Reproductive Health

STUDY PROTOCOL

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Safety, immunogenicity, efficacy, and effectiveness of Lassa fever vaccines in pregnant persons, children, and adolescents: a protocol for a living systematic review and meta-analysis

Jamile Ballivian[1*], Mabel Berrueta[1], Agustín Ciapponi[1], Juan Manuel Sambade[1], Katharina Stegelmann[1], Agustina Mazzoni[1], Ariel Bardach[1], Martin Brizuela[1], Daniel Comandé[1], Noelia Castellana[1], Edward P. K. Parker[2], Andy Stergachis[3], Xu Xiong[4], Flor M. Munoz[5] and Pierre M. Buekens[4]

Abstract

Background Lassa fever (LF), caused by the Lassa virus (LASV), is a zoonotic viral hemorrhagic disease endemic to West Africa, primarily transmitted through rodent excreta and infected bodily fluids. It poses significant public health challenges due to its high morbidity and mortality rates, particularly among at-risk populations like pregnant persons and children. Despite decades of research, vaccine development has been hindered by the virus's genetic diversity and complex epidemiology. While several vaccine candidates have been developed, none have received regulatory approval. Given the rapidly evolving vaccine landscape, a living systematic review (LSR) was selected to enable real-time evidence synthesis. This protocol outlines a living systematic review (LSR) to evaluate the safety, efficacy, effectiveness, and immunogenicity of LASV vaccines, providing evidence to guide public health interventions and vaccine recommendations.

Methods We will conduct a biweekly updated LSR and meta-analysis, systematically searching databases (e.g., MEDLINE, EMBASE, CENTRAL) and clinical trial registries from January 2014 onward to identify studies of LASV vaccines in pregnant persons, children, and adolescents. All study designs, including randomized trials, cohort studies, case–control studies, and case reports, will be eligible. Pairs of reviewers will independently assess eligibility, extract data, and evaluate the risk of bias. Primary outcomes include vaccine safety, efficacy, and effectiveness in pregnant persons (including neonatal outcomes), children, and adolescents, while secondary outcomes assess immunogenicity and reactogenicity. Data on adult populations will also be included, and results on this group will be reported as available. We will conduct paired meta-analyses, including prespecified subgroup and sensitivity analyses. We will use the grading of recommendations assessment, development, and evaluation approach to evaluate the certainty of evidence.

Discussion This LSR offers a dynamic framework to generate timely evidence on LASV vaccines for vulnerable populations. By integrating findings into an interactive Microsoft Power BI dashboard, stakeholders can access

*Correspondence:
Jamile Ballivian
jballivian@iecs.org.ar
Full list of author information is available at the end of the article

and utilize real-time updates to inform public health strategies. Despite challenges like study heterogeneity and vaccine platform variability, subgroup and sensitivity analyses will mitigate these issues. This review aims to support clinical trial designs, guide policy, and improve health outcomes in Lassa fever-endemic regions.

Study registration Two protocols were registered in the International Prospective Register of Systematic Reviews (PROSPERO) database: CRD42024514513 and CRD42024516754.

Keywords Lassa virus, Vaccine, Pregnancy, Children, Adolescents, Protocol, Systematic review, Meta-analyses

Background

The burden of disease caused by Lassa fever virus

Lassa fever (LF) is a zoonotic acute viral hemorrhagic disease that poses a significant public health challenge. It is caused by the Lassa virus (LASV), an RNA virus of the *Arenaviridae* family [1–3], which is endemic in rodent populations in West Africa [4]. Transmission to humans occurs through contact with rodents' excreta or blood and by consuming contaminated food or water [2, 5, 6]. Human-to-human transmission is also possible through exposure to the body fluids of infected individuals [7]. Discovered in Nigeria in 1969, LASV is endemic in the "Lassa fever belt" of West Africa [2, 8, 9]. The disease causes annual outbreaks in the affected regions, and cases have been sporadically imported to the United States, Japan, the United Kingdom, Germany, the Netherlands, and Israel [10]. LASV exhibits substantial genetic diversity, with six distinct strains identified, each associated with specific geographic regions [11–13].

LF is a substantial public health threat in the affected countries. Annually, an estimated 100,000–300,000 cases [9] and 5,000–10,000 deaths are reported [1, 14, 15]. The World Health Organization (WHO) urges a better understanding of LF in West Africa while warning against outdated, limited surveillance data [16]. Severe underreporting was shown by a recent study highlighting the discrepancy regarding national case fatality rates (CFR) [17]. With its high case numbers, LASV is the main causative agent for hemorrhagic fever worldwide [18]. The overall CFR for LASV infection reported in the literature was 1–2% [4]. However, during the LF outbreak in 2023 in Nigeria, the crude CFR, up to week 11, was 18.1% [19]. Most infections are mild or asymptomatic and do not require hospitalization [20]. Nevertheless, the CFR is higher in at-risk groups, such as pregnant persons and infants [21, 22].

LF is characterized by fever, fatigue, and headache [23]. Suspected cases may also suffer from hemorrhage and gastrointestinal and respiratory symptoms, such as vomiting, diarrhea, cough, and chest pain [4]. Common complications in patients infected with LF are hearing loss and encephalopathy [23, 24]. Although Lassa fever can impact individuals of all ages, children and pregnant persons face a significantly higher risk of severe complications and mortality, including obstetric outcomes such as fetal loss [21, 22, 25–28]. LF poses significant risks to pregnant persons and their fetuses. A systematic review and meta-analysis of 276 pregnant persons from Nigeria, Sierra Leone, and Liberia (1972–2019) reported a pooled maternal CFR of 33.73%, with pregnant persons being nearly three times more likely to die compared to non-pregnant persons [21]. Fetal outcomes were particularly poor, with a CFR of 61.5%. In addition to the typical clinical features of LF infection, such as fever, headache, and pharyngitis, infected pregnant persons experienced breast and retrosternal pain, vaginal bleeding, and preterm labor [21]. A recent retrospective cohort study of LF in pregnancy in Nigeria reported a 37% CFR among pregnant persons admitted to the hospital [29]. The high mortality rate may be due to the elevated viral load seen in pregnant persons and the strong affinity of the LASV for placental and vascular tissues [29]. Similarly, a prospective cohort study in Nigeria (2018–2020) found high rates of pregnancy loss, including miscarriages, stillbirths, and intrauterine deaths, highlighting the severe impact of Lassa fever during pregnancy [30].

Data on pediatric LF remains limited [10, 31]. A recent review analyzing six studies that included both adults and children reported a prevalence ranging from 0 to 40.5% in children [32]. Commonly observed symptoms in children included fever, vomiting, abdominal pain, cough, and headache, with hepatomegaly and splenomegaly also frequently reported. The CFR varied widely, from 6 to 49.3%, with two studies identifying higher CFRs in girls (36.8–80%) compared to boys (20–63.1%). Additionally, a cohort study from Sierra Leone reported a CFR of 63% [33]. Severe outcomes such as "swollen baby syndrome," characterized by generalized edema, abdominal distension and bleeding were described in one study, which documented a CFR of 75% [34]. These findings underscore the substantial morbidity and mortality associated with pediatric Lassa fever, highlighting the urgent need for effective diagnostic tools and treatment strategies tailored to this population.

Lassa fever vaccine development

LF vaccine research began in the 1970 s [35]. However, successful development has been challenging due to the genetic diversity of the virus [11]. Frequently occurring outbreaks, complex prevention dynamics, and limited surveillance data have increased the focus on LF in recent years [16, 36]. The disease has become a priority, and it was added to the WHO Research and Development Roadmap [16]. Since 2015, 34 vaccine candidates have been developed [37, 38]. Currently, four vaccine candidates (INO- 4500, MV-LASV, rVSVΔG-LASV-GPC, and EBS-LASV) are undergoing clinical trials [36, 37]. Three of these are in Phase I trials involving healthy adults aged 18–50 [36]. The first Phase II clinical trial for a Lassa fever vaccine recently started in West Africa, where the rVSVΔG-LASV-GPC vaccine is being tested in both adults and children [39]. Despite there are many candidates in the pipeline, no vaccine has been yet approved for LF, and no clinical trial has thus far included pregnant persons or children [36]. Given the diverse demographic characteristics and varying risk groups, tailored vaccine policies are essential to ensure effective implementation across populations.

A living systematic review (LSR) enables the continuous integration of emerging evidence and has been successfully used in outbreak settings such as COVID- 19 and mpox [40]. This approach allows for timely updates to inform vaccine policy and research as new data become available. With distinct vaccine platforms against LASV, such as viral-vector or DNA, it is crucial to understand and evaluate their safety and efficacy profiles. We aim to evaluate existing and emerging evidence on the safety, tolerability, efficacy/effectiveness, and immunogenicity of LF vaccine candidates in pregnant persons, children, and adolescents.

Methods

This living systematic review of LASV vaccines focusing on pregnant persons, children, and adolescents. will follow the Cochrane and World Health Organization (WHO) methods [41–43] and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA) statement [44, 45]. Two protocols were registered in the International Prospective Register of Systematic Reviews (PROSPERO) database following the PRISMA-P statement [46]: one for pregnant persons (CRD42024554330) and the other for children and adolescents (CRD42024556977).

Search strategy

Literature research will be conducted using the following sources: the Cochrane Library databases, MEDLINE, EMBASE, Latin American and Caribbean Health Sciences Literature (LILACS), Science Citation Index Expanded (SCI-EXPANDED), EPPI-Centre map of the current evidence on LASV/LF, WHO Database of publications on LASV/LF, LASV/LF-related Congresses, guidelines published by national and international professional societies (e.g., ACOG, RCOG, FIGO), preprint servers (e.g., ArXiv, BiorXiv, medRxiv, search. bioPreprint), and LASV/LF research websites.

A comprehensive search with no language restrictions will be conducted across these databases from January 2014 to current date. Biweekly searches will be used to ensure the inclusion of the latest relevant reports. Another data source will be reference lists of systematic reviews. These will be reviewed to identify additional relevant publications. Ongoing randomized controlled trials will be tracked in Clinicaltrial.gov and other trial registers (WHO, etc.). Contact with experts and hand-searching of reference lists of included studies and relevant systematic reviews will provide potentially missed studies from the search strategy.

Our literature search strategy will include the following search terms:

(Lassa Fever[Mesh] OR Lassa*[tiab] OR Lassa Virus[Mesh] OR LASV[tiab] AND (Vaccin*[Mesh] OR Vaccin*[tiab] OR INO- 4500[tiab] OR MV-LASV[tiab] OR rVSVΔG-LASV-GPC[tiab] OR RepliVAX*[tiab] OR EBS-LASV[tiab] OR ChAdOx1[tiab] OR Padovax[tiab] OR Baculovirus*[tiab]).

The search strategy will be periodically reviewed and refined to incorporate emerging terminology, new vaccine candidates, and additional data sources as the field evolves.

Study designs

This review will include pre-clinical and clinical trials, quasi-experimental, and observational (comparative and non-comparative) study designs, regardless of publication status, year, and language. Randomized controlled trials (RCTs) (all phase I, II, or III trials involving human subjects and animals), non-randomized CTs, uncontrolled before-after studies (UBAs), interrupted time series (ITSs), and adverse event/safety registries will be considered. Lastly, phase IV studies, cohort studies, case–control studies, cross-sectional studies, and case series will be included. Case reports will only be considered if reporting previously unknown or unexpected adverse events.

Types of participants

Study participants will include newborns, infants, children, adolescents, pregnant persons, and their fetuses, and adults, irrespective of prior exposure to LASV,

comorbidities, immune status, and risk group. Regarding the sample size, we will include observational studies reporting safety and efficacy or effectiveness outcomes with sample sizes of at least 50 subjects (commonly used in observational studies to ensure sufficient statistical power while being manageable for rare diseases). Case reports of infrequent adverse events will be included regardless of sample size. Animal studies will be included. General adult population data will be included to capture any data related to pregnant individuals.

Types of interventions

The intervention exposure considered will be LF vaccine candidates and licensed vaccines (when available), irrespective of doses and administration schedule. If available, data on heterologous ("mix-and-match") vaccination schedules and booster doses will also be included and analyzed.

Types of comparisons

Any control group will be considered, whether it involves standard care, no intervention, placebo, a different LASV vaccine, or any other "active" comparator, irrespective of co-interventions. Additionally, noncomparative studies will be included. The presence of a control group will not be obligatory.

Measures of effect

Odds ratios (ORs), Risk ratios (RRs), and Hazard ratios (HRs) with 95% confidence intervals (95% CIs) will be extracted for dichotomous outcomes, and Mean Difference (MD) or Standardized MD (SMD) will be extracted for continuous outcomes. We will report Vaccine efficacy/effectiveness (VE) for relevant clinical trials (of efficacy) and post-implementation observational studies (of effectiveness). We will also calculate proportions with 95% CIs for non-comparative studies.

Primary outcomes

Following immunization of pregnant persons

Safety outcomes

a) **Obstetric/neonatal outcomes after maternal vaccination:**

We will use the standardized case definitions developed by the Global Alignment of Immunization Safety Assessment in Pregnancy (GAIA) [47] project of prioritized obstetric and neonatal outcomes based on the standard Brighton Collaboration process and the Safety Platform for Emergency vACcines (SPEAC) guidance (https://brightoncollaboration.org/speac/) [48]. The outcomes include (but are not limited to):

- Obstetric outcomes: Maternal death, spontaneous abortion/miscarriage, induced abortion, stillbirth, preterm delivery, antenatal, perinatal, or maternal hemorrhage (antenatal/peripartum/postnatal), gestational diabetes mellitus, hypertensive disorders of pregnancy, pre-eclampsia/eclampsia, dysfunctional labor, non-reassuring fetal status, intrauterine fetal growth restriction.
- Neonatal outcomes: Neonatal death, prematurity or preterm birth, low birth weight, small for gestational age, neonatal infection, neonatal sepsis, neonatal encephalopathy, respiratory distress, failure to thrive, congenital anomalies including microcephaly.

b) **Serious adverse events (SAEs) and all-cause mortality related to vaccination (in vaccinated adults, pregnant people and their offspring).**
Regarding SAEs, all reported outcomes will be collected, and we will particularly focus on outcomes related to fetal loss (spontaneous abortion/miscarriage and stillbirth), neonatal mortality rate, infant mortality rate, maternal mortality rate and hospitalization for severe myalgia, hypovolemic hyponatremia, or atrial fibrillation.

c) **Adverse events of Special Interest (AESI) post-vaccination in pregnant persons (not related to pregnancy)**
Based on the outcomes recommended by SPEAC guidance on LF AESI [48], AESI include (but are not limited to): Myocarditis/Pericarditis, Polyserositis/Face & Neck Swelling, Hemorrhagic disease, Vaccine-associated Immune Thrombotic Thrombocytopenia (VITT), Thrombocytopenia, Anaphylaxis, Single Organ Cutaneous Vasculitis, Severe Lassa Fever infection (Acute Respiratory Distress Syndrome, acute kidney injury with KDIGO ≥ 2; NEWS2 ≥ 7; Liver Function Tests ≥ 3X upper limit of normal; shock; multiorgan failure; death), Acute aseptic arthritis, Aseptic meningitis, Acute Encephalitis, Myelitis, Generalized convulsion, Guillain-Barré Syndrome, Sensorineural Hearing Loss, Acute Kidney Injury, Acute Respiratory Distress Syndrome (ARDS), Acute Respiratory Distress Syndrome (ARDS), Alopecia.

Efficacy/effectiveness in the prevention of LASV infection according to the WHO-suggested case definition **Confirmed, Probable, or Suspected case of LASV infection (WHO case definition)** [49]**.**

Classification:

Suspected case: Any person with gradual onset of one or more of the following: malaise, fever, headache, sore throat, cough, nausea, vomiting, diarrhea, myalgia (muscle pain), central chest pain or retrosternal pain, or hearing loss and:

i. History of contact with excreta or urine of rodents; *OR*
ii. History of contact with a probable or confirmed Lassa fever case within a period of 21 days of onset of symptoms *OR*
iii. Inexplicable bleeding/hemorrhaging

Probable case: Any suspected case who died without collection of specimens for laboratory testing.

Confirmed case: Any suspected case with laboratory confirmation (positive IgM antibody, PCR or virus isolation).

Confirmed LF hospitalization.

Other complications attributed to LF

Immunogenicity

a. Humoral immune responses (titers of IgM, IgG, and combined; neutralizing antibodies in maternal serum at delivery and umbilical cord blood;).
b. Transplacental transfer ratios.
c. Magnitude and duration of antibody response

Others Case fatality rate (CFR) in mothers

Following immunization of infants, children and adolescents

Safety outcomes All reported safety outcomes will be included. We will use the standardized case definitions developed by the GAIA project to prioritize outcomes based on the standard Brighton Collaboration process and SPEAC guidance (https://brightoncollaboration.org/speac/). The outcomes include (but are not limited to):

a) **Serious adverse events (SAEs) and all-cause mortality related to vaccination** SAEs such as infant, children, and adolescent mortality rate and hospitalization for severe myalgia, hypovolemic hyponatremia, or atrial fibrillation.
b) **Adverse events (AEs) of Special Interest (AESI) post-vaccination in children:** Based on the outcomes informed by SPEAC [48] guidance, AESI include (but are not limited to): Myocarditis/Pericarditis, Polyserositis/Face & Neck Swelling, Hemorrhagic disease, Vaccine-associated Immune Thrombotic Thrombocytopenia (VITT), Thrombocytopenia, Anaphylaxis, Single Organ Cutaneous Vasculitis, Severe Lassa Fever infection (Acute Respiratory Distress Syndrome, acute kidney injury with KDIGO ≥ 2; NEWS2 ≥ 7; Liver Function Tests ≥ 3X upper limit of normal; shock; multiorgan failure; death), Acute aseptic arthritis, Aseptic meningitis, Acute Encephalitis, Myelitis, Generalized convulsion, Guillain-Barré Syndrome, Sensorineural Hearing Loss, Acute Kidney Injury, Acute Respiratory Distress Syndrome (ARDS), Acute Respiratory Distress Syndrome (ARDS), Alopecia.

Efficacy/effectiveness in the prevention of Lassa fever infection according to the WHO-suggested case definition

a) Confirmed, Probable or Suspected (WHO case definition) see 2.6.1.2.
b) Confirmed LF hospitalization.
c) Other complications attributed to LF vaccination in children.

Immunogenicity

a) Humoral response including titers of binding and neutralizing antibodies [geometric mean titers (GMT)] in serum after primary and/or booster vaccination schemes; seroresponse, seroconversion.
b) Duration of immune response

Others Case fatality rate (CFR) in children

Secondary outcomes

1. Viremia after vaccination: presence, magnitude, and duration of viremia in mother, newborn, infant, child, and adolescent.
2. Sympotomatic or Asymptomatic LASV infection after vaccination (determined by antibody or antigen detection in asymptomatic individuals).
3. Mother-to-child transmission: Presence and persistence of LASV detection and/or viral load in the placenta, fetal tissues, amniotic fluid, cord blood, vaginal fluids, breast milk, neonatal throat swabs, or other reported sources.

Data extraction and management

Selection

Pairs of reviewers will independently screen each title and abstract. For any studies or reports deemed potentially relevant, we will obtain the full texts. Review authors, working in pairs, will then independently assess these full texts and document reasons for excluding studies that do not meet the criteria. Any disagreements will be resolved through discussion with the review team. This process will be conducted using the web-based platform, Nested Knowledge (https://nested-knowledge.com/).

Data collection

Data for the study will be collected and securely stored using REDCap electronic data capture tools, hosted on data servers at the Institute for Clinical Effectiveness and Health Policy (IECS) in Buenos Aires, Argentina. Before formal data extraction begins, we will pilot the process on a sample of at least ten studies. Data will be independently extracted by pairs of review authors using a REDCap form, with any disagreements resolved through team discussion. If necessary, we will reach out to study authors to clarify any insufficiently reported data. Information on funding sources will also be gathered for each study included in the living systematic review (LSR).

Risk of bias assessment

Each study will be assessed based on its study design and relevant bias domains. For randomized controlled trials, we will apply the Cochrane risk of bias tool—version 2 (RoB2), covering five domains: randomization process, deviations from intended interventions, missing outcome data, outcome measurement, selective reporting, and an overall risk of bias evaluation [50]. For non-randomized intervention studies, the ROBINS-I tool will be utilized [51]. For controlled before-after studies, we will examine baseline measurements, characteristics of studies using a secondary site as a control, blinded assessment of primary outcomes, reliability of primary outcome measures, and follow-up of both professionals and patients to guard against exclusion bias. In uncontrolled before-after studies, the same criteria as controlled before-after studies will be applied, except for baseline measurement and characteristics for studies using a second site as control.

For interrupted time series studies, we will evaluate the risk of bias across seven domains: independence of the intervention from other changes, pre-specified shape of the intervention effect, likelihood that the intervention did not influence data collection, blinding of outcome assessors to intervention allocation, completeness of outcome data, selective outcome reporting, and any other bias sources. For controlled interrupted time series studies, we will add three additional domains specific to design-related validity threats: imbalance of baseline outcome measures, baseline comparability of intervention and control group characteristics, and protection against contamination. For non-comparative studies, the NIH Quality Assessment Tool will be applied [52]. After answering the different signaling questions, *yes, no, cannot be determined, not applicable, or not reported,* the raters will classify the study quality as good, fair, or poor. We will use the classifications low, high, or unclear risk of bias for consistency with the other designs. We will present GRADE certainty of evidence in the 'Summary of findings' tables.

Data synthesis plan

If suitable data are available, we will conduct meta-analyses for each comparison following the guidelines in the Cochrane Handbook for Systematic Reviews of Interventions, using a random-effects meta-analysis for the primary analysis. We will also carry out proportion meta-analyses to summarize frequencies from single-sample studies. Data analysis will be performed in R statistical software [53], primarily using the Meta, Metafor, and Tidyverse packages [54]. We will calculate pooled hazard ratios, risk ratios, or odds ratios with a 95% confidence interval (CI) for dichotomous outcomes, and mean differences or standardized mean differences for continuous outcomes. For non-comparative studies, we will calculate proportions with a 95% CI. To report efficacy or effectiveness outcomes, we will convert other outcome measures to vaccine efficacy/effectiveness, when possible, by assessing the risk of disease in vaccinated versus unvaccinated individuals and calculating the percentage risk reduction. Adjusted effect measures (e.g., by age or region) will be prioritized over unadjusted estimates, and heterogeneity will be explored through subgroup analyses.

Subgroup analysis

We will perform the following prespecified subgroup analyses when analyzing the primary outcomes:

- Pre-specified subgroups by pregnancy trimester (first, second, or third trimester)
- Age range of pediatric participants (0–27 days, 28 days–1 y, 0–4 y, 5–11 y, 12–17 y). These age categories were selected based on commonly used pediatric age groups in vaccine research and policy, reflecting developmental stages and immunization schedules.
- Age range of adult participants
- Risk status for infection of the participants (low or high)
- LASV vaccine administered

- Vaccine platform
- Dominant LASV virus variants
- Study design

Sensitivity analysis

Additional sensitivity analyses will be undertaken by excluding high-risk bias studies or using the fixed-effect model.

Data visualization

We will utilize an online interactive dashboard for data visualization, employing Microsoft Power BI. The most relevant variables related to all study populations, including adults, pregnant individuals, infants and children, will be selected and displayed in figures and tables. Since this project is a living systematic review, the living meta-analysis section will be accessible to users as an interactive tool developed as a Shiny application developed using R Studio [55]. The application will enable users to display meta-analyses of interest by applying filters such as age, region, vaccine platform, vaccine doses, and comparators. Additionally, predefined subgroup analyses will be available for users to choose from. The research team will develop an algorithm to determine the endpoints for each study in the living meta-analysis. The researchers will conduct a validation to ensure the accuracy of the endpoint selection algorithm. The dashboard will be updated weekly following the biweekly literature searches, and their maintenance will be overseen by the core research team at the Instituto de Efectividad Clínica y Sanitaria (IECS).

Discussion

The proposed LSR aims to address critical knowledge gaps in the safety, efficacy, effectiveness, and immunogenicity of Lassa virus (LASV) vaccines, focusing on vulnerable populations such as pregnant persons, children, and adolescents. By leveraging a biweekly evidence search and an innovative methodology, this LSR is designed to provide timely updates as new studies emerge, ensuring that its findings remain relevant to public health decision-making. The use of an online interactive dashboard powered by Microsoft Power BI further enhances the accessibility and dissemination of findings, allowing stakeholders to visualize data and track updates in real-time. Similar approaches have proven effective during other outbreak settings, such as COVID- 19 [40], demonstrating the value of living reviews in rapidly evolving research contexts.

The comprehensive search strategy employed in this review minimizes the risk of missing relevant studies, thereby enhancing the reliability of its conclusions. Furthermore, adherence to PRISMA guidelines and the use of rigorous methodological tools, such as the grading of recommendations assessment, development, and evaluation (GRADE) approach, underscore the review's commitment to high-quality evidence synthesis. Incorporating data from diverse populations, including children, pregnant persons, and adults, ensures that the findings address the needs of groups most at risk of severe Lassa fever outcomes. While the heterogeneity of study designs and vaccine platforms presents a potential challenge, the use of subgroup and sensitivity analyses will help mitigate these issues and provide more nuanced insights.

This LSR has the potential to significantly impact global health by informing vaccine recommendations, guiding clinical trial designs, and shaping public health policies in Lassa fever-endemic regions. By offering a dynamic, continuously updated evidence base, it supports informed decision-making for LASV vaccine deployment and highlights the value of living systematic reviews in rapidly evolving research areas [56].

Abbreviations

AEs	Adverse Events
AESI	Adverse Events of Special Interest
CFR	Case Fatality Rate
CI	Confidence Interval
CRD	Cochrane Risk of Bias Tool
DrPH	Doctor of Public Health
GAIA	Global Alignment of Immunization Safety Assessment in Pregnancy
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HR	Hazard Ratio
IgG	Immunoglobulin G
IgM	Immunoglobulin M
KDIGO	Kidney Disease: Improving Global Outcomes
LASV	Lassa Virus
LF	Lassa Fever
LILACS	Latin American and Caribbean Health Sciences Literature
LSR	Living Systematic Review
MD	Mean Difference
MESH	Medical Subject Headings
NEWS2	National Early Warning Score 2
OR	Odds Ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
RCTs	Randomized Controlled Trials
REDCap	Research Electronic Data Capture
RoB2	Cochrane Risk of Bias Tool, Version 2
RR	Risk Ratio
SAEs	Serious Adverse Events
SMD	Standardized Mean Difference
SPEAC	Safety Platform for Emergency Vaccines
VE	Vaccine Efficacy/Effectiveness
WHO	World Health Organization

Author contributions

JB, MB, AC, JMS, KS, AM, AB, MB, DC, NC, EPKP, AS, XX, FMM and PMB contributed to the conception and design of this study.

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Availability of data and materials
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Ethical approval is not necessary for this systematic review and meta-analysis that utilizes published data or data in the public domain. The findings from the systematic review and living meta-analysis will be shared widely through the online dashboards mentioned earlier. Additionally, one or more manuscripts summarizing findings will be submitted to a prominent peer-reviewed journal in this area, following the PRISMA statement/extension guidelines for reporting living systematic reviews.

Consent for publication
Not applicable. This study does not involve individual patient data or identifiable personal information requiring consent for publication.

Competing interests
The authors declare no competing interests.

Author details
[1]Instituto de Efectividad Clínica y Sanitaria (IECS-CONICET), Dr. Emilio Ravignani 2024 (C1414 CPV), Buenos Aires, Argentina. [2]Department for Infectious Disease Epidemiology and International Health, London School of Hygiene and Tropical Medicine, London WC1E 7HT, UK. [3]School of Pharmacy and School of Public Health, University of Washington, Seattle, WA, USA. [4]Celia Scott Weatherhead School of Public Health and Tropical Medicine, Tulane University, New Orleans, LA, USA. [5]Baylor College of Medicine, Texas Children's Hospital, 6621 Fannin St, Houston, TX 77030, USA.

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