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Ebola virus disease at the human–animal–environment interface: a scoping review of recent outbreaks, transmission dynamics, and future preventive strategies

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Abstract

Background Ebola Virus Disease (EVD) remains among the most lethal zoonotic hemorrhagic fevers, with case fatality rates (CFRs) of 25% to over 90%. Since 2018, successive major outbreaks; the 10th Democratic Republic of the Congo (DRC) epidemic (2018–2020), the 2021 Guinea resurgence, the Uganda Sudan ebolavirus outbreaks (2022, 2025), the 16th DRC (Kasai) outbreak (2025), and the 2026 Bundibugyo virus emergency declared a Public Health Emergency of International Concern have claimed thousands of lives, underscoring EVD's persistent threat at the human–animal–environment interface and critical preparedness gaps.

Objectives This scoping review synthesizes recent evidence on EVD outbreak dynamics, zoonotic transmission, genomic epidemiology, therapeutic and vaccine developments, and the sociocultural and ecological drivers of outbreaks.

Methods Following PRISMA-ScR, we searched PubMed, Embase, Cochrane Library, Web of Science, and Google Scholar (inception to May 2026), supplemented by WHO outbreak reports. Fifty eligible sources were included, over 90% published 2018–2026.

Results The DRC 10th outbreak (3,470 cases; CFR 66.2%) was exacerbated by armed conflict, nosocomial transmission, and community resistance. The 2021 Guinea resurgence was genetically linked to a 2014–2016 survivor, revealing viral persistence in immune-privileged tissues. The 2022 Uganda outbreak (164 cases; CFR 46.3%) highlighted super-spreading and inadequate infection control at private facilities. Frugivorous Pteropodidae bats remain the likely reservoir. Approved monoclonal antibodies Inmazeb and Ebanga showed 28-day mortality of 33.5% and 35.1% versus 49.7% for ZMapp; rVSV-ZEBOV protects against Zaire but not Sudan ebolavirus. Recent events reinforced these themes: 2025 Uganda (14 cases; CFR 29%) saw the first SUDV ring-vaccination trial; 2025 DRC-Kasai (64 cases; CFR 70.3%) was contained within ~3 months; and 2026 Bundibugyo again exposed absent countermeasures for non-Zaire species.

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Conclusion Integrated One Health surveillance, equitable therapeutic and vaccine access, community engagement, and genomic epidemiology must anchor future EVD prevention. Urgent investment in Sudan ebolavirus vaccines and outbreak-resilient health systems is essential.

Highlights/Novelties of the study

- This is the first comprehensive scoping review to integrate evidence from all three major post-2018 EVD outbreaks namely the DRC 10th epidemic, the 2021 Guinea resurgence, and the 2022 Uganda Sudan ebolavirus outbreak within a unified One Health framework.
- We provide a novel synthesis of genomic epidemiology alongside clinical, ecological, and sociocultural transmission determinants, bridging the gap between laboratory science and public health practice.
- The review critically appraises FDA-approved therapeutics (Inmazeb, Ebanga) and vaccine strategies (rVSV-ZEBOV) within the context of ongoing outbreaks caused by non-Zaire ebolaviruses for which no approved medical countermeasures currently exist.
- Our analysis highlights the paradigm-shifting finding that EVD can re-emerge years after an epidemic through persistence of Zaire ebolavirus in survivor immune-privileged tissues, with direct implications for long-term surveillance policies.

Keywords Ebola virus disease, One Health, Zoonotic spillover, Sudan ebolavirus, Outbreak preparedness, Monoclonal antibodies, rVSV-ZEBOV vaccine

Background and literature review

Historical context and global burden of Ebola virus disease

Ebola Virus Disease (EVD) is a severe and often fatal acute haemorrhagic fever caused by viruses belonging to the genus *Orthoebolavirus* (formerly *Ebolavirus*) within the family Filoviridae. Since its first description in 1976 along the Ebola River in the Democratic Republic of the Congo (DRC) then Zaire and simultaneously in Nzara, Sudan, EVD has emerged as one of the most feared infectious diseases known to medicine. The genus currently encompasses six recognized species: *Zaire ebolavirus* (ZEBOV), *Sudan ebolavirus* (SUDV), *Bundibugyo ebolavirus* (BDBV), *Taï Forest ebolavirus* (TAFV), *Reston ebolavirus* (RESTV), and the recently described *Bombali ebolavirus* (BOMV). Of these, ZEBOV, SUDV, and BDBV have caused documented human outbreaks with significant mortality, while RESTV appears non-pathogenic to humans [1, 2]. Beyond the genus *Ebolavirus*, the family *Filoviridae* also encompasses *Marburgvirus*, the etiological agent of Marburg virus disease, a clinically analogous and frequently lethal hemorrhagic fever underscoring the broader and continuing public health threat posed by filoviruses as a group [3].

The global burden of EVD, though dwarfed in absolute numbers by other infectious diseases, exerts a disproportionate impact on already fragile health systems in sub-Saharan Africa. Analysis of the Global Burden of Disease 2021 Study reveals that EVD, despite its lower absolute incidence compared to diseases such as HIV/AIDS or dengue fever, carries among the highest age-standardized disability-adjusted life year (DALY) rates per capita of all viral infectious diseases of poverty, inversely correlated with the Socio-Demographic Index (SDI) ($r = -0.2$, $P < 0.005$) [1]. These metrics underscore that the populations most exposed to EVD are systematically among the world's most medically underserved, thereby creating a cycle of vulnerability, delayed detection, and amplified transmission.

Before the 2013–2016 West African epidemic, individual EVD outbreaks were typically self-limiting events in remote forest communities, containing several dozens to a few hundred cases. The West African epidemic fundamentally transformed global understanding of EVD's pandemic potential: spanning Guinea, Sierra Leone, and Liberia over more than two years, it infected 28,616 individuals and claimed over 11,000 lives, inflicting an estimated economic loss of USD 6 billion in affected countries and upwards of USD 12 billion globally [2]. Retrospective seroprevalence studies at the index site in Meliandou, Guinea, subsequently revealed that the true toll including, subclinical and asymptomatic infections was broader than initially reported, with oral fluid-confirmed evidence of infection in community members who were not captured in official case counts [4].

Taxonomy, virology, and molecular epidemiology

Ebolaviruses are enveloped, non-segmented, negative-sense single-stranded RNA viruses with a characteristic filamentous morphology. The approximately 19-kilobase genome encodes seven structural proteins: the nucleoprotein (NP), viral protein 35 (VP35), VP40, the glycoprotein (GP), VP30, VP24, and the RNA-dependent RNA polymerase (L). The surface GP is the principal mediator of host cell attachment and membrane fusion, acting as the primary target for neutralising antibodies and vaccine-induced immunity [5].

Structurally, each virion is bounded by a host-derived lipid envelope studded with trimeric glycoprotein (GP)

spikes, beneath which the VP40 matrix and the minor matrix protein VP24 enclose a helical ribonucleoprotein complex in which NP, VP35, VP30, and the large (L) polymerase associate with the genomic RNA. The overall architecture and genome organization of the Ebola virion are summarized in Fig. 1.

Phylogenetic analyses of ZEBOV isolates across successive DRC outbreaks have defined four major lineages, with the 2018 North Kivu outbreak virus clustering distinctly from the 2014–2016 West African clade. Positive selection sites particularly in GP and VP24 have been identified, with key amino acid substitutions such as F443L in GP distinguishing the DRC lineage from West African strains [5]. These molecular signatures are epidemiologically informative and have direct implications for the development of broadly protective vaccines. Phylodynamic reconstructions of the West African epidemic in Sierra Leone have further demonstrated how viral genomic surveillance can resolve discrete transmission chains and infer the tempo and directionality of spread in near real time [6]. For the Sudan ebolavirus, the 2022 Mubende variant exhibited 96% amino acid similarity with historical SUDV sequences dating to the 1970s, demonstrating a remarkable degree of genomic conservation, which is highly promising for diagnostic and therapeutic development [7].

Bundibugyo ebolavirus, responsible for the 2007–2008 Uganda outbreak and the 2012 DRC outbreak in Isiro, presents a particularly compelling case study in molecular epidemiology. Retrospective sequencing of additional specimens from the 2012 outbreak challenged the prevailing hypothesis of a single-spillover-event origin and suggested that BDBV may have been circulating in the community for up to 50 days before official recognition a finding with profound implications for understanding the true onset of zoonotic spillover events [8].

The one health interface: ecological drivers and reservoir dynamics

The One Health framework, integrating human, animal, and environmental health provides the most conceptually coherent lens through which to understand EVD

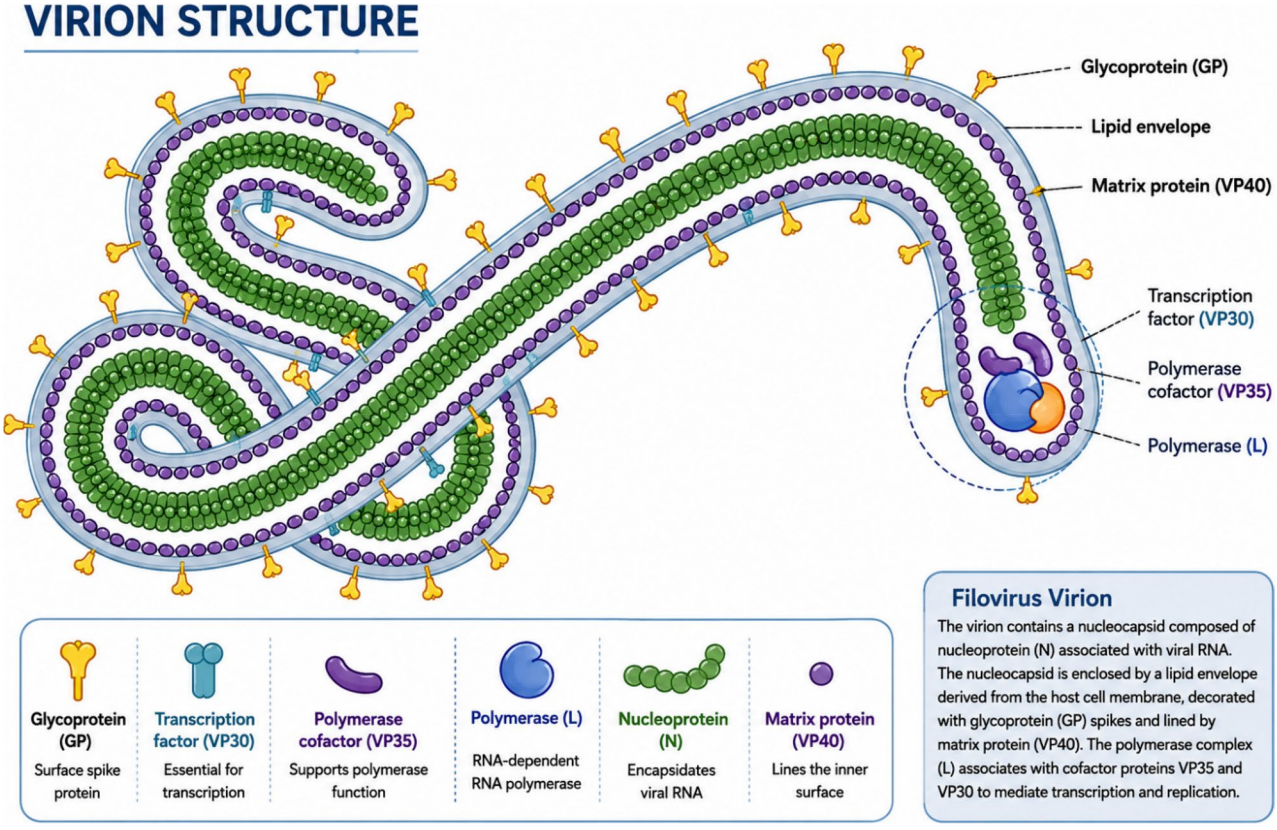

Fig. 1 Structure of the Ebola virus. Schematic structure and genome organization of the Ebola virion. The virion's surface is studded with glycoprotein (GP) spikes responsible for host-cell attachment, anchored in a lipid envelope derived from the host cell membrane, which is lined internally by the matrix protein VP40 that maintains structural integrity. Coiled within is the helical nucleocapsid, formed by the nucleoprotein (N, shown in green) that encapsidates the single-stranded viral RNA genome. The inset detail and legend identify the components of the polymerase complex, including the transcription factor VP30 (essential for initiating transcription), the polymerase cofactor VP35 (which supports polymerase function), and the large polymerase protein L (the RNA-dependent RNA polymerase), which together mediate viral transcription and genome replication. A summary box in the lower right reinforces these relationships, making the figure a clear educational overview of filovirus architecture and the functional roles of its seven structural proteins

emergence and persistence [9]. Converging evidence from ecological, virological, and seroepidemiological studies implicates frugivorous bats of the family *Pteropodidae* particularly species of the genera *Hypsignathus monstrosus*, *Epomops franqueti*, and *Myonycteris torquata* as the most plausible reservoir host for ZEBOV, although definitive proof of persistent bat infection under natural conditions remains elusive. The accelerated viral dynamics documented in bat cell lines wherein viral replication proceeds at rates far exceeding those observed in primate cell lines without triggering commensurate apoptotic or interferon responses offer a compelling mechanistic explanation for how bats may sustain filovirus infections without succumbing to disease [10].

Mechanistic mathematical models of viral dynamics in bat reservoir populations have demonstrated that the interplay between bat birth-pulse asynchrony, seasonal immune cycling, and population density creates periodic windows of heightened viral shedding windows that likely correspond temporally to observed EVD spillover events in adjacent human communities [11]. In vitro studies confirming that adipose tissue from both human- and bat-derived cell lines supports ZEBOV replication highlight the role of lipid-rich tissues as potential sites of viral persistence and immune evasion [12].

The human-bat interface is not merely a biological phenomenon but a deeply socioecological one. Studies in Sierra Leone's Bombali District documented frequent and diverse human interactions with bat populations including hunting of bats for consumption, bat guano collection for agricultural fertilizer, and residential cohabitation of bat colonies creating multiple, recurring exposure pathways that deforestation and agricultural expansion are intensifying by fragmenting forest habitats and displacing bat populations into closer proximity to human settlements [13].

Recent outbreak overview (2018–2026)

Between August 2018 and April 2020, the DRC experienced its 10th and most deadly EVD outbreak, centered in the North Kivu and Ituri provinces. With 3,470 confirmed and probable cases and a CFR of 66.2%, this epidemic surpassed all previous DRC outbreaks in scale. Its protracted course was shaped by a unique constellation of adversities: an active armed conflict with more than 100 armed groups operating in the affected region, multiple direct attacks against healthcare workers and Ebola response infrastructure, and deep community mistrust rooted in historical marginalization [14, 15]. Conflict dynamics, particularly Ebola-targeted civilian attacks, were found to increase the reproduction number (Rt) significantly Ebola-targeted violence events at the 95th percentile corresponded to an Rt of 1.52 (95% CI: 1.30–1.74) versus 1.06 at baseline [16].

In February 2021, Guinea declared its first EVD outbreak since the historic 2014–2016 epidemic, a resurgence that confounded epidemiologists in its apparent absence of any zoonotic spillover source. Whole-genome sequencing revealed that the 2021 Nzérékoré outbreak strain was not the product of a fresh bat-to-human transmission event but rather the reactivation of Zaire ebolavirus that had persisted in the body of a survivor of the 2014–2016 epidemic for more than five years. This watershed discovery published in *Nature* established EVD survivor-linked recurrence as a new paradigm with critical implications for long-term surveillance, survivor follow-up, and sexual transmission risk counselling [17].

Uganda's 2022 Sudan ebolavirus outbreak (September–November 2022), originating in Mubende District, resulted in 164 cases (142 confirmed, 22 probable) and 77 deaths (CFR 46.3%). Uniquely among recent outbreaks, SUDV represents a species for which no licensed vaccine or specific therapeutic currently exists, placing this outbreak in a category of heightened concern [18, 19]. Healthcare-associated transmission through private health facilities which lacked adequate infection prevention and control (IPC) capacity drove the early phase of the outbreak, with two super-spreader patients collectively linked to 51 confirmed secondary cases [20].

The tempo of EVD emergence accelerated markedly in 2025 and 2026, underscoring the dynamic and escalating nature of the filovirus threat. On 30 January 2025, Uganda declared its sixth Sudan ebolavirus outbreak, centered on the capital Kampala and ultimately spanning seven districts. Originating in a healthcare worker, the outbreak comprised 14 cases (12 confirmed and two probable) with four deaths (case fatality rate 29%) before being declared over on 26 April 2025 [21]. Critically, this event prompted the first-ever ring-vaccination trial against Sudan virus, deploying an investigational vaccine within days of outbreak confirmation a landmark intervention in the otherwise countermeasure-deficient SUDV landscape [22].

Subsequently, on 4 September 2025, the DRC declared its 16th EVD outbreak in the remote Bulape Health Zone of Kasai Province, caused by Zaire ebolavirus. The presumptive index case was a pregnant woman in her third trimester who developed hemorrhagic symptoms in August 2025. The outbreak ultimately comprised 64 cases (53 confirmed, 11 probable) and 45 deaths, corresponding to a high case fatality rate of 70.3%, with transmission concentrated in the Dikolo and Bulape health areas and five infections recorded among healthcare workers [23, 24]. Despite unfolding in a hard-to-reach rural setting with limited road, water, and telecommunication infrastructure, the outbreak was contained within approximately three months through an incident-management-system response that integrated rapid

investigation, community engagement, ring vaccination with the rVSV-ZEBOV vaccine, and embedded operational research; it was declared over on 1 December 2025 [23].

The threat has persisted into 2026. In May 2026, following an alert regarding a high-mortality illness in Ituri Province that killed several health workers, the DRC declared its 17th Ebola outbreak, this time caused by Bundibugyo virus, a species for which, as with SUDV, no licensed vaccine or specific therapeutic exists. Imported cases were detected in neighboring Uganda, and on 17 May 2026 the World Health Organization declared the event a Public Health Emergency of International Concern. As of 16 May 2026, eight laboratory-confirmed cases among 246 suspected cases and 80 suspected deaths had been reported across multiple Ituri health zones, with case counts rising thereafter as the situation continued to evolve [25]. The clustering of three discrete Ebola events, two distinct ebolavirus species across Uganda and the DRC in 2025, and a third species precipitating an international emergency in 2026 within an eighteen-month window represents the most intense period of filovirus activity since 2019 and provides the immediate impetus for this review [22].

Research gaps and study objectives

Despite the accumulation of substantial literature following each of these outbreaks, no comprehensive scoping review to date has synthesized evidence from all three major post-2018 EVD events within an integrated One Health framework encompassing zoonotic transmission, genomic epidemiology, clinical outcomes, therapeutic advances, and sociocultural drivers. Furthermore, previous reviews have largely addressed ZEBOV or the West African epidemic in isolation, leaving critical gaps around Sudan ebolavirus epidemiology, survivor-linked recurrence, and outbreak-specific super-spreading dynamics.

This scoping review therefore aims to: (i) systematically map the epidemiological landscape of major EVD outbreaks occurring between 2018 and 2026; (ii) characterise the transmission dynamics at the human–animal–environment interface; (iii) synthesise the evidence base for currently approved and emerging therapeutics and vaccines; (iv) appraise the sociocultural and structural factors modifying outbreak trajectories; and (v) identify priority research areas and policy recommendations to guide future EVD prevention and response.

Methods

Study design

This work was conducted as a scoping review in accordance with the methodological framework of Arksey and O'Malley (2005), subsequently refined by Levac et al. [26] and Tricco et al. [27], and adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) 2020 guidelines [28]. Scoping review methodology was selected over systematic review given the broad and multidisciplinary nature of the research question spanning virology, ecology, epidemiology, clinical medicine, and public health policy and the explicit aim of mapping the existing evidence landscape and identifying knowledge gaps rather than synthesizing a single quantitative outcome.

Eligibility criteria

Studies were included if they met all of the following criteria: (a) published as peer-reviewed original research articles, systematic reviews, or evidence-based review articles; (b) published in English; (c) focused on EVD in human populations or on animal reservoir/ecological research directly relevant to human spillover risk; (d) published between January 2013 and May 2026; and (e) reporting on one or more of the following domains: EVD outbreak epidemiology, transmission dynamics, zoonotic spillover, clinical features, therapeutic or vaccine trials, molecular/genomic epidemiology, One Health surveillance, or outbreak preparedness and response.

Studies were excluded if they: presented data exclusively on non-human primates or rodents without relevance to human spillover; were limited to in vitro or animal model studies without human applicability; were conference abstracts, letters without original data, editorials, or commentaries; or were published in predatory journals identifiable using the Beall's List criteria.

Study selection process and PRISMA flow

Systematic searches were conducted in five electronic databases: PubMed/MEDLINE, Embase, Cochrane Library, Web of Science, and Google Scholar (first 20 pages of results). Hand-searching of reference lists of included studies and key EVD-focused journals was performed to capture additional eligible literature. The search strategy employed a combination of Medical Subject Headings (MeSH) terms and free-text keywords: ("Ebola" OR "Ebolavirus" OR "ZEBOV" OR "SUDV" OR "BDBV" OR "EVD" OR "hemorrhagic fever") AND ("outbreak" OR "transmission" OR "reservoir" OR "One Health" OR "vaccine" OR "therapeutic" OR "epidemiology" OR "zoonosis" OR "spillover" OR "preparedness"). Date filters were applied from January 2013 to May 2026 to capture the post-West-African-epidemic era while including contextual background literature. The complete search was conducted in November 2024 and updated in May 2026, with official World Health Organization Disease Outbreak News consulted for the 2025–2026 events.

All retrieved records were imported into Rayyan AI, a systematic review management platform, for

deduplication and blind dual-reviewer screening. Two independent reviewers (A.N.O. and I.A.A.R.) independently screened titles and abstracts, followed by full-text assessment of eligible studies. Disagreements were resolved through consensus discussion with a third reviewer (L.G.F.). Inter-rater agreement was measured using Cohen's kappa ($\kappa = 0.84$), indicating near-perfect agreement during the full-text eligibility phase. The PRISMA 2020 flow diagram is presented in Fig. 2.

Data extraction and curation

Data were extracted by two reviewers using a standardized, piloted extraction form designed in Microsoft Excel, capturing the following fields for each included study: (i) study identification (first author, year, journal, DOI); (ii) study design and methodology; (iii) geographic setting and outbreak period; (iv) ebolavirus species; (v) key epidemiological parameters (case counts, CFR, reproduction number R_0/Rt, incubation period); (vi) transmission routes documented; (vii) animal reservoir data; (viii) clinical outcomes reported; (ix) intervention type (vaccine, therapeutic, IPC, surveillance); (x) study limitations and risk of bias. Data were synthesized narratively, and quantitative parameters were tabulated for comparative analysis across outbreaks (Table 1).

Statistical analysis and quality assessment

Given the heterogeneity in study design, setting, and outcomes, formal meta-analysis was not appropriate. Descriptive statistics were computed for continuous variables (median with interquartile range [IQR] for non-parametric distributions; mean ± standard deviation where normally distributed). Proportional outcomes (CFR, proportion of healthcare-associated cases) were reported with 95% confidence intervals (95% CI) calculated using the Wilson score method for proportions. Comparisons of CFR across ebolavirus species were performed using χ^2 tests, with statistical significance defined at $P < 0.05$.

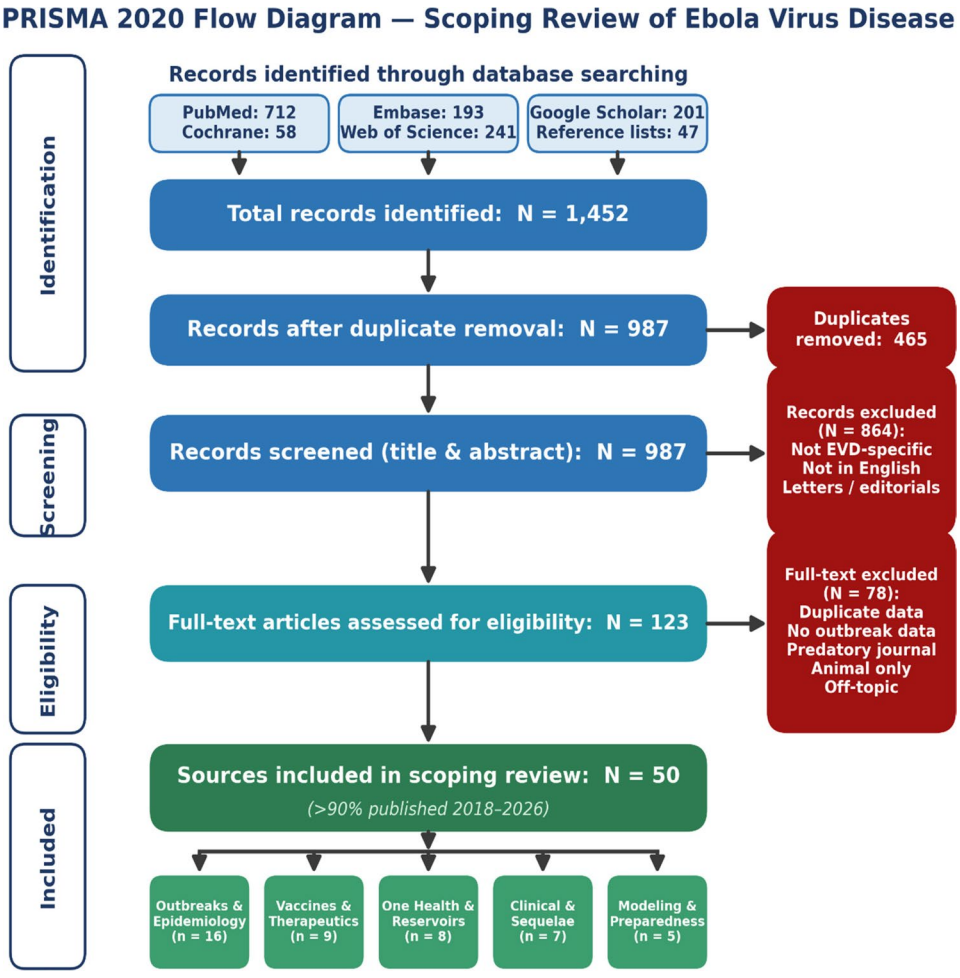

Fig. 2 PRISMA 2020 flow diagram illustrating the study selection process for this scoping review. From 1,452 initially identified records, 50 sources were ultimately included for evidence synthesis. κ = Cohen's kappa inter-rater reliability statistic

Table 1 Comparative epidemiological characteristics of major EVD outbreaks included in this scoping review (2018–2026)

Outbreak Location	Year	Ebolavirus Species	Total Cases (Confirmed)	CFR (%)	R_0 / Rt	Key Features	Reference
DRC (North Kivu, Ituri)	2018–2020	ZEBOV	3,470	66.2%	~1.8 initial Rt ~ 1.06 avg	Armed conflict; healthcare-associated spread; IDP displacement; longest DRC outbreak	[14–16, 29]
DRC (Équateur)	2020	ZEBOV	130	56.9%	Est. 1.5–2.0	Remote forest region; limited infrastructure; rapid response containing spread	[30]
Guinea (Nzérékoré)	2021	ZEBOV	23	73.9%	Est. 1.4	Survivor-linked recurrence; genetically identical to 2014–16 West African strain; 5 + years persistence	[17]
DRC (Équateur)	2022	ZEBOV	5	60.0%	N/R	Rapid containment; remote locale; aggressive ring vaccination	[31]
Uganda (Mubende et al.)	2022	SUDV	164	46.3%	1.25 overall	No approved vaccine/treatment; super-spreading events; private facility IPC failures; multi-district spread	[7, 18, 20, 32]
Uganda (Kampala)	2025	SUDV	14 (12)	29.0%	N/R	Sixth Ugandan SUDV outbreak; first SUDV ring-vaccination trial; rapid containment in < 3 months	[21, 22]
DRC (Bulape, Kasai)	2025	ZEBOV	64 (53)	70.3%	N/R	16th DRC outbreak; remote rural setting; incident-management-system response; contained in ~ 3 months	[23, 24]
DRC/Uganda (Ituri)	2026[†]	BDBV	246 susp. (8 conf.)[†]	N/E[†]	N/R	17th DRC outbreak; no licensed BDBV vaccine; PHEIC declared 17 May 2026; imported cases in Uganda	[25]

CFR Case Fatality Rate, R_0 Basic Reproduction Number, *Rt* Time-varying Reproduction Number, *ZEBOV* Zaire ebolavirus, *SUDV* Sudan ebolavirus, *BDBV* Bundibugyo ebolavirus, *IDP* Internally Displaced Person, *IPC* Infection Prevention and Control, *PHEIC* Public Health Emergency of International Concern, *N/R* Not reported, *N/E* Not yet established, *DRC* Democratic Republic of the Congo

[†]The 2026 Bundibugyo virus outbreak was ongoing at the time of writing; figures are provisional World Health Organization counts as of 16 May 2026 and the outbreak-specific CFR had not yet been established

Quality appraisal was performed using the Appraisal Tool for Cross-Sectional Studies (AXIS) for observational studies and the Critical Appraisal Skills Program (CASP) checklists for cohort studies and systematic reviews. Risk of bias was independently assessed by two reviewers and is reported in Supplementary Table S1. The Joanna Briggs Institute (JBI) Scoping Review Checklist confirmed methodological alignment with scoping review standards for all 50 included sources.

Results

Overview of included studies

Fifty sources were included in this scoping review, comprising 45 peer-reviewed studies together with five additional items documenting the most recent (2025–2026) outbreaks of which two were peer-reviewed analyses and three were official World Health Organization (WHO) outbreak reports. Forty-six of the 50 sources (92.0%) were published after 2018, and collectively they represent data from more than 12 countries across sub-Saharan Africa, Europe, and North America. The peer-reviewed studies comprised 16 original epidemiological investigations, 9 vaccine and therapeutic analyses, 8 One Health and reservoir ecology studies, 7 clinical outcome studies, 3 mathematical modelling studies, and 2 global burden analyses, complemented by a 2026 filovirus-preparedness policy review. The most commonly studied geographic settings were the DRC and Uganda. The predominant ebolavirus species studied was Zaire ebolavirus, followed by Sudan ebolavirus, with Bundibugyo virus featuring prominently in the 2026 outbreak. Fig. 3 presents the temporal distribution and scale of major outbreaks covered.

Comparative epidemiological characteristics of recent outbreaks

The 2025 and 2026 outbreaks reinforce several patterns evident across the earlier events. The 2025 DRC (Kasai) Zaire ebolavirus outbreak retained a very high case fatality yet was contained far more rapidly than the protracted 2018–2020 epidemic, reflecting pre-positioned vaccine stockpiles, rapid ring vaccination, and an experienced incident-management structure [23, 24]. The 2025 Uganda SUDV outbreak similarly arose from a healthcare-worker index case and again confronted the absence of a licensed Sudan-virus vaccine, partially offset for the first time by an emergency ring-vaccination trial [21, 22]. The 2026 Bundibugyo virus emergency extends this pattern to a third ebolavirus species lacking licensed countermeasures, and its emergence in a conflict-affected, mining-influenced area of Ituri exemplifies the ecological and security drivers discussed below [25].

Transmission dynamics and the one health interface

Figure 4 schematizes the One Health triad of transmission pathways documented in the included literature. The zoonotic spillover interface where animal reservoir host exposure events translate into primary human infection represents the critical entry point into all EVD epidemics [9].

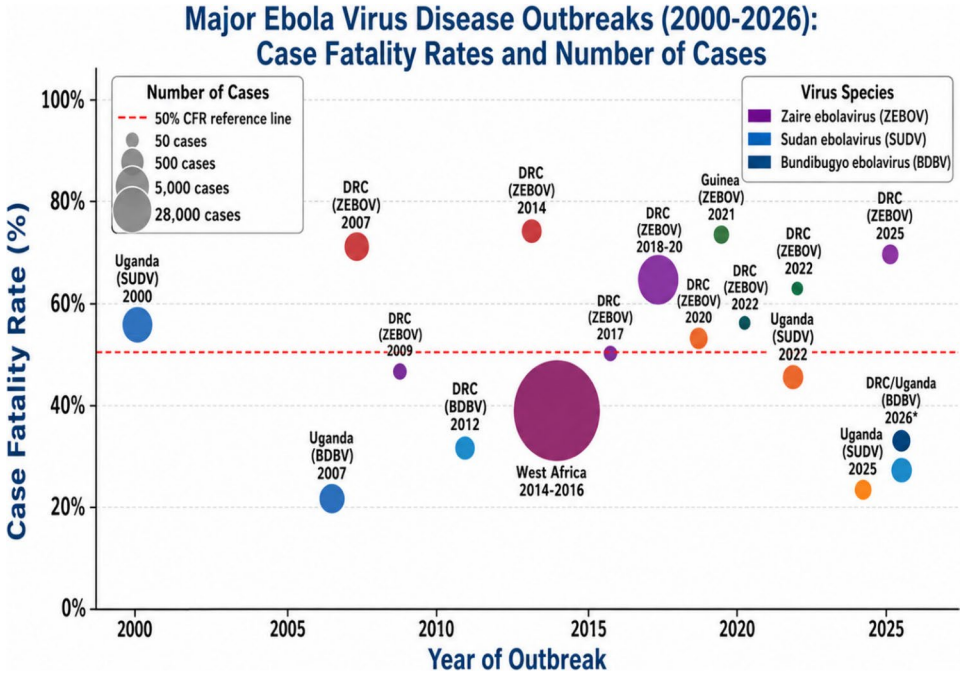

Fig. 3 Temporal distribution of major Ebola Virus Disease outbreaks from 2000 to 2026, illustrating case fatality rates (y-axis) and relative case burden (bubble size). The 2014–2016 West African epidemic represents the largest recorded outbreak; the 2025 DRC (Kasai) and 2025 Uganda events and the 2026 Bundibugyo virus emergency mark the most recent activity. CFR = case fatality rate; ZEBOV = Zaire ebolavirus; SUDV = Sudan ebolavirus; BDBV = Bundibugyo ebolavirus. The 2026 Bundibugyo virus outbreak was ongoing at the time of writing; the corresponding point reflects provisional World Health Organization suspected-case figures and apparent CFR as of 16 May 2026. Data derived from WHO outbreak reports

Frugivorous bats of the family *Pteropodidae* including, hammer-headed bats (*Hypsignathus monstrosus*) and epauletted fruit bats (*Epomops franqueti*) are the foremost reservoir candidates for ZEBOV. Experimental studies using human- and bat-derived adipose cell lines have confirmed the permissiveness of bat cell types to EVD infection and replication [12]. Mechanistic modelling of viral dynamics in bat reservoir populations demonstrates that seasonal birth pulses, which transiently amplify population density and introduce large cohorts of immunologically naive juveniles, create predictable "spillover windows" of heightened environmental contamination and human exposure risk [11]. Human hunting of bushmeat including, bats, non-human primates, and forest antelopes — coupled with the handling of fresh carcasses, constitutes the primary documented mechanism of primary (index) case generation across nearly all historical outbreaks [13].

Healthcare-associated (nosocomial) transmission emerged as a particularly dominant pathway during recent outbreaks. During the 2022 Uganda SUDV outbreak, healthcare-associated cases constituted 26% of all confirmed cases during the early outbreak phase, with transmission linked specifically to inadequate IPC practices at private health facilities that lacked the training or resources to identify and isolate suspected cases promptly [18]. Two super-spreader patients (Patient A and Patient B) were linked collectively to 51 secondary confirmed cases, with transmission mediated by family contact, faith-based healing practices, and post-mortem ritualistic handling [20]. Detailed reconstruction of the outbreak's origin traced the initial chain of transmission to a single index patient, highlighting the diagnostic delays that preceded formal recognition of the outbreak [29].

Sexual transmission of ZEBOV from convalescent survivors particularly through semen in which viable virus can persist for 470–565 days post-clinical recovery was definitively established during the West African epidemic and remains a critical concern for survivor follow-up programs. The 2021 Guinea resurgence, caused by genetically identical virus recovered from a survivor of the 2014–2016 epidemic more than five years after their initial infection, represents the most dramatic illustration of this phenomenon in a real-world outbreak setting [17].

Clinical features, case fatality rates, and special populations

The incubation period of EVD ranges from 2 to 21 days, with a median of 6–12 days across studies reviewed (Table 1). The clinical presentation is characterized by an abrupt-onset febrile illness accompanied by myalgia, headache, fatigue, and gastrointestinal manifestations (nausea, vomiting, diarrhea). Hemorrhagic

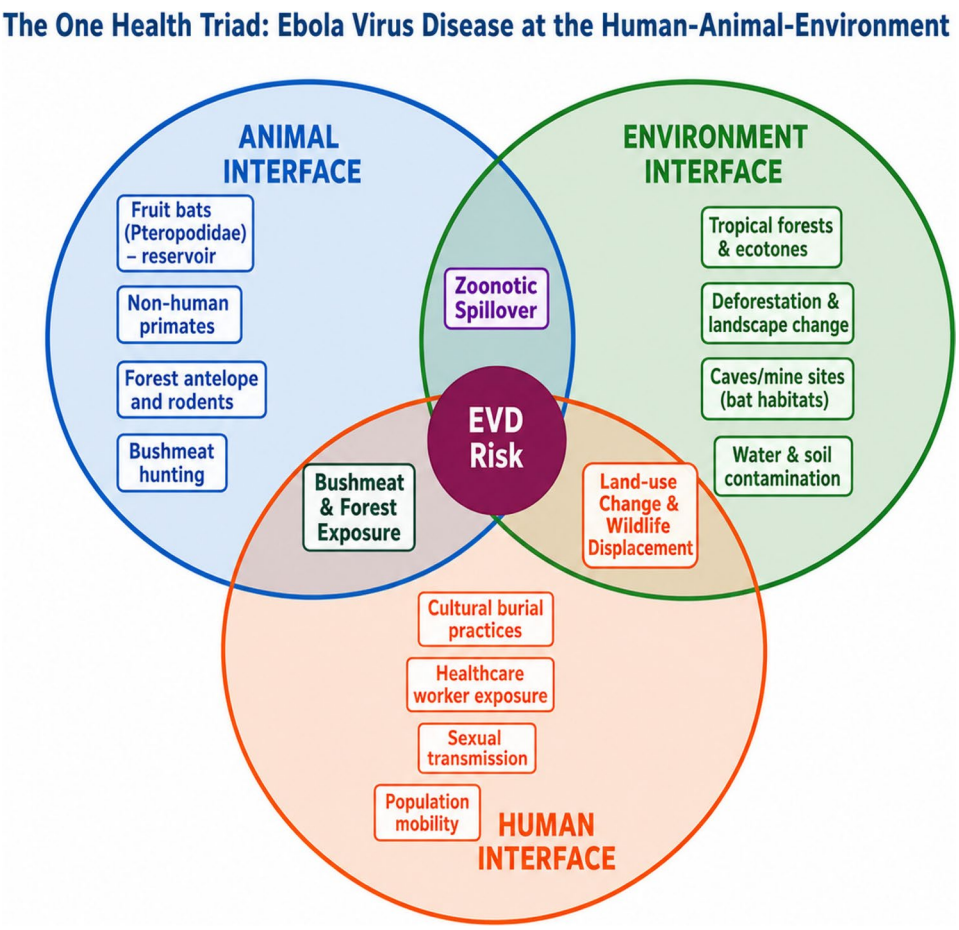

Fig. 4 The One Health Triad depicting the convergence of animal (blue), environmental (green), and human (orange) domains that collectively determine Ebola Virus Disease risk. Overlap zones represent interface areas of heightened zoonotic and anthroponotic transmission probability

manifestations historically considered the hallmark of EVD were surprisingly uncommon during the 2022 Uganda outbreak, affecting only 13% (21/164) of cases [18]. This observation reinforces the challenge of clinical diagnosis in outbreak settings where hemorrhagic features may be absent, particularly for SUDV, which exhibits a lower frequency of hemorrhage than ZEBOV.

Because the early clinical syndrome is non-specific and overlaps with malaria, typhoid fever, and other viral haemorrhagic fevers, laboratory confirmation—typically by reverse-transcription polymerase chain reaction (RT-PCR) detection of viral RNA, supported where available by rapid antigen assays—remains central to diagnosis. The frequent absence of overt haemorrhage, particularly with Sudan ebolavirus [18], together with the documented co-circulation of Crimean–Congo haemorrhagic fever during the 2022 Uganda outbreak [30], complicates differential diagnosis and reinforces the value of integrated, multi-pathogen laboratory surveillance during outbreaks.

Case fatality rates vary substantially by ebolavirus species (Fig. 5A). The mean CFR for ZEBOV across included studies was 67.4% (range 39.5%–89%), for SUDV 52.3% (range 40%–70%), and for BDBV 29.6%, reinforcing the understanding that Bundibugyo ebolavirus carries a more favorable prognosis. Pregnancy constitutes a major risk modifier: a systematic review and meta-analysis of 28 studies documented an absolute maternal mortality risk of 67.8% (95% CI: 49.8–83.7%) and near-universal fetal loss (76.9% fetal death; 98.5% neonatal mortality), underscoring the urgent need for inclusive clinical trial designs [31].

Age-specific outcomes during the 2022 Uganda SUDV outbreak revealed that children under 10 years had the highest case fatality rate (74%; 17/23 cases), a pattern not previously well-characterized for SUDV [18]. Post-Ebola syndrome, a constellation of multi-organ sequelae persisting for months to years after clinical recovery represents a significant long-term burden on survivor populations. Studies from Sierra Leone documented musculoskeletal symptoms, uveitis, neurological deficits, and reproductive complications in EVD survivors more than 2.5 years after discharge, with overlapping symptom clusters suggesting a heterogeneous, multi-system

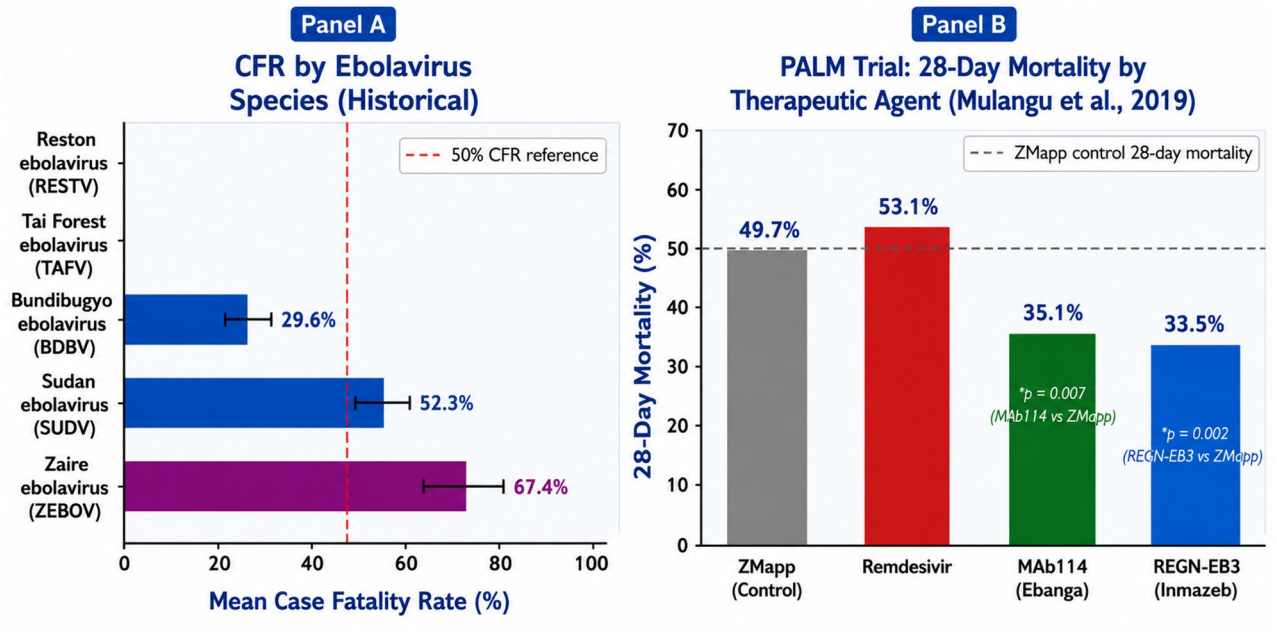

Fig. 5 Panel **A** Mean case fatality rates (CFR) with ± 1 standard error by Ebolavirus species derived from historical outbreak data included in this review. Panel **B** Comparative 28-day mortality rates across investigational therapeutic agents in the PALM (Pamoja Tulinde Maisha) randomised controlled trial conducted during the 2018–2020 DRC outbreak [33]. Asterisks denote statistical significance vs. ZMapp control (**$p < 0.01$). ZEBOV = Zaire ebolavirus; SUDV = Sudan ebolavirus; BDBV = Bundibugyo ebolavirus

pathophysiology [32]. Within the PREVAIL survivor cohort in Liberia, demographic analyses identified specific factors associated with survivors presenting for ophthalmological evaluation, reflecting the substantial ocular morbidity that characterizes post-Ebola syndrome [34]. Mental health consequences are equally profound: a representative cross-sectional study in the DRC found that 62.0% of individuals residing in EVD-affected health zones met criteria for severe depressive symptoms, with stigmatization doubling to quadrupling the risk of depression [35].

Vaccines and therapeutics

The period 2018–2024 represents an unprecedented era in EVD medical countermeasure development. The PALM (Pamoja Tulinde Maisha) randomised controlled trial, conducted within the DRC 2018–2020 outbreak, enrolled 681 patients and compared four investigational agents against ZMapp as the reference standard. MAb114 (Ebanga; ansuvimab) and REGN-EB3 (Inmazeb; atoltivimab-maftivimab-odesivimab) demonstrated 28-day mortality rates of 35.1% and 33.5%, respectively, versus 49.7% for ZMapp ($P = 0.007$ and $P = 0.002$, respectively), leading to the early termination of ZMapp and remdesivir arms and ultimately to FDA approval of both antibody products in 2020 [33]. Fig. 5B illustrates the comparative trial outcomes.

Mechanistic studies of the rVSV-vectored Zaire ebolavirus glycoprotein vaccine (rVSV-ZEBOV; Ervebo) which received FDA approval in December 2019 — have elucidated the polyclonal and convergent antibody response it elicits, demonstrating that repeated vaccination drives the accumulation of glycoprotein-specific memory B cells and broadly neutralizing antibody clones [36]. Critically, prior vaccination with rVSV-ZEBOV was demonstrated not only to not interfere with, but to synergistically improve, the efficacy of post-exposure passive monoclonal antibody therapy, providing a biological basis for combining active vaccination with passive immunotherapy strategies in high-risk contacts [37]. Proteomic-genomic analyses have identified two major neutralization-sensitive sites on the Ebolavirus glycoprotein the glycan cap and the fusion loop which are accessible to convalescent plasma-derived antibodies, informing next-generation vaccine antigen design [38].

Despite these advances, a critical therapeutic vacuum persists for non-Zaire ebolavirus species. No licensed vaccine exists for SUDV, BDBV, or TAFV. The 2022 Uganda SUDV outbreak was managed entirely with supportive care; aggressive fluid and electrolyte management, symptomatic treatment, and infection control without access to species-specific therapeutics [39]. A survey of the published research landscape documented only 20 SUDV-focused research studies globally, with none conducted in Uganda [19]. This profound asymmetry between species-specific research investment and epidemiological risk is a critical gap requiring urgent redress (Fig. 6).

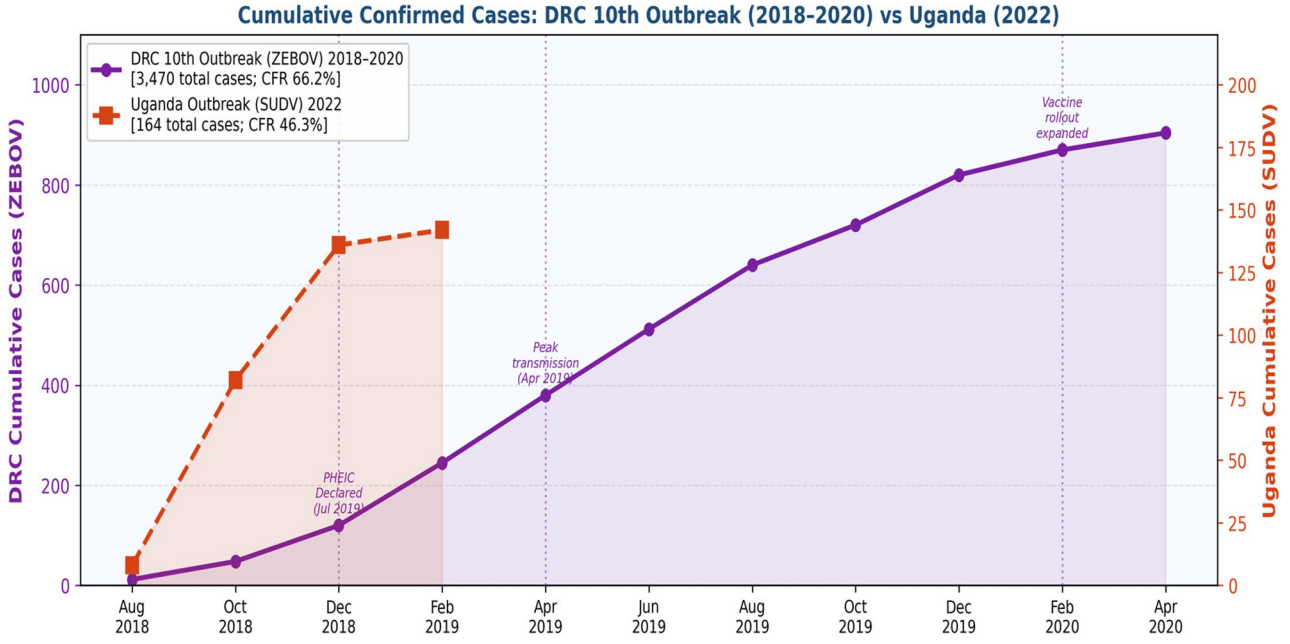

Fig. 6 Comparative cumulative confirmed case trajectories of the DRC 10th outbreak (ZEBOV, 2018–2020; left y-axis, purple) and the Uganda 2022 Sudan ebolavirus outbreak (SUDV; right y-axis, orange). PHEIC = Public Health Emergency of International Concern declared July 2019. Data adapted from published WHO situation reports and peer-reviewed surveillance studies

Outbreak response, preparedness, and community engagement

Figure 6 Illustrates the contrasting epidemic curves of the DRC 10th outbreak and the Uganda 2022 SUDV outbreak, highlighting how response capacity and environmental context shaped outbreak trajectories.

Safe and dignified burials (SDB) constituted a cornerstone of EVD response during the DRC 10th outbreak, given the high viral load in post-mortem corpses and the risk of transmission during traditional burial practices. Of 14,624 SDB requests processed by the International Federation of Red Cross and Red Crescent Societies, 99% were responded to and 89% achieved within the 24-hour target window. Overall SDB success (all components implemented) was 61%, impeded primarily by security-related disruptions and community and family non-acceptance [40]. Community-based contact isolation strategies in DRC's Beni and Mabalako health zones demonstrated superior outcomes compared to standard contact tracing alone: community-isolated contacts, once confirmed, had a case fatality rate of 12.5% versus 48.4% ($P = 0.0001$) and experienced significantly shorter onset-to-isolation intervals (1.3 vs. 4.8 days, $P < 0.0001$) [41].

Contact tracing during the Uganda 2022 outbreak identified 3,844 contacts (mean 22 per case). Contacts who were known and listed before symptom onset had significantly reduced time to isolation (4 vs. 6 days, $P = 0.007$) and were 84% less likely to infect others (incidence rate ratio: 0.16; 95% CI: 0.08–0.32) compared to non-known prior contacts [42]. Qualitative research in Mubende and Kassanda districts identified five thematic drivers of the outbreak: individual knowledge gaps, interpersonal and cultural risk amplifiers (including traditional healing and exhumation practices), community-level economic vulnerabilities, organizational health system failures (delayed laboratory results, poor recording systems), and policy deficits in One Health integration [43].

Neighboring countries' preparedness was a critical determinant of whether cross-border spread occurred. Uganda's preparedness response during the DRC 10th outbreak which included pre-deployed rapid response teams, cross-border surveillance, ring vaccination of contacts at border points, and interoperable case definition alignment with DRC prevented importation despite geographical proximity [44, 45]. Free care policies implemented during the DRC outbreak led to measurable increases in health facility utilization, underscoring the importance of removing financial barriers to care-seeking during epidemics [46]. Sustainable preparedness frameworks must embed EVD response capacities within routine primary healthcare systems rather than relying exclusively on emergency vertical structures [47]. Mathematical transmission models reinforce this operational imperative, indicating that quarantine and isolation measures, when implemented with sufficient coverage and timeliness, can drive the effective reproduction number below the epidemic threshold [48].

Table 2 Summary of included studies by category, geographic setting, ebolavirus species, and study design

Category (*n* studies)	Representative Studies (*n*)	Geographic Focus	Ebolavirus Species	Primary Outcome	Key Findings
Outbreak Epidemiology (*n* = 16)	Kabami 2024 [18], Kraemer 2020 [14], Kelly 2020 [16], Medley 2020 [15], Komakech 2024 [20]	DRC, Uganda, Guinea, Neighbouring Countries	ZEBOV, SUDV	Case counts, CFR, Rt	Conflict amplifies Rt; super-spreading linked to healthcare facilities; community isolation reduces CFR; survivor-linked recurrence documented
Vaccines & Therapeutics (*n* = 9)	Mulangu 2019 [33], Ehrhardt 2019 [36], Cross 2020 [37], Gilchuk 2021 [38], El Ayoubi 2024 [49]	DRC (clinical trial); USA (lab); International	ZEBOV	28-day mortality; antibody titres	MAb114 and REGN-EB3 superior to ZMapp ($p < 0.01$); rVSV-ZEBOV synergises with mAb therapy; no licensed SUDV vaccine
One Health & Reservoirs (*n* = 8)	Brook 2020 [10], Gentles 2020 [11], Garnett 2023 [12], Euren 2020 [13], Sikakulya 2019 [9]	Sierra Leone, Pan-African, Experimental	ZEBOV (experimental)	Viral dynamics; bat-human interface	Bat cell lines support EVD replication; seasonal birth pulses create spillover windows; bushmeat hunting is primary exposure pathway
Clinical & Sequelae (*n* = 7)	Bond 2021 [32], Wallace 2024 [34], Cénat 2022 [35], Kayem 2022 [31]	Sierra Leone, Liberia, DRC	ZEBOV, SUDV	Survivor symptoms; mental health; pregnancy outcomes	62% severe depression in EVD-affected zones; 98.5% neonatal mortality; musculoskeletal and ocular sequelae persisting > 2.5 years
Molecular Epidemiology (*n* = 5)	Fang 2024 [5], Hulseberg 2021 [8], Jansen van Vuren 2019 [6], Balinandi 2023 [7], Keita 2021[17]	DRC, Sierra Leone, Uganda, Guinea	ZEBOV, SUDV, BDBV	Phylogenetic lineages; adaptive evolution	4 ZEBOV lineages; F443L substitution marks DRC 2018 clade; SUDV 2022 is 96% similar to 1970s strains; Guinea 2021 genetically identical to 2014-16 survivor virus
Preparedness & Modelling (*n* = 5)	Kluge 2018 [28], Dénes 2019 [48], Kraft 2020 [50], Ryan 2022 [47], Potter 2023 [45]	Global, DRC neighbours, USA, Uganda	General/multiple	Epidemic control; IHR compliance; R_0	IHR embedding in national health systems essential; quarantine can reduce R_0 below 1.0 with high coverage; HCW seroconversion avoided with strict IPC

CFR Case Fatality Rate, *ZEBOV* Zaire ebolavirus, *SUDV* Sudan ebolavirus, *BDBV* Bundibugyo ebolavirus, *DRC* Democratic Republic of the Congo, *IHR* International Health Regulations, *HCW* Healthcare Worker, *IPC* Infection Prevention and Control, *mAb* Monoclonal antibody

Evidence summary: included study characteristic (Table 2)

Discussion

EVD remains an enduring and evolving threat

This scoping review, drawing on 50 sources published predominantly between 2018 and 2026, confirms that EVD has transitioned from a recurring but geographically isolated epidemic threat to a complex, multifaceted global health security challenge. Distinct outbreak scenarios the resource-exhausting DRC 10th epidemic, the paradigm-altering Guinea survivor resurgence, the medically defenseless Uganda SUDV outbreaks of 2022 and 2025, the rapidly contained 2025 DRC (Kasai) Zaire ebolavirus outbreak, and the 2026 Bundibugyo virus emergency collectively illuminate the diverse ways in which Ebola viruses exploit vulnerabilities at the human–animal–environment interface, within fragile health systems, and among immunologically naive populations facing species for which no licensed countermeasure exists.

The clustering of these 2025–2026 events is itself analytically instructive, carrying two divergent lessons [22, 25]. On one hand, the 2025 Kasai outbreak demonstrated tangible progress: a Zaire ebolavirus epidemic in a remote, infrastructure-poor setting was extinguished within approximately three months through pre-positioned rVSV-ZEBOV stockpiles, prompt ring vaccination, and an experienced incident-management system a marked operational improvement over the prolonged 2018–2020 epidemic [23]. On the other hand, the 2025 Uganda SUDV outbreak and the 2026 Bundibugyo virus emergency reaffirmed that the countermeasure gap for non-Zaire species remains a critical and still-unaddressed vulnerability, leaving responders dependent on supportive care and, at best, investigational vaccines deployed under emergency trial protocols [21, 22].

The finding that survivor-linked recurrence can precipitate full-scale outbreaks five or more years post-recovery represents a major paradigm shift in EVD epidemiology since the 2014–2016 West African epidemic demonstrated the virus's pandemic potential. The Guinea 2021 outbreak challenged the fundamental assumption that EVD elimination is achievable once clinical cases resolve — a challenge that demands a fundamental rethinking of survivor follow-up programs, sexual transmission counselling, and the duration of EVD surveillance after outbreak declaration [17]. These findings align with growing mechanistic understanding of how ZEBOV establishes persistence in immunologically privileged anatomical sites the anterior chamber of the eye, the testes, the central nervous system where antibody-mediated immune surveillance is attenuated [32].

Conflict, structural fragility, and outbreak amplification

The DRC 10th outbreak provides an empirically documented case study in how armed conflict and governance failures amplify epidemic trajectories. The demonstration that Ebola-targeted violence events significantly elevated the reproduction number in some health zones pushing Rt beyond 1.5 has important implications for the design of humanitarian response frameworks [16]. Conventional outbreak response tools such as contact tracing, ring vaccination, and safe burials become operationally impracticable when security is compromised, as evidenced by the 39% SDB failure rate during periods of peak insecurity [40]. Responses must therefore be simultaneously clinical, epidemiological, and diplomatic requiring the integration of conflict resolution mechanisms, community engagement strategies, and adaptive security protocols into EVD response architectures.

The therapeutic landscape and the SUDV vaccine deficit

The PALM trial results published in the New England Journal of Medicine represent one of the most significant milestones in the history of EVD treatment [33]. The success of MAb114 and REGN-EB3 in reducing 28-day mortality by approximately one-third compared to ZMapp transforms EVD within the bounds of ZEBOV from a disease with near-universal mortality at high viral loads to one with potentially manageable outcomes when monoclonal antibody therapy is initiated early. The demonstration that prior rVSV-ZEBOV vaccination synergizes with post-exposure antibody treatment [37] suggests that combined active-passive immunization strategies should be prioritized for high-risk healthcare workers and frontline response staff in endemic regions.

The Uganda 2022 SUDV outbreak starkly exposed the consequences of species-specific research and development asymmetry. Despite SUDV's well-documented capacity to cause substantial outbreaks including, the initial 1976 Sudan outbreak (CFR 53%), the 2000 Uganda outbreak (CFR 53%), and the 2022 epidemic, only a handful of investigational SUDV vaccines have entered early-phase trials, and none were available for deployment [19]. Syntheses of the 2022 Uganda outbreak have distilled its principal lessons among them the need for pre-positioned candidate vaccines, strengthened infection prevention within the private health sector, and regional vaccine manufacturing capacity as strategic priorities for sub-Saharan Africa [51]. The rVSV-ZEBOV vaccine, despite its proven efficacy against ZEBOV, offers no cross-protection against SUDV given the approximately 47% amino acid divergence in their respective glycoproteins. The development of broadly protective panfilovirus vaccines potentially utilizing multivalent or consensus GP antigen platforms represents an urgent and unmet research priority [49].

One health frameworks for prevention

A recurring theme across the included literature is the insufficiency of purely human-health-focused outbreak response in the absence of coordinated animal surveillance and environmental monitoring [9]. The One Health framework provides an operational architecture for addressing the multi-domain drivers of EVD: reducing forest encroachment and bushmeat hunting risk through ecologically integrated livelihoods; monitoring bat population dynamics and viral shedding seasonality to anticipate spillover risk windows; and embedding zoonotic disease surveillance into routine veterinary and agricultural services [11, 13]. The detection of concurrent Crimean–Congo hemorrhagic fever cases during the Uganda SUDV outbreak further illustrates how syndromic overlap among viral hemorrhagic fevers complicates differential diagnosis and reinforces the value of integrated, multi-pathogen laboratory surveillance [30]. Sustained international scientific collaboration exemplified by global virology consortia that coordinate cross-border research priorities and pathogen surveillance remains indispensable to closing the knowledge gaps surrounding emerging filoviruses [52].

The International Health Regulations (2005) provide the international legal framework for these cross-sectoral efforts, but evidence suggests that national health systems must more deeply embed IHR core capacities into their primary healthcare infrastructure rather than maintaining them as parallel vertical emergency structures [28]. Countries bordering endemic regions that proactively invested in these capacities as Uganda demonstrated during the DRC 10th outbreak can successfully prevent importation even with sustained cross-border pressure [44, 45].

Healthcare worker safety and nosocomial transmission

A particularly concerning dimension of recent outbreaks is the disproportionate risk experienced by healthcare workers (HCWs). Inadequate IPC training and infrastructure especially in private and community-level health facilities was a primary driver of healthcare-associated EVD transmission in both the DRC and Uganda outbreaks. In contrast, the Emory University SCDU experience demonstrated that with meticulous infection control protocols and trained, motivated staff, zero occupational seroconversion can be achieved even when managing confirmed EVD patients in non-endemic settings [50]. These findings underscore the urgent need to extend IPC training beyond tertiary government hospitals to the full spectrum of healthcare delivery points including private clinics, faith-based facilities, and community health posts that represent first points of contact for symptomatic patients in most outbreak settings.

Limitations

Several limitations must be acknowledged in interpreting the findings of this scoping review. First, as a scoping rather than systematic review, formal meta-analysis of quantitative outcomes across studies was not performed; the heterogeneity in study designs, outbreak contexts, and outcome definitions precluded pooled effect estimates, and findings reflect narrative synthesis. Second, publication bias is a recognized limitation of all literature reviews: negative or null findings, particularly from small outbreak investigations, are less likely to be published in indexed journals, potentially skewing the evidence base toward dramatic or newsworthy outbreak scenarios. Third, the majority of included ecological and reservoir studies employed experimental or in vitro designs that, while mechanistically informative, may not fully capture the complexity of natural bat-to-human transmission dynamics in situ.

Fourth, language restriction to English-language publications may have excluded relevant data from French-language publications potentially significant given that French is the primary language of scientific publication in several of the most-affected countries, including the DRC and Guinea. Fifth, the rapidly evolving nature of outbreak literature means that some studies included here represent preliminary findings that may be updated or revised in subsequent publications; readers are advised to consult primary sources and WHO situation reports for the most current epidemiological data. Finally, the qualitative assessment of study quality, while systematic, involves inherent subjectivity, and inter-rater disagreements though resolved through consensus reflect the interpretative challenges inherent in cross-disciplinary evidence appraisal.

Conclusions and future directions

Ebola Virus Disease stands at an important juncture in 2026. Its epidemiology has been reshaped by the recognition of survivor-linked recurrence, its therapeutic options have expanded for Zaire ebolavirus, and the rapid containment of the 2025 DRC (Kasai) outbreak signals real operational gains; yet a serious countermeasure deficit persists for non-Zaire species, exposed by the 2025 Uganda Sudan-virus outbreak and the 2026 Bundibugyo virus emergency that prompted a Public Health Emergency of International Concern [22, 25]. Drawing on the major post-2018 outbreaks through the 2025–2026 events, this review highlights the following priorities for research and policy:

- Prioritize Sudan and Bundibugyo ebolavirus vaccines: multivalent filovirus vaccines combining SUDV, BDBV, and ZEBOV glycoprotein antigens warrant accelerated development, using adaptive, outbreak-responsive trial designs of the kind pioneered during the DRC 10th epidemic.
- Sustain long-term survivor programs: serial viral RNA testing, immunological monitoring, sexual-transmission counselling, and psychosocial and mental-health support should be institutionalized for survivors and affected communities, given documented viral persistence beyond five years and the substantial burden of post-Ebola syndrome and depression.
- Strengthen One Health surveillance at the animal–human interface: prospective serological, virological, and ecological monitoring of bat reservoirs, aligned with known birth-pulse seasonality, can help anticipate spillover windows and pre-position outbreak-response resources.
- Reform infection prevention and control across all healthcare tiers: IPC training, protective equipment, and rapid diagnostic capacity must reach private, faith-based, and community facilities, not only tertiary government hospitals, because these are the first points of contact for EVD-suspect patients.
- Embed preparedness within national health systems and governance: integrating IHR core capacities, real-time whole-genome sequencing, and accountability mechanisms into routine health services—rather than maintaining vertical emergency structures—would support resilient responses and help distinguish new spillover events from survivor-linked recurrences.

In sum, the post-2018 EVD landscape calls for a response that is grounded in One Health principles, integrated across human, animal, and environmental health, enabled by genomic and immunological advances, and equitably resourced for the populations most at risk. Many of the scientific tools needed to blunt future epidemics now exist; translating them into protection will depend on sustained investment, political commitment, and international cooperation.

Key take-home messages

- The 2021 Guinea outbreak established survivor-linked recurrence as a new EVD transmission paradigm, with genetically identical ZEBOV persisting in an immune-privileged site for over five years post-recovery.
- The 2022 Uganda Sudan ebolavirus outbreak exposed a critical gap: no licensed vaccine or specific therapeutic exists for non-Zaire ebolavirus species, representing an urgent unmet medical need.
- Healthcare-associated transmission through inadequately equipped private facilities drove early

spread in the Uganda 2022 SUDV outbreak; IPC training must extend across all healthcare tiers.
- Super-spreading events — shaped by cultural practices, delayed isolation, and healthcare-seeking patterns — can be substantially mitigated through intensive contact tracing and community engagement.
- MAb114 (Ebanga) and REGN-EB3 (Inmazeb) reduce 28-day EVD mortality by approximately 30% versus previous standard care and should be positioned in outbreak-preparedness stockpiles.
- The One Health framework, integrating bat reservoir dynamics, ecological surveillance, and community behavioural factors, offers the most comprehensive approach to preventing primary spillover events.
- Genomic sequencing should be embedded as a real-time outbreak investigation tool to distinguish new spillover events from survivor-linked recurrences and to track super-spreading chains with precision.

Authors' contributions
M.B.S. : Conceptualisation, Resources, Investigation, Analysis, Preparation of tables and figures, Writing and reviewing manuscript. V.N. : Resources, Investigation, Writing and reviewing manuscript. All authors reviewed and approved the final version of the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This manuscript was conceptualized, designed, written, and critically revised by the author. Artificial intelligence (AI) language model tools were used solely to assist in formatting, preliminary literature sorting, and language editing of specific draft paragraphs. All intellectual content, including the search strategy, eligibility criteria, data extraction, synthesis of findings, interpretation of results, and conclusion formulation, was performed exclusively by the author. The author accepts full responsibility for the accuracy and integrity of the work.

Competing interests
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