNERS adaptive platform trial	*WHO Priority 1* *Component of Inmazeb (EBOV)*
Therapeutic	**Remdesivir**	Gilead Sciences	RNA polymerase inhibitor (antiviral)	In vitro and preclinical activity against BVD	Prioritized for evaluation in the PARTNERS adaptive platform trial[1]	*WHO Priority 1* *Prioritized in combination with mAb therapy*
Therapeutic	**Obeldesivir**	Gilead Sciences	Oral prodrug of remdesivir (PEP)	Antiviral activity Prioritized for PEP among high-risk contacts	EBO-PEP BUNDI trial (ANRS)[2]	*Oral administration may facilitate PEP in field settings*
Therapeutic	**Inmazeb (REGN-EB3)**	Regeneron	Three-mAb cocktail (reference)	Limited BDBV cross-reactivity Not prioritized for BVD trials	Not prioritized	*FDA-approved for EBOV only* *WHO advises against use outside research for BVD*

[1] PARTNERS adaptive platform trial launched 2 July 2026
[2] EBO-PEP trial launched 14 July 2026

BVD = Bundibugyo virus disease; EBOV = Zaire ebolavirus; SUDV = Sudan virus; GP = glycoprotein; mAb = monoclonal antibody; NHP = non-human primate; PEP = post-exposure prophylaxis; CEPI = Coalition for Epidemic Preparedness Innovation; UTMB = University of Texas Medical Branch, Galveston; WHO Technical Advisory Group recommendations issued 28 May 2026

The 2026 outbreak has accelerated evaluation of candidate vaccines, therapeutics, and post-exposure prophylaxis strategies. The table summarizes leading countermeasures under investigation. No candidate has demonstrated clinical efficacy against BDBV disease in humans, and no licensed BDBV-specific medical countermeasures are currently available.

Table

Panel 2: Research priorities for Bundibugyo Ebolavirus Preparedness and Response

Virology and pathogenesis

- What are the principal determinants of BDBV tissue tropism and organ-specific disease?
- Which immune responses correlate with protection against infection and severe disease?
- What is the frequency, duration, and clinical significance of viral persistence?
- How do BDBV replication kinetics and immune evasion mechanisms differ from those of EBOV & SUDV?

Clinical and epidemiologic research

- What host and viral factors predict severe disease and mortality?
- What is the full clinical spectrum of BVD infection, including mild and asymptomatic disease?
- What are risk factors for severe disease and mortality – including age, pregnancy, comorbidities, nutritional status, host genetics, viral load, immune responses, time to presentation, and access to supportive care?
- What are the drivers of transmission within households, healthcare facilities, & communities?
- How do viral load, symptom stage, and body-fluid shedding correlate with infectiousness?
- What are the long-term clinical, neurological, ocular, auditory, reproductive, and mental health sequelae of BVD infection?

Vaccines and therapeutics

- Can EBOV vaccines provide meaningful protection of humans in a BVD outbreak?
- Can multivalent or pan-ebolavirus vaccines provide durable cross-species protection?
- Which vaccine platforms provide the optimal balance of immunogenicity, durability, scalability, and outbreak readiness?
- Which broadly neutralising monoclonal antibodies or antibody combinations provide the greatest protection against diverse ebolavirus species?
- Can broadly neutralising monoclonal antibodies such as MBP134 provide clinically meaningful protection against BVD?
- Does remdesivir have a role in BVD disease when administered early or in combination with antibody therapy?
- What role do antiviral agents and host-directed therapies have in BVD treatment?
- Which post-exposure prophylaxis trial designs can enroll contacts rapidly enough to generate interpretable evidence?

- How can ring-vaccination, manufacturing, stockpiling, and adaptive trial designs be optimized for small or geographically dispersed outbreaks?

Clinical care

- Which components of supportive care provide the greatest survival benefit?
- How can advanced supportive care —including oxygen therapy, vasopressors, and renal replacement therapy— be adapted for resource-constrained outbreak settings?
- What models of outbreak critical care are scalable and sustainable?
- What point-of-care diagnostics and monitoring tools most improve clinical decision-making?

Care of survivors

- What is the burden and pathophysiology of post-BVD sequelae?
- How durable are humoral and cellular immune responses after recovery?
- What is the risk of relapse or transmission associated with persistent infection?
- How should prospective survivor cohorts be designed to define long-term clinical, virological, immunological, and psychosocial outcomes?
- What models of survivor care are feasible in affected regions?

Preparedness and implementation science

- How can outbreak clinical trials and studies be activated more rapidly?
- Can investigational vaccines, therapeutics, and post-exposure prophylaxis strategeis be made trial-ready before outbreaks occur?
- How can species-inclusive diagnostics be integrated into acute febrile illness algorithms and deployed through decentralized laboratory networks?
- Which implementation strategies best sustain infection prevention and control readiness between outbreaks?
- Which community engagement and risk communication strategies most improve care-seeking, reporting, contact tracing, and acceptance of public health measures?
- Which investments in laboratory systems, surveillance, infection prevention and control, and workforce development provide the greatest preparedness benefits?
- What governance and data-sharing models best support equitable outbreak research?

The limited experience with Bundibugyo ebolavirus has left substantial gaps in understanding of disease pathogenesis, transmission, clinical outcomes, medical countermeasures, survivor health, and outbreak

preparedness. These research priorities provide a framework for generating evidence and strengthening species-inclusive, outbreak-ready preparedness before future outbreaks occur.

Figure



Figure 1. Integrated Framework for Species-Inclusive Filovirus Preparednes
Species-inclusive filovirus preparedness requires integrated systems spanning surveillance, diagnostics, clinical care, countermeasures, research, workforce, governance, financing, and One Health. Together, these components support a continuous cycle of preparedness, detection, response, recovery, and capacity building.