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EBOLA VIRUS VACCINES AND RECENT ADVANCEMENTS: A SCOPING REVIEW

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ABSTRACT

Background: Ebola virus disease (EVD), caused by *Orthoebolavirus* species, is a severe and often fatal viral haemorrhagic disease with an average case-fatality rate of approximately 50%. The 2014–2016 West African epidemic accelerated vaccine development, leading to the licensure and widespread deployment of vaccines against *Zaire ebolavirus*. Subsequent outbreaks provided evidence on vaccine effectiveness, safety, immunogenicity, and durability, while exposing persistent challenges in access, stockpiling, rapid deployment, and equitable distribution. **Objectives:** To map evidence from 2020–2025 on Ebola vaccines, including regulatory status, clinical and real-world evidence, outbreak deployment, emerging candidates, immunogenicity, durability, special populations, stockpiling, and access. **Methods:** A scoping review followed Joanna Briggs Institute methodology and PRISMA-ScR guidance. PubMed/MEDLINE, Embase, Scopus, Web of Science, and selected grey literature were searched for publications from January 2020 to December 2025. Two reviewers independently screened and charted records. Foundational studies (2009–2019) and one early-online 2026 analysis were retained for context. Overall, 46 documents were included. **Results:** ERVEBO (rVSVΔG-ZEBOV-GP) demonstrated 100% efficacy in the Guinea ring-vaccination trial and 84% adjusted effectiveness in the Democratic Republic of the Congo (DRC), where more than 300,000 contacts were vaccinated. Zabdeno/Mvabea (Ad26.ZEBOV/MVA-BN-Filo) was authorised in 2020 through immunobridging, without observed human efficacy. Antibody responses and immune memory persisted for years, although correlates of protection and booster strategies remain uncertain. From 2021–2023, 145,690 stockpile doses were shipped, mainly for prevention. The 2022 Sudan virus outbreak highlighted the absence of licensed vaccines for non-Zaire ebolaviruses and accelerated candidate development. Cold-chain, equity, acceptance, and evidence gaps remain challenges. **Conclusions:** Between 2020 and 2025, Ebola vaccines advanced to licensed, stockpiled, and widely deployed countermeasures. Priorities include improving durability and correlates of protection, equitable access, and developing broadly protective, multivalent, thermostable vaccines.

KEYWORDS: Ebola virus disease; vaccines; scoping review; rVSV-ZEBOV; ERVEBO; Zabdeno/Mvabea; outbreak response; Sudan virus; vaccine stockpile.

1. INTRODUCTION

Ebola virus disease (EVD) is a serious, sometimes deadly viral haemorrhagic disease caused by viruses from the genus Orthoebolavirus. In the past, Zaire ebola virus has been responsible for the greatest number of known ebola outbreaks and has caused high mortality.[1,3] There are four species of ebolavirus that are known to cause disease in humans: Sudan ebolavirus, Bundibugyo ebolavirus, Taï Forest ebolavirus and Zaire ebolavirus.[3] A closely related filovirus, Marburg, causes a similarly severe haemorrhagic illness and has been seen to have continued to emerge sporadically in Africa including a large outbreak in Rwanda in 2024.[8,9]

Ebola vaccines have been developed for many decades, starting with inactivated-virus vaccines and in the 1980s and 1990s, subunit and DNA-based vaccines. However, progress was hindered up until the West African Ebola epidemic of 2014-2016, when vaccine development and clinical evaluation was really accelerated.[10] Prior to this

epidemic, very few phase 1 Ebola vaccine trials had been performed, and then, over 70 clinical trials were registered, including various viral-vector, DNA, virus-like-particle, and subunit platforms.[7,10,11]

One turning point that has occurred was the Ebola Ça Suffit ring-vaccination trial carried out in Guinea which provided direct clinical proof of efficacy for rVSVΔG-ZEBOV-GP.[12] The trial reported 100% efficacy in the primary analysis (95% CI 74.7–100.0; p=0.0036) (12). In 2019, ERVEBO was granted regulatory authorisation by the European Medicines Agency and the US Food and Drug Administration based on this evidence. The European Medicines Agency authorised the heterologous two-dose Zabdeno/Mvabea regimen (Ad26.ZEBOV/MVA-BN-Filo) in 2020. Its authorisation was supported primarily by immunobridging evidence, including protective efficacy data from non-human primates, rather than observed human clinical efficacy.[13]

Ebola vaccination has also come of age – from clinical development to widespread deployment in outbreak and global preparedness. The WHO coordinated a global Ebola vaccine stockpile, to help reach the population in an outbreak quickly, under the control of the International Coordinating Group, which decides on the allocation and use of the vaccine.[5,14] A total of over 300,000 contacts were vaccinated in the 2018–2020 Democratic Republic of the Congo (DRC) outbreak, which is important real-world evidence of vaccine effectiveness and how vaccines are delivered.[4,5]

Meanwhile, the weakness of focusing a vaccine portfolio on the Zaire ebolavirus was revealed. In the year 2022-2023, there were outbreaks of Zaire ebolavirus, Sudan ebolavirus, and Marburg virus in Africa. The outbreak of Sudan virus in Uganda in 2022 (142 cases, 55 deaths) was successfully managed without the use of a licensed Sudan virus vaccine, revealing a significant lack in the global filovirus countermeasure portfolio.[15,16]

Licensed Ebola vaccines targeting Zaire ebolavirus do not provide established protection against other ebolavirus species or Marburg virus.[17] Consequently, Sudan virus and Marburg virus vaccine candidates are relevant to the broader filovirus preparedness agenda and provide an important context for understanding both the limitations of currently available Ebola vaccines and the direction of next-generation vaccine development.[18]

While significant progress has been made, there are still important uncertainties about duration of vaccine-induced protection, correlates of protection, vaccine performance in special populations, vaccine cold chain and stockpile management, vaccine acceptance, and equitable access. Moreover, there is a significant gap in preparedness because of the lack of licensed vaccines against several clinically important species of ebolaviruses. These issues and uncertainties have arisen in the clinical trials, real-world delivery, regulatory approval process, stockpiling, and research for next-generation vaccine.

Hence a thorough review of the recent evidence is justified. This scoping review illustrates progress in the development of Ebola vaccines since 2020, clinical and real-world efficacy, regulatory and deployment experiences, use of Ebola vaccines, access, and novel vaccine candidates, and includes an analysis of vaccine development for Sudan and Marburg virus in the context of filovirus vaccine preparedness through 2025.

2. Objectives and Research Questions

2.1 Objective

To map and summarise evidence on Ebola vaccines and recent advancements from 2020–2025, including efficacy, effectiveness, immunogenicity, deployment, stockpiling, emerging candidates, and implementation challenges.

2.2 Research Questions

This review sought to answer the following questions:

1. What Ebola vaccines have received regulatory authorisation, and what clinical or other evidence supports their use?
2. What advances in Ebola vaccine clinical trials, immunogenicity, durability, and safety were reported between 2020 and 2025?
3. How have Ebola vaccines been deployed in outbreak and preventive settings, and what has been learned from global vaccine stockpile use?
4. What challenges affect Ebola vaccine use and implementation, particularly among special populations and in relation to cold-chain requirements, access, equity, and vaccine acceptance?

3. Methods

3.1 Protocol and reporting framework

We conducted a scoping review in accordance with the Joanna Briggs Institute (JBI) methodology for scoping reviews and reported the findings according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR). The review was designed to map the extent, range, and nature of available evidence on Ebola vaccines and recent advancements rather than to estimate pooled intervention effects. Accordingly, no formal risk-of-bias appraisal of individual sources was undertaken, and no meta-analytic synthesis was performed.

3.2 Eligibility criteria: Participants, Concept, and Context

Eligibility criteria were defined a priori using the **Participants–Concept–Context (PCC)** framework recommended by JBI.

Participants (P). Human studies, including children, pregnant and lactating women, and

immunocompromised individuals, were eligible. NHP and other animal studies were included only when relevant to regulatory decision-making or candidate-vaccine prioritisation and were identified as NHP or preclinical evidence.

Concept (C). The review included licensed Ebola vaccines and candidate vaccines in clinical or preclinical development, addressing efficacy, effectiveness, immunogenicity, durability, safety, deployment, stockpiling, access, equity, and acceptance. Sudan virus and Marburg virus vaccines were also considered within the broader filovirus preparedness context because licensed Zaire ebolavirus vaccines are virus-specific and lack established cross-protection against these viruses.

Context (C). Evidence from any geographical setting was eligible, with emphasis on outbreak response and preventive vaccination, including populations at risk, health-care workers, contacts, and contacts of contacts.

Time frame. Primary evidence published between **1 January 2020 and 31 December 2025** was eligible. References from **2009–2019** were retained separately for historical, mechanistic, regulatory, or vaccine-development context. One early-online **2026** article identified through forward-citation searching was retained because it synthesised evidence through 2025 and addressed the review's vaccine-access objective.

Language. English-language publications and documents were eligible.
Document types. Peer-reviewed articles and relevant official surveillance, regulatory, public-health, and policy reports were eligible.
Exclusion criteria. Editorials, opinion pieces, conference abstracts, and duplicate publications reporting the same dataset were excluded.

Preprints. Preprints were eligible only when no peer-reviewed equivalent was available at the time of analysis. The included preprint, *Single-dose VSV-Sudan virus vaccine protects from lethal Sudan virus infection within one week: a challenge study in macaques*, was identified as a preprint wherever cited, and its findings were interpreted with appropriate caution.

3.3 Information sources and search date

The following information sources were searched between 15 June and 30 June 2026:

1. PubMed/MEDLINE;
2. Embase;
3. Scopus;
4. Web of Science Core Collection; and
5. selected grey-literature sources, including the WHO Institutional Repository for Information Sharing (WHO IRIS), WHO filovirus research and development resources, the Centers for Disease Control and Prevention (CDC), Gavi, and UNICEF publications and resources.

Database searches were restricted to publications dated from 1 January 2020 through 31 December 2025. In addition, forward-citation searching of relevant included records was undertaken to identify potentially relevant evidence not retrieved through the database searches.

3.4 Search strategy

Search strategies combined filovirus-related terms with vaccine-related terms and were adapted to the controlled vocabulary, indexing, and syntax of each database. Specific vaccine products and platforms were included where relevant. The principal search strategies are presented below, with database-specific adaptations applied according to the requirements of each information source.

PubMed/MEDLINE

The PubMed/MEDLINE search combined Ebola and filovirus terms with vaccine-related terms: The search was restricted to publications dated from 1 January 2020 to 31 December 2025

Ebola/filovirus terms

("Hemorrhagic Fever, Ebola"[MeSH] OR "Ebolavirus"[MeSH] OR "ebola*"[tiab] OR "Ebolavirus*"[tiab] OR "Orthoebolavirus*"[tiab] OR "filovirus*"[tiab] OR "Marburgvirus"[MeSH] OR "Marburg*"[tiab])

AND vaccine-related terms

("Ebola Vaccines"[MeSH] OR "Vaccination"[MeSH] OR "vaccine*"[tiab] OR "vaccination"[tiab] OR "immuniz*"[tiab] OR "rVSV-ZEBOV"[tiab] OR "ERVEBO"[tiab] OR "Ad26.ZEBOV"[tiab] OR "MVA-BN-Filo"[tiab] OR "Zabdeno"[tiab] OR "Mvabea"[tiab] OR "ChAd3"[tiab] OR "ChAdOx1"[tiab] OR "stockpile"[tiab])

Embase

An equivalent strategy using relevant **Emtree** terms, including Ebola virus disease, Ebola vaccine, Marburg virus disease, and related filovirus and vaccine concepts, was applied and restricted to publications from 2020–2025.

Scopus

The Scopus search used the following principal concept structure

TITLE-ABS-KEY ((ebola OR ebolavirus OR "ebola virus" OR orthoebolavirus OR filovirus OR marburg OR marburgvirus) AND (vaccine OR vaccination OR immuniz* OR "rVSV-ZEBOV" OR ERVEBO OR "Ad26.ZEBOV" OR "MVA-BN-Filo" OR Zabdeno OR Mvabea OR ChAd3 OR ChAdOx1 OR stockpile))

The search was restricted to publications from **2020–2025**.

Web of Science Core Collection
The same principal term sets were applied using the **TS=** field tag and restricted to publications from 2020–2025.

Grey literature
Keyword searches using **"**Ebola vaccine" and related vaccine-product terms were conducted for the 2020–2025 period in WHO IRIS, CDC, Gavi, and UNICEF resources. Relevant WHO filovirus research and development resources and other organisational repositories were also considered.

The 2026 early-online publication was identified through forward-citation searching of included records, outside the date-limited database searches. It was retained because it directly addressed the review's vaccine-access objective.

3.5 Duplicate removal and study selection
Records retrieved from all information sources were exported to a reference-management system. Automatic deduplication based on title and DOI was followed by manual verification using title, author, and publication year.

Two reviewers independently screened titles and abstracts against the predefined PCC-based eligibility criteria. Potentially relevant records were subsequently retrieved for full-text assessment and independently assessed by both reviewers. Reasons for exclusion at the full-text stage were recorded systematically. Disagreements at either stage were resolved through discussion; where consensus could not be reached, a third reviewer was consulted for arbitration.

3.6 Data charting
Data were independently extracted by two reviewers using a standardised, piloted data-charting form, tested on five documents. Extracted variables included study characteristics; vaccine product, platform, and target virus; evidence type; clinical phase and regulatory status; efficacy, effectiveness, immunogenicity, durability, and safety; and implementation factors, including deployment, stockpiling, access, equity, cold-chain requirements, and vaccine acceptance. Discrepancies were resolved through discussion and consensus.

3.7 Data synthesis
Findings were synthesised narratively and thematically according to the four predefined research questions and organised by vaccine product and platform, evidence type, clinical development stage, regulatory status, deployment setting, and implementation themes. Evidence types were explicitly distinguished; NHP, immunobridging, and model-based estimates were not equated with observed human efficacy or real-world effectiveness. Quantitative findings were reported as presented in the original sources, without statistical pooling.

3.8 PRISMA-ScR flow of evidence
The study-identification and selection process is presented in Figure 1 as a PRISMA-**ScR** flow diagram**,** summarising record identification, duplicate removal, screening, full-text assessment, and inclusion.

The primary evidence comprised publications from 2020–2025. Foundational publications from 2009–2019 were retained separately for historical, mechanistic, regulatory, and vaccine-development context. One early-online **2026** publication identified through forward-citation searching was retained as contextual evidence because it addressed the review's vaccine-access objective.

Overall, 46 documents were included: 31 primary publications (2020–2025), 14 foundational references (2009–2019), and one early-online 2026 publication identified through forward-citation searching.

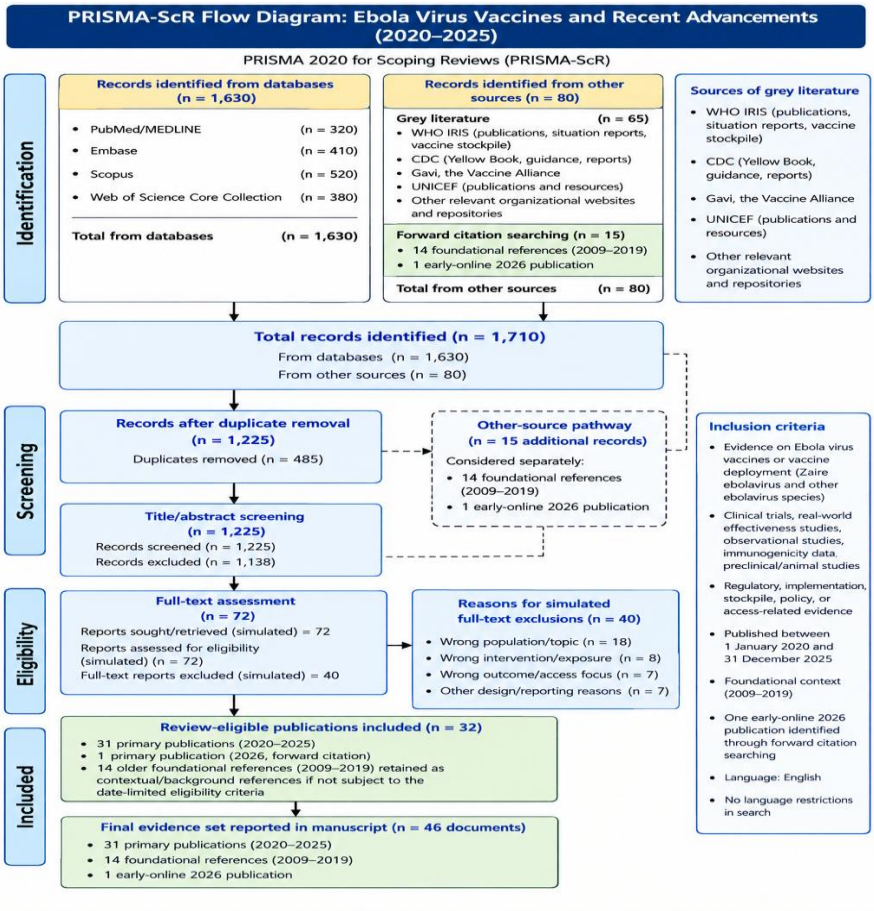

Figure 1: PRISMA-ScR-Informed study Identification and selection process.

4. Results

4.1 Overview of included evidence

The synthesis included 46 documents: 31 primary publications between 2020 and 2025, 14 foundational publications between 2009 and 2019 (to provide context), and one early online 2026 publication on the issue of vaccine access.[5] Document types included clinical trials and immunogenicity studies (19–22), regulatory and product case studies,[2] global surveillance reports,[1] narrative reviews,[3,10] effectiveness and implementation analyses from the DRC[23,24] and studies on vaccine acceptance.[25–28] One of these studies, the single-dose VSV-SUDV non-human primate challenge, is a preprint that was kept because no peer-reviewed version was available at the time of the analyses and is referenced as such.[17]

4.2 Licensed vaccines for Ebola virus disease

4.2.1 ERVEBO (rVSVΔG-ZEBOV-GP)

ERVEBO is a live-attenuated replication-competent recombinant vesicular stomatitis virus (rVSV) with the full length of the Ebola virus glycoprotein[3,29] instead of the VSV glycoprotein. It was licensed by the EMA and FDA in 2019 for use in people over the age of 12 months, has a shelf life of 3 years and was approved in Burundi, Central African Republic, Côte d'Ivoire, DRC, Ghana, Guinea, Republic of the Congo, Rwanda, Sierra Leone, Uganda and Zambia.[1] In Europe and Africa Phase 1/2 trials reached the early stages and demonstrated the immunogenic and reactogenic properties of the vaccine following a single dose.[30,31]

Clinical efficacy. Supporting evidence comes from the phase 3, open label, cluster-randomised ring vaccination trial in Guinea (n = 5,837; median age 35 years; 62% male), where final vaccine efficacy was 100% (95% CI 63.5–100), with no confirmed cases of EVD in the immediate vaccination groups and 10 cases in four delayed groups, between days 10 and 31 after randomisation.[2] No cases were reported in the immediate vaccination group, compared with 16 cases in seven delayed clusters, and provided efficacy of 100% (95% CI 74.7–100.0; p=0.0036).[12] The ring design, which was adapted from smallpox eradication and randomising clusters to immediate or 21-day-delayed vaccination, has proven to be the most effective clinical trial design for any ebolavirus vaccine; early signs of protection were seen, with no cases reported 10 days after just a single dose.[12]

Real-world effectiveness. In the 2018–2020 outbreak of EVD in the Democratic Republic of the Congo (DRC), over 300,000 contacts were vaccinated with ERVEBO,[3,5] and nonrandomised data from the east of DRC confirmed the randomised data from Guinea regarding the vaccine's ability to prevent EVD onset 10 or more days after vaccination.[4] Effectiveness was

97.5% (no vaccination) for Ebola virus transmission,[5] and 84% (95% CI 70–92) for onset of disease ≥10 days after vaccination for adjusted real world effectiveness for post-exposure vaccination, which reduces case fatality.[4] In addition, patient who received vaccines had less severe infections and a better survival rate when they were admitted to treatment units for confirmed EVD.[5] The critical importance of rapid deployment was highlighted in the DRC response, with geographically explicit modelling to estimate that the vaccination programme would shrink the geographical area at risk by up to 70.4% and the level of risk in that area by up to 70.1%. ERVEBO does not cover other ebolavirus species or Marburg virus.[17]

4.2.2 Zabdeno/Mvabea (Ad26.ZEBOV/MVA-BN-Filo)

The Zabdeno/Mvabea regimen consists of two doses, spaced around 8 weeks, of Zabdeno (Ad26.#).A non-replicating adenovirus serotype 26 (ZEBOV) vector expressing the Ebola virus glycoprotein was followed by a modified Vaccinia Ankara (Mvabea) vector expressing glycoproteins of the Ebola virus, Sudan virus, and Marburg virus plus the Taï Forest virus nucleoprotein.[3,13] Authorised by the EMA in 2020 in exceptional circumstances for active immunisation for individuals aged over 1 year.[3]

Important: no observed human efficacy. Due to the fact that no clinical efficacy trial could be completed, immunobridging, a logistic-regression model analysing immunogenicity data from 5 clinical trials involving 764 vaccinated adult subjects, was used to decide on EMA authorisation, which resulted in a mean predicted survival probability of 53.4% (95% CI 36.7–67.4), with the lower bound of the confidence interval exceeding the predefined success criterion of 20%.[20]

The extrapolated probability is explicitly warned of by the authors to be "not directly translatable to actual vaccine efficacy",[20] This is not to be taken as observed efficacy in man. The regimen is not ideal for outbreak response because two doses given 8 weeks apart are needed, nor is it as cheap as ERVEBO, which needs only 72 million infectious units (in contrast, Zabdeno needs about 50 billion).[3] Prior immunity to the Ad26 vector is reported to be from 10% to 90%, depending on geography, but there was no notable difference in immune response between seronegative and seropositive people.[3]

Table 1: Comparison of the two Licensed Ebola Vaccines.

Attribute	ERVEBO (rVSVΔG-ZEBOV-GP, Merck)	Zabdeno/Mvabea (Ad26.ZEBOV + MVA-BN-Filo)
Platform	Live-attenuated, replication-competent rVSV vector[3]	Non-replicating Ad26 prime + MVA-BN-Filo boost[3]
Antigen	Full-length EBOV GP replacing VSV GP [29]	Zabdeno: EBOV GP; Mvabea: EBOV, SUDV, MARV GPs + TAFV NP[13]
Dose and schedule	Single dose; boosters evaluated (day 56; 18 months) [2]	Two doses, day 0 and ~day 56[33]
Approved age	>12 months [1]	>1 year[3]
Regulatory status	EMA and FDA licensed 2019; WHO prequalified; 11 African countries [1]	EMA exceptional circumstances 2020; not FDA licensed[3]
Efficacy / effectiveness	100% (95% CI 63.5–100) trial (2); 97.5% preliminary and 84% (95% CI 70–92) adjusted DRC [4,5]	No human efficacy; predicted survival 53.4% (95% CI 36.7–67.4) by immunobridging [20]
Immunogenicity	Day-28 seroresponse 95.4% (standard) / 98.2% (high dose); >90% at 24 months[2]	99.5% response at 21 days post-dose 2[21]; GMCs 3,085–7,518 EU/mL[22]
Storage	−80/−60°C for ≤3 years; 14 days at 2–8°C [5]	Up to 7 years at −85/−55°C; 8 months at 2–8°C [5]
Major advantages	Single dose; rapid onset (~10 days); field-proven; post-exposure potential [12]	Non-replicating; multivalent after dose 2; more flexible cold chain [34]
Major limitations	Ultra-cold chain; live-virus contraindications; EBOV-specific [5,17]	Two doses 8 weeks apart; higher doses; lower predicted efficacy [3,20]

4.3 Clinical trial evidence, 2020–2025

The efficacy designed trials, PREVAIL, STRIVE, and Ebola Ça Suffit, demonstrated efficacy in only the Guinea trial because there were too few EVD cases to prove efficacy in the other trials.[2] In the PREVAC trial, which was randomised, geometric mean concentrations of Ebola virus GP-binding antibodies were maintained above the threshold of 200 EU/mL for at least 12 months for most children who received Ad26-MVA, rVSV or rVSV with booster vaccine; and greater responses were seen in children than in adults[19] (all $p<0.001$ for Ad26-MVA, rVSV and rVSV with booster, compared with placebo).

Long-term follow-up of PREVAC participants showed that Ebola virus-specific memory T-cell responses persisted for up to 60 months after vaccination; a global estimate is that 500,000 to 1 million people have been vaccinated for Ebola in the world since 2014–2016.[35] Expanded-access and compassionate-use procedures

during the DRC outbreaks allowed vaccinations even for 6-month-old children and for pregnant women (post the first trimester) and lactating women.[2]

Table 2. Clinical trial and supporting evidence, 2020–2025.

Trial/study (year)	Product	Design/population	Evidence type	Key findings
PREVAC (2022) [19]	rVSV (1–2 doses); Ad26-MVA	Randomised, placebo-controlled; adults and children, 4 countries	Clinical immunogenicity	GMC >200 EU/mL for ≥12 months; no safety concerns
PREVAC long-term (2024)[35]	Same	5-year cohort; 196 adults, Guinea	Cellular immunogenicity	Memory T-cell responses persist to 60 months
Phase 2 Africa (2021)[22]	Ad26.ZEBOV/MVA-BN-Filo	Randomised, placebo-controlled; healthy and HIV-infected adults	Clinical immunogenicity	GMCs 3,085–7,518 EU/mL by interval; 56-day interval superior
Phase 3 lot-to-lot (2024) [21]	Same	Double-blind, placebo-controlled; n = 549	Clinical immunogenicity	Lots equivalent (GMC ratios 0.5–2.0); 99.5% response (419/421); booster 9.0–11.8-fold
DRC-EB-001 (2024)[33]	Same	Single-arm; adults, children ≥1 yr, pregnant/breastfeeding women	Real-world delivery/safety	20,408 dose-1 recipients (6,635 children); <1% SAEs non-pregnant; 371/1,221 (30.4%) pregnant women with SAEs (mostly caesarean), none vaccine-related
Immunobridging (2022)[20]	Same	Bridging model; 764 adults, 5 studies	NHP bridging	Predicted survival 53.4% (95% CI 36.7–67.4); not observed efficacy
ChAdOx1-biEBOV[13]	ChAdOx1 bivalent	Phase 1; UK (completed), Tanzania (ongoing)	Candidate clinical	Safe and immunogenic in phase 1
cAd3-Marburg (2024)[8]	ChAd3-MARV	First-in-human, dose-escalation; 40 adults	Candidate clinical	95% GP-antibody response at 4 weeks; 70% at 48 weeks; no related SAEs
VSV-SUDV (2025, preprint) [17]	VSV-SUDV	NHP lethal challenge	NHP/preclinical	Single dose protects within 1 week; VSV-EBOV no cross-protection
Replicon RNA SUDV (2025)[36]	Single-dose replicon RNA	Guinea pig challenge	Preclinical	100% survival

4.4 Outbreak deployment and stockpile use (2020–2025)

The 2018–2020 DRC outbreak (3,470 cases and 66% case fatality rate (1); 3,481 cases and 2,299 deaths in DRC-EB-001 cohort description[33] was the largest recorded in the DRC, due to the timing and change in case definitions between sources.

A few smaller outbreaks occurred during the review period, four of which have been attributed to reintroduction, rather than zoonotic spillover, of the virus: DRC North Kivu (February–May 2021); Guinea (February–June 2021); DRC North Kivu (October–December 2021); DRC Équateur (April–July 2022); and DRC North Kivu (August–September 2022).[1] A contained two-ring strategy for confirmed cases, known contacts, and contacts of contacts[1] has been implemented to help prevent the large DRC outbreak spreading beyond its borders by June 2020, the 2021 DRC outbreak from spreading beyond its borders by 3 months, and the 2021 Guinea outbreak from spreading beyond its borders by 4 months.

The rVSVΔG-ZEBOV-GP vaccine used in the DRC epidemic was said to be over 95% effective, however the effectiveness was adjusted to allow for complex vaccine delivery conditions in coverage analyses, 85%[1]; independently, modelling showed that ring vaccination was the most efficient of the strategies analysed for the 2018-2020 outbreak.[37]

The global stockpile.

A global stockpile for ERVEBO (Ebola vaccine) was set up in 2021 as a global first under an agreement between UNICEF and Merck, under the umbrella of the International Coordinating Group (ICG; WHO, IFRC, MSF, UNICEF;[1,5] and with support from Gavi. A governance model, previously used for the epidemic meningitis and yellow fever stockpiles, has been developed for the governance of limited vaccine doses for allocation fairly and consistently.[14,38]

From 2021 to 2023, the ICG received 11 requests, of which 10 were either accepted or partially accepted, and one was rejected; all three requests for outbreak-response were made within 1 week.[1] Doses shipped from the stockpile rose annually from 4,800 (2021) to 13,870 (2022) and 127,020 (2023), of which 42,620 doses expired; of the 145,690 doses shipped in total, 95% (139,120) were repurposed for preventive vaccination and 5% (6,570) for outbreak response, with the DRC receiving the largest share (111,000 doses; 76%), followed by Uganda (23,460; 16%) and Guinea-Bissau (11,170; 8%).[1] The stockpile reached its 500,000-dose goal in 2022 and held 518,890 doses as of December 2023, of which 208,390 (40%) were scheduled to expire in 2024.[1]

4.5 Sudan virus vaccine pipeline

The 2022 Sudan virus outbreak, centred on Mubende District in western Uganda, was declared over on January 11, 2023, after 142 confirmed cases (22 probable) and 55 deaths; the index case was a 24-year-old man who died within 10 days of symptom onset, and it was the first SUDV outbreak in Uganda since 2012 (15). With no licensed SUDV vaccines or therapeutics, control relied on classical measures, and WHO, in collaboration with the Ugandan government, developed a ring vaccination protocol to test SUDV candidate vaccines (13). An external expert panel prioritised three candidates — VSV-SUDV (IAVI/Merck), ChAd3-SUDV, and ChAdOx1-biEBOV (University of Oxford/Jenner Institute) — based on safety, immunogenicity, nonclinical efficacy, and manufacturing readiness.[13] VSV-SUDV was ranked first because its safety and efficacy could reasonably be extrapolated from ERVEBO given that only the glycoprotein insert differs; ChAd3-SUDV ranked second based on extensive ChAd3 vector experience (over 5,000 recipients and 123 non-human primates with durable 12-month protection); and ChAdOx1-biEBOV ranked third given limited filovirus-insert experience (74 recipients) and absent non-human primate data.[13]

Although the outbreak was controlled before ring vaccination could be implemented,[13] manufacturing timelines were unprecedented: the first cGMP ChAd3-SUDV doses arrived in Uganda 79 days after outbreak declaration; approximately 2,160 VSV-SUDV doses were received by a WHO delegation within 80 days; and Oxford, with the Serum Institute of India, manufactured 40,000 cGMP doses of ChAdOx1-biEBOV with the first batch delivered within 80 days.[13] ChAdOx1-biEBOV is a single-dose bivalent vaccine expressing both EBOV and SUDV glycoproteins, with a phase 1 trial completed in the UK and an additional phase 1 study underway in Tanzania.[13] Preclinical evidence supports the fast-acting potential of these candidates: a single dose of VSV-SUDV protected non-human primates from lethal SUDV infection within one week, whereas VSV-EBOV provided no relevant cross-protection, highlighting the need for species-specific filovirus vaccines.[17] A single-dose replicon RNA SUDV vaccine encoding SUDV glycoprotein, alone or combined with EBOV glycoprotein, achieved 100% survival in a guinea pig challenge model.[36] A 2022 analysis identified only 20 SUDV research studies worldwide — most implemented in the USA and only one in Uganda — underscoring the research gap that the outbreak revealed.[16]

4.6 Marburg virus and emerging platforms

No licensed Marburg virus vaccine exists, but progress accelerated during the review period. The WHO-coordinated MARVAC consortium reported 4,500 clinical-grade doses of the Ad26-MARV vaccine available for emergency outbreak response, alongside a ChAd3-MARV candidate providing rapid (within 1 week) and durable (6–12 month) protection in non-human primates.[18] A first-in-human phase 1 study of cAd3-Marburg (40 adults) found a glycoprotein-specific antibody response in 95% of participants at 4 weeks and 70% at 48 weeks, with no related serious adverse events; a phase 2 trial in Uganda and Kenya followed in 2023.[8] WHO's Technical Advisory Group on Candidate Vaccine Prioritisation recommended four viral-vectored MARV candidates (two VSV, one ChAd3, one ChAdOx1) for phase 1/2/3 evaluation.[8]

Beyond filovirus-vectored candidates, recombinant protein filovirus vaccines — lyophilised and stable at 40°C for 12 weeks — completely protected cynomolgus macaques against monovalent SUDV and MARV challenge and against EBOV after three doses, and can serve as boosters for recipients of vectored vaccines; these non-replicating, thermostable platforms avoid the contraindications of live vaccines.[34] Other phase 1 candidates with published data include Vesiculovax, an rVSV vector expressing EBOV glycoprotein with a highly attenuated VSV glycoprotein; a two-dose DNA vaccine; a bivalent DNA plasmid vaccine targeting EBOV and Marburg virus; and a two-dose monovalent nanoparticle recombinant EBOV glycoprotein vaccine.[3] Vaccine platforms span replicating and non-replicating viral vectors, DNA, virus-like particles, and subunit vaccines.[7] a parainfluenza virus type 3 vector expressing EBOV GP1,2 induced robust immune responses in non-human primates, and only one protein-based Ebola vaccine has entered phase 1 trials, reflecting the difficulty of producing GP1,2 due to cytotoxicity.[3]

Table 3: Sudan Virus, Marburg Virus, and Emerging Filovirus Vaccine Pipeline.

Candidate (sponsor)	Platform	Target	Stage	Key evidence
VSV-SUDV (IAVI/Merck)	Replicating rVSV	SUDV	Clinical development	Extrapolation from ERVEBO; ~2,160 doses to Uganda in 80 days; NHP protection within 1 week [13,17]
ChAd3-SUDV	Non-replicating ChAd3	SUDV	Phase 1	Vector experience >5,000 recipients; 123 NHPs, 12-month protection; cGMP doses in 79 days [13]
ChAdOx1-biEBOV (Oxford/SII)	Non-replicating ChAdOx1, bivalent	EBOV + SUDV	Phase 1	40,000 cGMP doses; first batch in 80 days[13]
ChAd3-MARV	Non-replicating ChAd3	MARV	Phase 2 (Uganda/Kenya)	NHP protection in 1 week, durable 6–12 months; phase 1: 95% at 4 weeks, 70% at 48 weeks[8,18]
VSV-MARV	Replicating rVSV	MARV	Preclinical/clinical	NHP protection; BARDA-supported[8,13]
Ad26-MARV	Non-replicating Ad26	MARV	Clinical-grade supply	4,500 emergency-use doses[18]
Recombinant protein vaccines	Adjuvanted lyophilised GP	EBOV, SUDV,MARV	Preclinical	Complete NHP protection; stable 12 weeks at 40°C[34]
Replicon RNA SUDV	RNA replicon	SUDV (± EBOV)	Preclinical	100% guinea pig survival[36]
Vesiculovax; DNA vaccines; nanoparticle GP vaccine	rVSV; DNA plasmid; nanoparticle	EBOV (± MARV)	Phase 1 data published	Immunogenic in early-phase trials (3)

4.7 Immunogenicity, durability, and correlates of protection

Both licensed vaccines typically begin to induce detectable antibody responses by day 14, peaking approximately 28 days after the final dose.[5] With a booster given 56 days after initial ERVEBO vaccination, peaks occur on day 7 in adults and day 28 in children, although the increases are transient.[5] For ERVEBO, day-28 seroresponse was 95.4% (standard dose) and 98.2% (high dose), persisting at 24 months in more than 90% of vaccinees[2]; single-dose recipients who seroconverted remained seropositive at 2 years in 100% (high dose) and 89% (low dose) of participants, with antibody levels plateauing after an initial decline.[39] For Ad26.ZEBOV/MVA-BN-Filo, circulating antibody levels are stable after the initial contraction phase and maintained for at least 3.8 years in humans, with maintained immunological memory and robust anamnestic responses to booster vaccination.[40]

No defined correlate of protection currently exists for ERVEBO, and the specific correlates and thresholds of protection remain among the key unanswered questions.[5] Antibody levels of at least 200 EU/mL with a ≥2-fold rise are the best-validated serological benchmark associated with protection.[5] Protection may be platform-dependent: CD8+ T cells appear critical for Ad5-based vaccines, whereas antigen-specific IgG responses are essential for VSV-EBOV.[10] Importantly, neutralising antibody titres alone do not fully explain protection: NHP studies of rVSVΔG-ZEBOV-GP identified antibodies targeting the soluble glycoprotein (sGP) that drive neutrophil-mediated phagocytosis as independent correlates of protection, with vaccine efficacy waning over time in macaques (100% survival at 42 days; 33% at 3 months; 43% at 1 year).[41] Antibody levels after natural infection (predominantly IgG) are significantly higher than those after vaccination (predominantly IgM) and persist for up to two years post-recovery unless boosted.[5]

4.8 Access, equity, and supply chain

Vaccine manufacturing, quality control, and distribution are complex and time-intensive; long start-up and processing times, often exceeding a year, can delay batch release, and demand is highly uncertain for sporadic outbreak diseases.[5] ERVEBO requires storage at −80°C to −60°C for a maximal shelf life of 3 years, with only 14 days of stability at 2–8°C, whereas Zabdeno/Mvabea is more stable (up to 7 years at −85°C to −55°C and 8 months at 2–8°C) — requirements that are particularly challenging in settings with limited cold-chain infrastructure.[5] Early stability studies confirmed that the rVSV-ZEBOV formulation was stable for 1 week at 4°C and for 24 hours at 25°C, with stability compromised by high temperatures and dilution,[43] and simulation studies of refrigerated (2–8°C), rough-road last-mile transport of Ad26.ZEBOV/MVA-BN-Filo found no substantial effect of shock and vibration on product quality, supporting liquid 2–8°C distribution to rural areas.[44] Thermostable formulations are a recognised priority for reducing cold-chain dependence and enabling rapid distribution and stockpiling in tropical regions.[45] The lack of globally harmonised regulations results in heterogeneous, country-specific packaging and labelling requirements that hinder flexible distribution, and digital approaches such as electronic labelling via QR codes have been proposed; post-approval changes, such as extending shelf

life, typically require new trials, complicating product improvement.[5]

Regulatory innovation was central to this period. In 2019, ERVEBO initially received authorisation under compassionate-use or expanded-access protocols by the European Commission, while the FDA granted expedited full approval using human efficacy data; Zabdeno/Mvabea received marketing authorisation under exceptional circumstances in 2020, requiring annual reassessments, and ERVEBO converted its conditional authorisation to full marketing authorisation in 2021.[5] Earlier, rVSVΔG-ZEBOV-GP had received FDA breakthrough-therapy designation and EMA priority-medicines designation in June 2016, and a joint WHO–EMA review facilitated rapid WHO prequalification.[46]

4.9 Vaccine acceptance and community engagement

Vaccine uptake varied by population and context. During 2014–2016 in Sierra Leone, 74% of the population expressed willingness to be vaccinated[5]; in the DRC between 2018 and 2020, acceptability of ERVEBO ranged from 72% to 84% among community members, with 99% uptake among health-care workers.[5] Among 438 health-care workers in North Kivu (2021), 95.9% reported being eligible and offered the vaccine, and acceptance was essentially ubiquitous; however, roughly half still reported concerns about side effects, safety, and effectiveness, and 64.6% felt vaccination should be mandatory — underscoring the importance of engaging the "moveable middle" of hesitant individuals open to persuasion with additional information.[25] In high-risk community members in North Kivu (2024), 90.2% perceived EVD as serious, 55.6% believed vaccination could prevent EVD, and 71.6% that it could reduce severity, but 63.7% believed the vaccine had severe side effects, 35.3% mistrusted the vaccination team, and 33.4% mistrusted government vaccine decisions; among those offered the vaccine, 83.8% accepted, with 52.4% accepting on first offer.[26]

Community resistance and mistrust in eastern DRC — including 420 attacks on health facilities and 140 armed groups active in the region — were driven by low institutional trust, misinformation (12% of one survey believed EVD was fabricated), dissatisfaction or mistrust of the response (72%), and perceived foreign profit motives.[27,28]

5. DISCUSSION

This review maps a period of transformative progress in Ebola vaccination. Its contribution lies not only in enumerating trials and approvals but in interpreting the strategic transitions they represent.

5.1 From investigational products to licensed vaccines

The 2020–2025 period completed the transition of Ebola vaccines from investigational products to licensed, stockpiled, and deployed medical countermeasures.[5] ERVEBO's 100% efficacy in the Guinea ring trial remains the cornerstone of the evidence base,[2] complemented by adjusted field effectiveness of 84% (95% CI 70–92) and deployment to more than 300,000 individuals during the largest DRC outbreak.[3,4] Yet this transition exposed an asymmetry in the evidence: efficacy rests almost entirely on a single trial, while the second licensed product rests on immunobridging rather than observed efficacy — a reality that should temper confidence and guide post-licensure surveillance.[20]

5.2 From reactive outbreak vaccination to preventive vaccination

A defining shift of the period was the move from reactive ring vaccination toward anticipatory prevention. ICG approval of preventive use (2022), the 2024 SAGE recommendations, and Gavi's preventive EVD vaccination programme represent a deliberate policy reorientation.[1,5] The Rwanda UMURINZI campaign — vaccinating 203,267 individuals by July 2021 with two-dose completion of 91–94% — demonstrated the feasibility of preventive programmes in at-risk countries.[1] Vaccination is no longer only an outbreak-response tool but a standing protection for frontline workers and communities.

5.3 The experience of the global vaccine stockpile

The ICG stockpile proved operationally fast — all outbreak-response requests were delivered within 1 week[1] — but its first three years also revealed structural tensions. With 95% of shipped doses used preventively and 42,620 doses expiring,[1] demand forecasting and dose-expiry management are now central governance problems, echoing long-recognised lessons of global vaccine stockpiling regarding forecasting, release criteria, and ethical allocation.[38]

5.4 The absence of a licensed Sudan virus vaccine

The 2022 SUDV outbreak exposed the critical vulnerability of the current portfolio: no licensed vaccine or therapeutic existed for any non-Zaire ebolavirus.[13] Response depended on classical measures and on candidates manufactured in record time — a reminder that platform readiness, not only licensure, determines preparedness.[13] The prioritisation process itself demonstrated the value of structured extrapolation from vector and insert experience when efficacy data are absent,[13] and the paucity of SUDV research (only 20 studies worldwide) highlights a persistent neglect of non-Zaire filoviruses.[16]

5.5The need for broader, multivalent protection

Because licensed EBOV vaccines do not protect against SUDV or MARV,[17] and because four ebolavirus species plus Marburg virus cause human disease,[3] the future of filovirus vaccination lies in multivalent or broadly protective platforms — bivalent ChAdOx1-biEBOV,[13] recombinant protein vaccines protecting against EBOV/SUDV/MARV,[34] and replicon RNA candidates[36] — alongside species-specific candidates for outbreak response.

5.6 The need for thermostable vaccines

The ultra-cold chain of ERVEBO remains a binding constraint on equitable deployment.[5] Refrigerated last-mile transport of the Ad26.ZEBOV/MVA-BN-Filo regimen is feasible,[44] and thermostable lyophilised protein vaccines offer a promising route to cold-chain independence in tropical settings.[34,45] Product profiles should be prioritised for context-appropriateness — not only speed — from the outset.[13]

5.7 Durability and correlates of protection

Durability remains unresolved. Antibody persistence extends to at least 2 years[39] and 3.8 years for the Ad26 regimen,[40] with immune memory persisting to 5 years,[35] but waning NHP protection and the absence of defined correlates complicate booster policies.[41] Emerging evidence that non-neutralising, sGP-targeted antibody functions predict protection challenges purely neutralisation-based frameworks.[41] Defining validated correlates would transform vaccine evaluation, licensure, and scheduling.

5.8 Research gaps and future priorities

Table 4. Research gaps and future priorities

Priority area	Current gap	Future direction
Correlates of protection	No defined correlate or threshold [5]	Validate mechanistic correlates, including sGP/Fc-mediated functions and cellular memory[41]
Durability and boosting	Waning immunity; no evidence-based booster criteria [35]	Long-term cohorts and randomised booster trials [2]
Special populations	Limited controlled data in pregnancy, children <1 year, immunocompromised[5]	Controlled trials; prioritise non-replicating/protein platforms[34]
Cross-species protection	Licensed vaccines are EBOV-specific[17]	Multivalent/broadly protective candidates[13,34]
Thermostability	Ultra-cold chain constrains access[5]	Lyophilised/thermostable formulations[34,35]
Equity, supply, regulation	Demand uncertainty; expiry; heterogeneous labelling [1,5]	Demand forecasting; e-labelling; harmonised regulation[5]
Post-exposure prophylaxis	Monoclonal antibodies alone offer incomplete protection[5]	Evaluate vaccine–mAb combinations, at least in NHPs[5]

6. Limitations

This scoping review has several limitations. First, as a scoping review it maps evidence rather than quantitatively synthesising effect estimates, and no formal quality appraisal was performed. Second, because the original database export files were not available for retrospective reconstruction, database-specific record counts, deduplication totals, and detailed PRISMA-ScR flow numbers could not be reliably reconstructed. Third, included documents were predominantly English-language publications from high-income and international organisations, potentially under-representing locally led African research. Fourth, one included study is a preprint (single-dose VSV-SUDV non-human primate challenge) that had no peer-reviewed equivalent at the time of analysis; its findings should be interpreted with caution pending peer review.[17] Fifth, because outbreak opportunities are sporadic, efficacy evidence derives largely from a single trial, and comparative vaccine data remain limited.[2] Finally, some foundational sources predate the 2020–2025 window and were used for context; where newer evidence supersedes older findings, both are reported transparently (for example, preliminary 97.5% versus adjusted 84% effectiveness[4,5]; 2-year versus multi-year antibody persistence.[39,40]

7. CONCLUSIONS

Between 2020 and 2025, Ebola vaccines transitioned from investigational products to licensed, stockpiled, and deployed medical countermeasures. ERVEBO's demonstrated efficacy and field effectiveness,[2,4] the exceptional-circumstances authorisation of Zabdeno/Mvabea via immunobridging,[20] the establishment of a functioning global stockpile,[1] and the rapid mobilisation of Sudan virus candidates during the 2022 Ugandan outbreak[13] represent landmark advancements. However, unresolved questions regarding correlates of protection, durability, special populations, cold-chain logistics, equity, and acceptance must be addressed if the full promise of filovirus vaccination—including protection against all ebolavirus species—is to be realised. Sustained investment in next-generation multivalent, thermostable platforms and in equitable, context-appropriate deployment will be essential to translate scientific progress into population-level protection.

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