Health-economic impacts of age-targeted and sex-targeted Lassa fever vaccination in endemic regions of Nigeria, Guinea, Liberia, and Sierra Leone: a modelling study

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Summary

Background Lassa fever is an emerging zoonotic disease endemic to west Africa. Several vaccines aimed at preventing Lassa fever are currently under development, creating a need to assess how best to administer them once licensed for human use. We aimed to project the health-economic burden of Lassa fever from 2025 to 2037 across age and sex groups in subnational administrative divisions of west Africa with endemic *Lassa mammarenavirus* transmission and to estimate the cost-effectiveness of targeting Lassa vaccination to different risk groups.

Methods In this vaccine-impact modelling study, we developed a mathematical model using a zoonosis risk map and epidemiological data from recent and ongoing cohort studies to predict the health-economic burden of Lassa fever across age and sex groups in endemic regions. We simulated vaccination campaigns targeting different risk groups to estimate the cost-effectiveness of various strategies for Lassa vaccine administration. Threshold vaccine costs (TVCs), which represent the break-even price per dose of vaccine administered, were estimated in international dollars (INT$ 2023), accounting for health-care costs, productivity losses, and monetised disability-adjusted life-years (DALYs) averted by vaccination.

Findings Lassa fever was estimated to cause 6·23 (95% uncertainty interval (UI) 4·21–8·42) hospitalisations, 0·75 (0·48–1·10) deaths and 31·1 (17·7–52·2) DALYs per 100 000 person-years. Vaccine strategies targeting adolescents–adults aged 15–49, older adults aged 50 years and older, and women of childbearing age (WCBA) aged 15–49 years prevented, respectively, the most hospitalisations, deaths, and DALYs per 100 000 vaccine doses. Under base case assumptions, the most cost-effective strategy (greatest net monetary benefit) was untargeted vaccination for a vaccine costing INT$2 per dose, and targeting adolescents–adults at $5 per dose. At $10 per dose or more, none of the considered strategies were cost-effective. The highest TVC for a single-dose vaccine was estimated at $7·39 (95% UI 4·33–11·60) when targeting adolescents–adults, followed by $6·69 (4·17–9·85) when targeting older adults, $6·10 (3·56–9·74) when targeting WCBA, and $1·94 (1·10–3·10) when targeting children.

Interpretation Targeting of adolescents–adults appears to generate the greatest health-economic value per vaccine dose. However, the most cost-effective vaccination strategy will depend on vaccine price.

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Introduction

Lassa fever is an emerging viral haemorrhagic disease caused by *Lassa mammarenavirus* (LASV). LASV is endemic to west Africa and phylogenetic data support that most human infections result from zoonotic transmission (so-called spillover) from the Natal multimammate mouse, *Mastomys natalensis*.[1–3] Millions of LASV spillovers are estimated to occur annually throughout west Africa,[4,5] and although most human infections remain asymptomatic or cause only mild febrile illness,[6] burden estimates suggest that Lassa fever causes approximately 24 000 hospitalisations and 4000 deaths annually throughout the region.[7]

Although no vaccines against Lassa fever are currently licensed, enrolment in the first phase 2 clinical trial of a Lassa vaccine began in 2024 and several other vaccines are in development,[8–11] highlighting a pressing need to assess how best to use a Lassa vaccine once licensed for human use. A recent study estimated that untargeted, population-wide preventive Lassa vaccination campaigns probably require a low vaccine price to be cost-effective at willingness-to-pay thresholds that reflect health-care spending opportunity costs in endemic areas.[7,12]

To maximise cost-effectiveness, most vaccines included in national immunisation programmes preferentially target higher-risk groups. However, although children appear to be at highest risk of LASV infection,[13] most hospitalised patients are middle-aged adults,[14] mortality risk is estimated to increase with age,[15] and pregnant

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Research in context

Evidence before this study

Lassa fever is a common but widely under-reported emerging zoonotic disease endemic to west Africa. At least four Lassa vaccine candidates have entered clinical trials. We searched PubMed and preprint archives MedRxiv and BioRxiv up to March 31, 2025, for journal articles using the search terms ("LASV" OR "Lassa") AND "vaccin*" AND ("burden" OR "health-econ*" OR "econ*" OR "projection") without data or language restrictions. Several articles address Lassa vaccine candidates currently in development, including laboratory studies, experiments in animal models, and one first-in-human phase 1 clinical trial. Reviews and editorials discuss extensive gaps in Lassa fever surveillance, recent efforts to scale up vaccine investment and challenges in designing efficient vaccination campaigns. Only our previous study has attempted to estimate the potential impacts of Lassa vaccination on population health or economies, suggesting that population-wide preventive vaccination is more cost-efficient than reactive outbreak response vaccination. However, estimates of Lassa fever burden in specific population groups are needed to inform target prioritisation and predict the health and economic benefits of different possible vaccine allocation strategies.

Added value of this study

We synthesised data from a *Lassa mammarenavirus* (LASV) zoonosis risk map and recent and ongoing prospective cohort studies in Lassa-endemic regions to provide the first estimates of the health-economic burden of Lassa fever stratified by age, sex, and pregnancy status. We then simulated the introduction of a novel Lassa vaccine administered preventively among the general population in areas of Nigeria, Guinea, Liberia, and Sierra Leone identified as having endemic LASV transmission. We assessed a series of age-targeted and sex-targeted vaccination campaigns, in addition to untargeted vaccination, and estimated projected impacts of these campaigns on health outcomes across different population groups. We estimated the economic benefits of vaccination under various scenarios and calculated incremental cost-effectiveness ratios and net monetary benefit across a range of hypothetical vaccine costs. We also calculated threshold vaccine costs, which describe the threshold price per dose at which vaccination is estimated to become a cost-effective investment. These costs were estimated from a modified societal perspective accounting for health-care costs and impacts of morbidity and mortality on economic productivity and disability-adjusted life-years.

Implications of all the available evidence

The benefits of vaccination are predicted to vary greatly across target groups owing to the group-specific risks of different Lassa fever outcomes, including hospitalisation, death, post-acute hearing loss, and fetal and neonatal demise. Children bore the greatest infection burden but were by far the least cost-effective target. Untargeted vaccination was estimated to be the most cost-effective strategy for a low-cost vaccine (international dollars [INT$]; INT$2 per dose), whereas targeting adolescents–adults aged 15–49 years was the most cost-effective strategy at $5 per dose. However, at $10 per dose or more, none of the considered vaccine strategies were cost-effective. Across a range of scenarios and sensitivity analyses, threshold vaccine costs were highest when targeting adolescents–adults, suggesting that prioritising this group is probably the most cost-effective strategy for allocating a low number of doses, offering the greatest health-economic returns per dose of vaccine administered. However, the most cost-effective target group could vary if vaccine efficacy were to vary across age groups or provide protection against particular Lassa fever outcomes, such as hearing loss or neonatal demise, more than others. Vaccine efficacy assumptions underlying these results are hypothetical, because, to date, no vaccine efficacy estimates are available and no correlates of protection have been identified for any Lassa vaccine candidates. Monitoring Lassa vaccine efficacy against different Lassa fever outcomes and in different population groups in clinical trials will therefore be crucial to inform future decision making around target prioritisation.

women bear particularly high risks of mortality and fetal and neonatal demise.[16] Such risk heterogeneity makes it unclear who to target for greatest returns on vaccine programme investment, and no studies to date have assessed how vaccine impact could vary across risk groups—a crucial consideration for forthcoming Lassa vaccination programmes.

In this vaccine impact modelling study, we aimed to project the health-economic burden of Lassa fever from 2025 to 2037 across age and sex groups in subnational administrative divisions of west Africa with endemic LASV transmission and to estimate the cost-effectiveness of targeting Lassa vaccination to different risk groups, including children aged 2–14 years, women of childbearing age (WCBA) aged 15–49 years, all adolescents and adults aged 15–49 years, and older adults aged 50 years and older.

See **Online** for appendix

Methods

Model overview

We previously developed a mathematical model that predicts human Lassa fever burden throughout west Africa.[7] Here, this model was extended to characterise Lassa fever risk across age and sex groups, and to estimate the cost-effectiveness of conducting risk-targeted Lassa vaccination campaigns in areas with endemic LASV transmission. The spillover incidence map underlying the model's infection projections is shown in figure 1 and an illustrated model schematic is provided in the appendix (p 2).

Following WHO's Lassa fever risk map from March, 2024, endemic areas were defined as the 19 first-level subnational administrative units (eg, states in Nigeria) reporting at least five Lassa fever cases annually.[17]

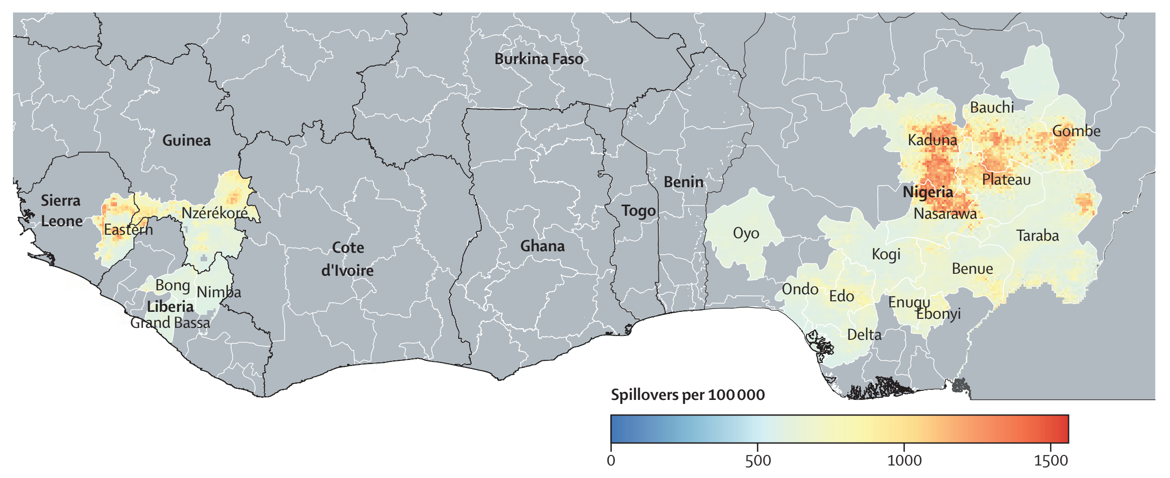

Figure 1: **Estimated incidence of zoonotic Lassa virus infection (spillover) per 100 000 population in 2019 at the level of 0·05° × 0·05° grid cells in the 19 areas classified as endemic by use of WHO's 2024 Lassa fever risk map**

Zoonosis incidence was predicted by Smith and colleagues,[7] building on a geospatial risk map from Basinski and colleagues.[5] Although the incidence estimates shown here exclude areas not classified as endemic, they result from region-wide geospatial estimation that borrows data across the whole of west Africa.

Population sizes and their distributions by age, sex, and pregnancy status from 2025 to 2037 were defined by use of UN World Population Prospects and geospatial population estimates from WorldPop (appendix pp 2–5).[18–20]

Ethical approval was not necessary as this study relied on publicly available data. The study team included Lassa fever researchers from endemic countries who contributed expert opinion on the interpretation of data, feedback on interim results, and insights into vaccine scenarios.

Data sources

Our previous work estimated 710 (95% UI 671–750) LASV spillover infections per 100 000 population across these 19 areas in 2019 (appendix p 6).[7] Here, data from the ongoing Enable cohort study were harnessed to adjust these estimates to account for age-specific spillover risk.[21] A Bayesian serocatalytic model was fitted to age-stratified seroprevalence data from Enable's interim results to estimate the force of infection and proportion of human LASV infections occurring across age groups (appendix pp 6–8).[13] Age-specific incidence in 2019 was multiplied by annual population projections to project forward in time. To account for seasonality, national-level Nigeria Centre for Disease Control and Prevention (NCDC) case data were used to distribute LASV infections at the weekly level, accounting for Lassa fever's incubation period and lags to case reporting (appendix p 9).

A previous estimate that 19·3% (95% UI 10·2–32·7) of infections coincide with symptoms (of any severity) was used, assuming no association with age or sex.[6,7] In a sensitivity analysis, symptom risk was assumed to increase with age (appendix p 10). Age-specific and sex-specific risk of severe Lassa fever and hospitalisation were calculated by scaling a previous infection-hospitalisation risk estimate by use of laboratory-confirmed hospital case data from the NCDC (appendix p 11).[7,14]

Among hospitalised cases, age-specific case-fatality risk was estimated with data from two arms of the LASCOPE study (appendix pp 11–13).[15,22] Increased risk of death in pregnant women relative to non-pregnant women was accounted for,[16] while maintaining stable overall age-specific case-fatality risk in men and women, as reported in LASCOPE (appendix pp 12–13).[15] Previous meta-analyses were augmented with data from LASCOPE to estimate the proportion of pregnant women hospitalised with Lassa fever who lose their fetus or have neonatal loss (appendix pp 14–15).[15,16,22] Final risk estimates stratified by age and sex are provided in the appendix (p 14).

Sensorineural hearing loss (SNHL) is a common sequela of Lassa fever, which tends to occur suddenly during convalescence.[23] Individual patient-level data from a prospective cohort study were used to quantify SNHL risk, duration and associated disability (appendix pp 16–19).[24] Available literature suggests that post-acute SNHL is not limited to severe cases or strongly associated with age or sex,[23,24] so SNHL risk was applied to anyone surviving symptomatic disease, but in sensitivity analysis was limited only to those surviving hospitalisation.

Vaccine characteristics followed WHO's target product profile for a Lassa vaccine.[25] These include a one-dose schedule and a 2-week delay to immunological response, after which the recipient acquires 10 years of partial protection from disease and its downstream health-economic consequences (appendix pp 20–22). A sensitivity analysis was included considering a vaccine eliciting a 5-year immunological response (appendix p 22). No estimates of vaccine efficacy are available and no correlates of protection have been identified among Lassa vaccines that have undergone assessment in clinical trials, so hypothetical vaccine efficacy assumptions were made. In the base case analysis, a vaccine was 70% effective against all symptomatic disease, but efficacies of 50%, and 90% were considered and scenarios with greater vaccine efficacy against severe disease than moderate disease were included. There was assumed to be no association between vaccination uptake and infection risk or serostatus and no vaccine adverse effects were considered.

A range of preventive vaccination campaigns were simulated in four target groups living in Lassa-endemic areas: children aged 2–14 years, WCBA aged 15–49 years, all adolescents–adults aged 15–49 years, and older adults aged 50 years and older (appendix pp 20–21). Untargeted vaccination administered to all individuals aged at least 2 years was also evaluated. Campaigns were designed as 3-year mass vaccination programmes with doses administered seasonally to align with periods of reduced LASV transmission (April 1 to Oct 31, from 2025 to 2027). Each year, campaigns covered 25% of individuals throughout the age range of the target group, reaching 75% coverage after 3 years with an excess 10% of doses added annually to account for wastage. The remaining model parameters are detailed in the appendix (pp 22–23).

Outcomes

Our model was used to predict baseline health-economic outcomes in the absence of vaccination (comparator), and outcomes occurring in vaccinated individuals, averted proportionally to vaccine efficacy (intervention). Final outcomes in each area are aggregated at the level of sex, pregnancy status, and age group, reported both annually and as cumulative totals over the full model horizon (2025–37). Detailed model outcome calculations are described in the appendix (pp 24–32).

Health outcomes include: zoonotic LASV infections; cases of Lassa fever; defined as reported or unreported symptomatic LASV infections and stratified into moderate cases or severe cases; Lassa fever hospitalisations; Lassa fever deaths (including neonatal deaths); fetal losses; cases of SNHL among Lassa fever survivors; and disability-adjusted life-years (DALYs).

Economic outcomes include: health-care costs, stratified by setting (outpatient or inpatient) and payer (government-reimbursed or out-of-pocket); instances of catastrophic health-care expenditure or impoverishing health-care expenditure resulting from out-of-pocket health-care costs; productivity losses due to reduced labour force participation because of acute symptomatic disease, SNHL, or death (calculated by use of a human capital approach; see appendix pp 29–31); monetised DALYs, quantified by use of country-specific health opportunity costs;[12] and the monetised value of life lost and life-years lost, calculated, respectively, by use of value of statistical life and value of statistical life-years approaches.

For **Model** see www.github.com/drmsmith/lassaRiskVac

Statistical analysis

Model outputs were used in a health-economic evaluation to estimate the cost-effectiveness of vaccination campaigns against a usual care alternative. This analysis was done assuming a modified societal perspective, in which societal costs are presented as the sum of health-care costs, productivity losses and monetised DALYs attributed to Lassa fever, and the total economic benefit of vaccination as the societal costs averted by vaccine. Five hypothetical vaccine programme costs were considered (international dollars [INT$]; INT$2, $5, $10, $20, or $50 per dose), implicitly covering all administration costs and potential productivity losses associated with vaccination. Incremental cost-effectiveness ratios were calculated along the efficiency frontier as the incremental change in costs (combined vaccine programme costs, health-care costs, and productivity losses) per additional DALY averted. Net monetary benefit was calculated for each vaccination campaign as the total economic benefit of vaccination minus total vaccine programme costs. Threshold vaccine costs (TVCs) were defined as the price per vaccine dose at which the benefit-to-cost ratio equals one, calculated as the total economic benefit of vaccination divided by the number of doses administered. In the base case analysis, TVCs were calculated by use of societal costs, but monetised life-years lost (the value of statistical life-years approach) was used instead in sensitivity analysis. Finally, cost-effectiveness acceptability curves were generated to evaluate how cost-effectiveness varies depending on variable willingness-to-pay thresholds. Costs beyond the first year of the study horizon (2025) are discounted at 3·5% annually, or 0% in sensitivity analysis. Monetary outcomes are reported in international dollars (INT$) 2023.

Probabilistic sensitivity analysis was done by use of Monte Carlo simulations to randomly draw input parameters from estimated distributions for 500 model runs, including: area-level zoonosis incidence rates; age-stratified LASV seroprevalence and force of infection; and the probabilities, durations, and disability weights associated with different health states. All outcomes are reported as means and 95% uncertainty intervals (95% UIs) of outcome distributions across all probabilistic sensitivity analysis runs. Partial rank correlation coefficients were calculated to assess the impacts of input parameter uncertainty on outcome uncertainty. Burden estimates are reported following the GATHER statement (appendix pp 32–33). Health-economic analyses are reported following the CHEERS statement (appendix pp 34–35).

All analyses were run with R version 4.3.0.

Role of the funding source

The Coalition for Epidemic Preparedness Innovations (CEPI) commissioned this analysis. Internal Lassa fever experts were involved in study design by providing knowledge on input parameters and vaccine administration. An earlier version of this work was provided as a report to CEPI.

Results

From 2025 to 2037 in the 19 included endemic areas, our model predicted a cumulative 8·68 million (95% UI 8·19 million–9·15 million) human LASV infections. Growing populations in endemic regions coupled with our assumption of stable annual transmission risk from the rodent host translated to gradually increasing LASV infections year-over-year, from 609 000 (575 000–643 000) in 2025 to 724 000 (683 000–763 000) in 2037 (figure 2). In the absence of vaccination, these infections led to a substantial health burden, resulting in a cumulative 401 000 (228 000–672 000) DALYs (table 1).

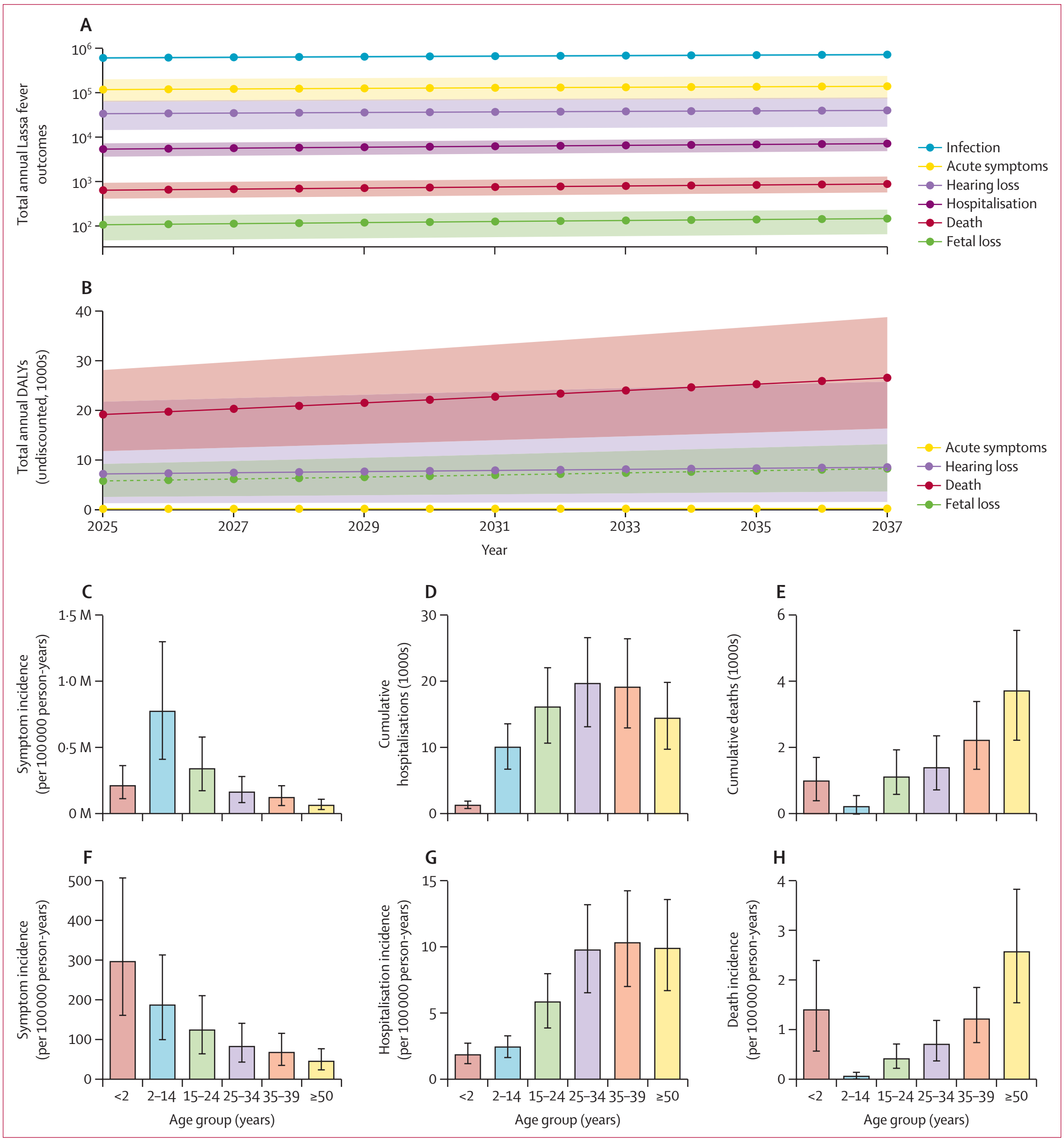

Figure 2: **Projected burden of Lassa fever from 2025 to 2037 in the absence of vaccination and associations with age under base case assumptions**
(A) Change over time in the annual number of infection outcomes (log scale). Acute symptoms refers to all symptomatic cases. (B) Change over time in annual DALYs associated with Lassa fever; DALYs due to acute symptoms combine those due to moderate disease and severe disease; DALYs due to fetal loss (dashed line) are only included in the sensitivity analysis. (C) The cumulative total number of symptomatic cases, stratified by age group. (D) The cumulative total number of Lassa fever hospitalisations, stratified by age group. (E) The cumulative total number of Lassa fever deaths, stratified by age group. (F) The cumulative incidence of symptomatic cases per 100 000 person-years, stratified by age group. (G) The cumulative incidence of Lassa fever hospitalisation per 100 000 person-years, stratified by age group. (H) The cumulative incidence of Lassa fever death per 100 000 person-years, stratified by age group. In panels A and B, lines represent means and shading represents 95% uncertainty intervals (UIs). In panels C through to G, bar heights represent means and error bars represent 95% UIs. Neonatal deaths occurring subsequent to maternal Lassa fever are counted as deaths in children younger than 2 years. Fetal losses are not counted as deaths. DALYs=disability-adjusted life-years.

The cumulative economic burden of Lassa fever in terms of societal costs—the sum of health-care costs, productivity losses and monetised DALYs—was estimated at $923 million (95% UI 555 million–1·42 billion). An alternative measure of Lassa fever's economic burden, the monetised value of life-years lost by use of a value of statistical life-years approach, was estimated at $2·76 billion (1·75 billion–4·16 billion). Inpatient treatment costs far outnumbered outpatient treatment costs, and Lassa fever deaths were responsible for the majority of productivity losses and monetised DALYs (appendix p 39). However, hearing loss, which in our base

	Cumulative totals	Cumulative totals per 100 000 person-years
Health burden		
Lassa virus infection	8·68 million (8·19 million–9·15 million)	674 (636–711)
Symptomatic cases	1·67 million (884 000–2·86 million)	130 (68·6–222)
Hospitalisation	80 300 (54 200–108 000)	6·23 (4·21–8·42)
Sensorineural hearing loss	477 000 (204 000–933 000)	37·1 (15·8–72·4)
Death	9660 (6220–14 200)	0·75 (0·48–1·10)
Fetal loss	1600 (710–2560)	0·12 (0·06–0·20)
DALYs	401 000 (228 000–672 000)	31·1 (17·7–52·2)
Economic burden		
Health-care costs, INT$ 2023	177 million (116 million–247 million)	13 700 (8990–19 200)
Catastrophic health-care expenditure	80 100 (54 100–108 000)	6·22 (4·20–8·40)
Impoverishing health-care expenditure	47 400 (32 000–64 000)	3·68 (2·49–4·97)
Productivity losses, INT$ 2023	706 million (402 million–1140 million)	54 900 (31 200–88 400)
Monetised DALYs, INT$ 2023	39·9 million (21·9 million–74·2 million)	3100 (1700–5760)
Monetised value of life lost, value of statistical life approach, INT$ 2023	2·53 billion (1·63 billion–3·74 billion)	197 000 (127 000–291 000)
Monetised value of life-years lost, value of statistical life-years approach, INT$ 2023	2·76 billion (1·75 billion–4·16 billion)	215 000 (136 000–323 000)

Data are n (uncertainty intervals), unless stated otherwise. Symptomatic cases include both moderate and severe symptomatic infections. DALYs=disability-adjusted life-years. INT$=International dollar.

Table 1: **Projected mean (95% uncertainty interval) cumulative total health and economic burden of Lassa fever from 2025 to 2037 in the absence of vaccination under base case assumptions**

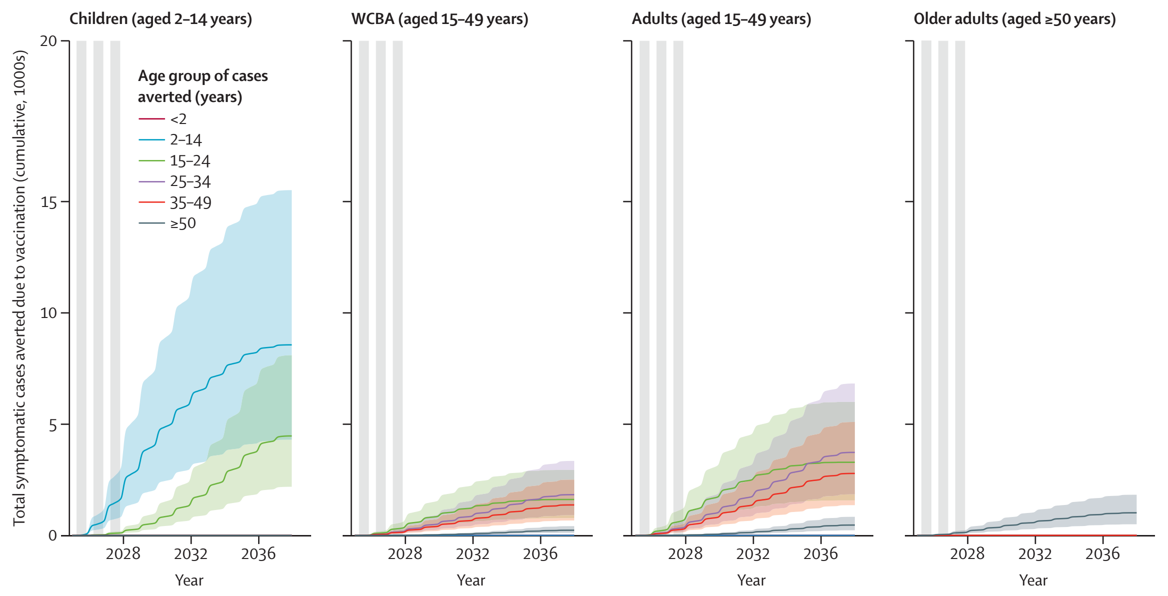

Figure 3**: Evolution of age-specific vaccine impacts through time**

The weekly total cumulative number of symptomatic Lassa fever cases in different age groups (colours) averted by vaccination in one exemplar area (Edo, Nigeria) from Jan 1, 2025, to Dec 31, 2037. Grey vertical bars indicate periods of Lassa vaccine distribution and panels compare results when targeting different groups for vaccination. Thick lines and shaded areas represent means and 95% uncertainty intervals, respectively, for a one-dose vaccine 70% effective against all symptomatic disease and eliciting an immunological response lasting 10 years (base case assumptions). The adults target group includes adolescents and adults. WCBA=women of childbearing age.

case analysis was assumed to result from 29% of symptomatic cases, made major contributions to productivity losses (25%) and monetised DALYs (37%).

The projected burden of Lassa fever varied greatly across age groups (figure 2). Annual LASV infection incidence per 100 000 population decreased with age, from 1540 (95% UI 1320–1770) in children younger than 2 years to 232 (207–255) in those aged 50 years and older (appendix p 36). Children aged 2–14 years experienced nearly half (46%) of all infections (appendix p 37). In contrast to the highest infection burden in the youngest age groups, middle-aged adults accounted for the most hospitalisations, whereas older adults accounted for the most deaths. Pregnant women accounted for 2·1% of symptomatic cases but a disproportionally large share (5·6%) of deaths (appendix p 37). Children younger than 2 years were second only to adults aged 50 years and older in terms of mortality risk per person-year. Total DALYs were similar across age groups but DALYs per 100 000 person-years were greatest in children younger than 2 years (appendix p 38).

Modelled vaccination campaigns were implemented seasonally over a 3-year period, resulting in heterogeneous vaccine impacts through time (figure 3; appendix pp 40–43). Targeting of children aged 2–14 years averted the most symptomatic cases, whereas targeting of adolescents–adults aged 15–49 years averted the most hospitalisations, deaths, and DALYs (figure 4; appendix p 44). However, these two groups required the most vaccine doses (appendix p 20). When accounting for vaccine benefits relative to the number of doses administered, the most efficient strategy for preventing symptomatic disease was targeting children aged 2–14 years, for preventing hospitalisations was targeting adolescents–adults, for preventing deaths was targeting older adults aged 50 years and older, and for preventing DALYs was targeting WCBA (figure 4). In contrast to targeted vaccination (appendix pp 45–46), for untargeted vaccination the age distributions of vaccine benefits resembled the underlying age

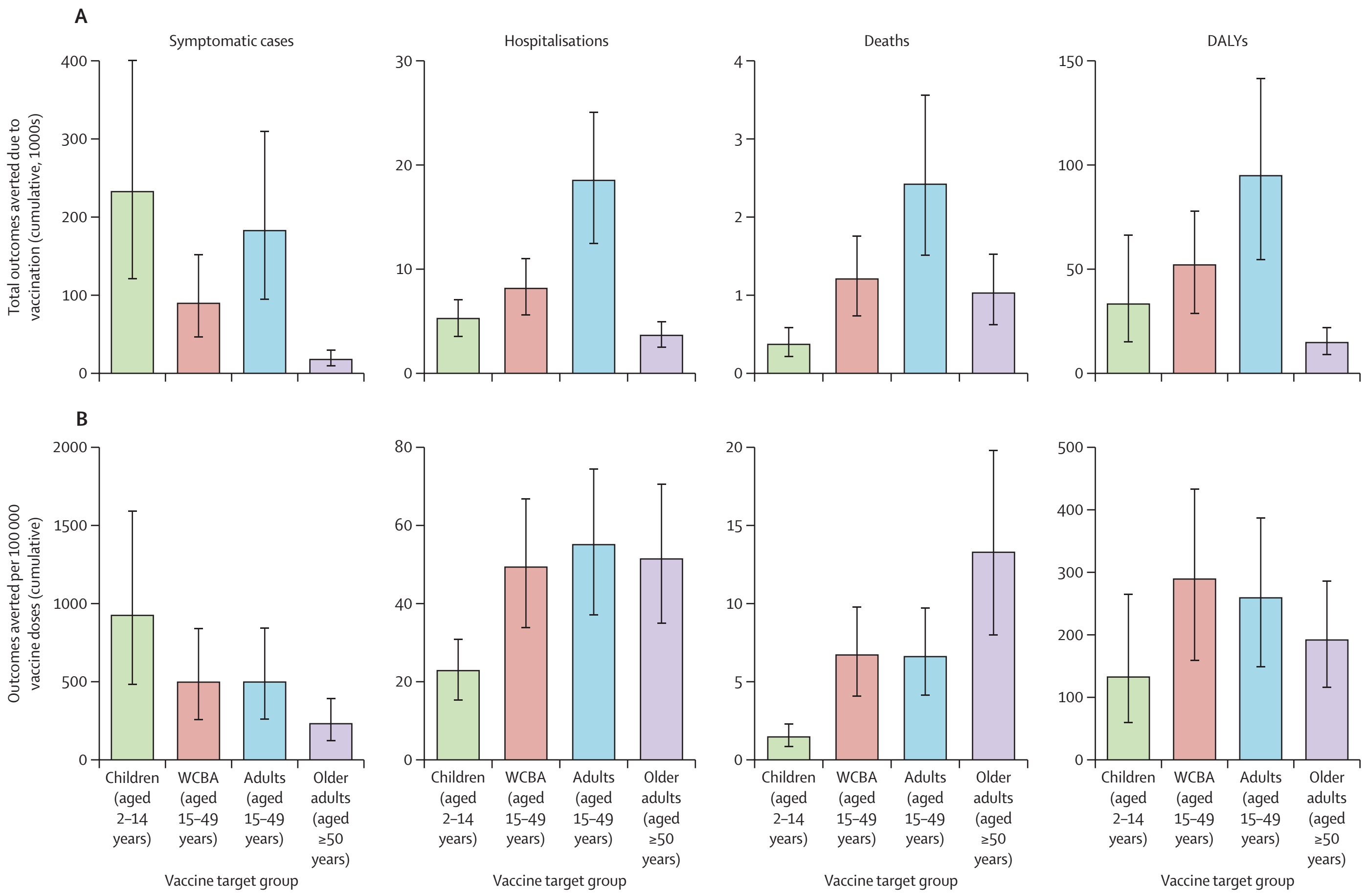

Figure 4: **Comparing the cumulative health impacts and efficiencies of targeting different risk groups for vaccination with a one-dose Lassa fever vaccine having 70% efficacy against all symptomatic disease and an immunological response lasting 10 years (base case assumptions)**

(A) Impact: cumulative total health outcomes averted by vaccination across all 19 areas from 2025 to 2037. (B) Efficiency: cumulative total health outcomes averted per 100 000 doses of vaccine administered. DALYs exclude fetal loss. Bar heights represent means. Error bars represent 95% uncertainty intervals. The adults target group includes adolescents and adults. DALYs=disability-adjusted life-years. WCBA=women of childbearing age.

	Children (aged 2–14 years)	Women of childbearing age (aged 15–49 years)	Adolescents and adults (aged 15–49 years)	Older adults (aged 50 years and older)	All (older than 2 years)
Net monetary benefit, INT$ 2023					
$2*	−1·51 million (−22·0 million to 26·8 million)	71·6 million (27·2 million to 135 million)	191 million (82·7 million to 340 million)	35·3 million (16·3 million to 59·0 million)	225 million (79·7 million to 419 million)
$5*	−74·6 million (−95·0 million to −46·2 million)	19·3 million (−25·2 million to 82·6 million)	84·8 million (−23·7 million to 234 million)	12·7 million (−6·23 million to 36·5 million)	22·9 million (−122 million to 217 million)
$10*	−196 million (−217 million to −168 million)	−68·0 million (−112 million to −4·59 million)	−92·5 million (−201 million to 56·5 million)	−24·8 million (−43·8 million to −1·10 million)	−314 million (−459 million to −119 million)
$20*	−440 million (−460 million to −412 million)	−242 million (−287 million to −179 million)	−447 million (−555 million to −298 million)	−100 million (−119 million to −76·3 million)	−987 million (−1130 million to −792 million)
$50*	−1·17 billion (−1·19 billion to −1·14 billion)	−766 million (−810 million to −702 million)	−1·51 billion (−1·62 billion to −1·36 billion)	−326 million (−344 million to −302 million)	−3·01 billion (−3·15 billion to −2·81 billion)
Threshold vaccine cost, INT$ 2023					
Break-even cost	1·94 (1·10 to 3·10)	6·10 (3·56 to 9·74)	7·39 (4·33 to 11·60)	6·69 (4·17 to 9·85)	5·34 (3·18 to 8·23)

Data are n (uncertainty intervals). Net monetary benefit is calculated using a range of hypothetical costs per dose of vaccine administered and represents the difference between the total costs and benefits of each vaccination campaign. Threshold vaccine costs correspond to the break-even cost, representing the projected economic return per dose of vaccine administered, considering a modified societal perspective including health-care costs, productivity losses, and monetised disability-adjusted life-years. Results for sensitivity analyses are shown in the appendix (pp 63–66). *Cost per vaccine dose, INT$ 2023. INT$=international dollar.

Table 2: **Estimated mean (95% uncertainty interval) health-economic outcomes across vaccine target groups under base case assumptions**

distributions of disease (appendix p 47). Projected vaccine impacts depended importantly on vaccine efficacy assumptions (appendix pp 48–49).

The economic benefits of targeted vaccination campaigns were always greatest when targeting adolescents–adults, under base case assumptions preventing $253 million (95% UI 148 million–396 million) in societal costs (appendix pp 52–54). However, the most economically cost-efficient strategy again depended on the outcome considered (appendix pp 50–51). Targeting of adolescents–adults was most efficient in terms of health-care costs and productivity losses, whereas targeting of WCBA was most efficient in terms of monetised DALYs and monetised life-years. Targeting of children was by a considerable margin the least efficient strategy across all economic outcomes considered.

The most cost-effective strategy (greatest net monetary benefit) under base case assumptions was untargeted vaccination given a vaccine costing $2 per dose, targeting adolescents–adults at $5 per dose, and no vaccination at $10 per dose or more (table 2). Incremental cost-effectiveness ratios varied substantially depending on the cost per vaccine dose (appendix p 55), but the order of vaccine strategies along the efficiency frontier was largely consistent across sensitivity analyses (appendix pp 56–62). Cost-effectiveness planes are shown in the appendix (pp 67–74). Cost-effectiveness results were consistent across sensitivity analyses, with two exceptions: when not discounting future costs, untargeted vaccination and targeting of adolescents–adults were equally cost-effective at $5 per dose, whereas targeting of adolescents–adults was the most cost-effective strategy at $10 per dose; and for a vaccine eliciting a 5-year instead of a 10-year immune response, targeting of adolescents–adults was most cost-effective at $2 per dose, whereas no vaccination was most cost-effective at $5 per dose or more (appendix pp 63–64). Net monetary benefit was calculated by use of estimated country-specific willingness-to-pay thresholds (appendix p 24), but cost-effectiveness acceptability curves show how cost-effectiveness could vary if assuming alternative thresholds (appendix pp 75–82).

The highest TVC for a single-dose vaccine was estimated at $7·39 (95% UI 4·33–11·60) when targeting adolescents–adults, followed by $6·69 (4·17–9·85) when targeting older adults, $6·10 (3·56–9·74) when targeting WCBA, $5·34 (3·18–8·23) for untargeted vaccination and $1·94 (1·10–3·10) when targeting children (table 2). This order of vaccine target groups by TVC was robust to sensitivity analyses with four exceptions: older adults aged 50 years and older yielded the highest TVCs if SNHL is assumed only to occur after severe disease; or for a vaccine eliciting a 5-year immune response; WCBA yielded second instead of third-highest TVCs if not discounting future costs; and if considering averted monetised life-years lost instead of averted societal costs as the metric of vaccine benefit, TVCs were highest when targeting WCBA (appendix pp 65–66).

Discussion

This study projected the burden of Lassa fever in endemic regions of west Africa from 2025 to 2037 and estimated the health-economic benefits and cost-effectiveness of targeting Lassa vaccination to different groups on the basis of age and sex. Benefits of vaccination varied greatly across target groups, reflecting heterogeneity in underlying risk. Targeting adolescents and adults regardless of sex was the most efficient strategy for preventing health-care costs and productivity losses, whereas targeting WCBA was most efficient for preventing DALYs and monetised life-year losses. Children bore the greatest infection burden but were by far the least cost-effective target owing to their low estimated risks of severe disease and death on infection. Across a range of scenarios and sensitivity analyses, TVCs were highest when targeting adolescents and adults aged 15–49 years, suggesting that, from a societal perspective, prioritising this group would lead to the greatest health-economic returns per dose of vaccine administered. However, the cost-effectiveness of any forthcoming Lassa fever vaccination campaigns will ultimately depend on vaccine price, estimates of which are not currently available. Furthermore, the most cost-effective target group could vary if vaccine efficacy were to vary across risk groups, for instance if vaccine-induced immune responses vary with age or provide protection against particular outcomes, such as hearing loss or neonatal demise, more than others. Monitoring vaccine efficacy against different outcomes across population groups in clinical trials will therefore be crucial to inform future decision-making around target prioritisation.

We synthesised data from several recent and ongoing prospective cohort studies to estimate Lassa fever risk across age and sex groups. Interim results from the Enable study provided an opportunity to estimate age-specific infection risk,[13,21] whereas data from the LASCOPE study in Nigeria,[15] including new results from the paediatric cohort,[22] provided further opportunities to characterise age-specific and sex-specific risks. We also accounted for aspects of Lassa fever's health-economic burden not considered previously, including data-driven characterisation of the risk, duration, quality-of-life impacts, and economic consequences of post-acute SNHL.[24]

Lassa fever is concentrated in areas that face a challenging burden of many diseases,[26] and there are opportunity costs to investing in Lassa vaccination in lieu of alternative interventions. Estimates of vaccine programme cost-effectiveness are therefore crucial to guide Lassa vaccine investment decisions. Under base case assumptions, TVC estimates ranged from $1·94 per dose to $7·39 per dose, suggesting that per-dose returns on investment could vary by nearly four-fold across the considered vaccination strategies, highlighting the importance of well targeted vaccine administration for optimal health-care resource allocation. The TVC for untargeted vaccination ($5·34 per dose) was about 32% higher than our previous estimate for a population-wide campaign in endemic areas under similar vaccine efficacy assumptions ($2·03 for a 2-dose schedule, translating to approximately $4·06 for a one-dose schedule), which had a shorter time horizon and did not account for future productivity losses owing to SNHL.[7]

Some elements of Lassa fever's burden remain poorly characterised. Data describing mild or moderate disease and post-acute sequelae are particularly scarce.[27] Three parameters that contributed most to economic outcome uncertainty were symptomatic disease risk, SNHL risk, and SNHL duration (appendix p 83). We did sensitivity analyses around these parameters. Accounting for an alternative age structure in moderate disease risk did not affect which vaccination strategies were most cost-effective. However, when SNHL risk was limited to only severe cases, targeting older adults aged 50 years and older led to the greatest TVC. Further, mean DALY incidence increased from 31 DALYs per 100 000 person-years to 38 DALYs per 100 000 person-years in a sensitivity analysis including fetal loss DALYs, which assumed each lost foetus would have lived to life expectancy at birth, thereby representing an upper bound to potential fetal loss DALYs.[28] Despite these uncertainties, our main conclusions regarding vaccine cost-effectiveness were largely robust to sensitivity analyses. However, our estimates might nonetheless be conservative, as costs were limited to health-care resource use, lost economic productivity and reduced health-related quality of life. Owing to data limitations, it was not possible to consider potential additional costs, such as those related to informal caregiving or transportation, although these are probably of secondary importance relative to the costs captured in our analysis.

Two remaining uncertainties relate to the previously reported zoonosis risk map used to estimate LASV incidence.[5,7] First, distinct LASV lineages were not explicitly accounted for, although there is a suggestion of variable disease severity across regions.[29] It is unclear whether age-specific and sex-specific risks of hospitalisation and death, quantified here with Nigerian data, differ in Guinea, Liberia, or Sierra Leone. Although potential differences are unlikely to influence our conclusions, as more than 90% of predicted infections occurred in Nigeria, vaccine target prioritisation decisions in the Mano River region should nonetheless take local epidemiological patterns into account. Similarly, our use of pooled seroprevalence data to characterise infection risk by age group throughout Lassa fever's endemic range could mask true spatial heterogeneity in age-specific risk.

Second, although we propagate incidence uncertainty throughout our simulations, the map's predictive accuracy is difficult to validate. However, another, more recent, bottom-up geospatial modelling study provides an opportunity for comparison. Across 19 endemic areas, we estimated 130 (95% UI 69–222) symptomatic cases per 100 000 person-years, compared with Moore and colleagues who estimated 80 to 390 cases per 100 000 person-years across the 20 highest incidence areas (when also assuming no seroreversion and full immunity among seropositives).[30] Although some degree of LASV seroreversion does occur, seroreverted individuals are believed to have reduced Lassa fever risk relative to the serologically naive, so to remain conservative we considered a model without seroreversion, therefore probably underestimating infection incidence. However, by fitting infection-hospitalisation risks and case-fatality risks to laboratory-confirmed hospital case data from Nigerian states with extensive Lassa fever surveillance programmes in place, we ensured that our model faithfully reproduced best-available, prospectively collected, age-stratified and sex-stratified estimates of annual hospitalisations and deaths—the main predicted drivers of Lassa fever's health-economic burden.

In conclusion, our analysis has provided detailed Lassa fever burden estimates stratified by age and sex, allowing us, for the first time, to evaluate the potential impacts and cost-effectiveness of Lassa vaccination strategies targeting different population groups. These results could inform prioritisation strategies for forthcoming Lassa vaccines.

Contributors

KBP and TDH acquired funding and supervised the work. AAT administered the project. DRMS, MCAO, HRS, and KMH reviewed the literature and synthesised the data. DA, OOA, BNA, AC, WAF, DSG, KJ, SAO, JS, and DAW provided expert input on Lassa fever epidemiology and the value and interpretation of data. DRMS and AAT developed the vaccine administration strategies. KBP did the serocatalytic modelling. DRMS developed all other model components, did the analyses, and produced the results. DRMS, KBP, TDH, and AAT interpreted the results. The underlying data were verified by DRMS, KBP, and TDH, and all authors had full access to the study data and accept responsibility for the decision to submit for publication. DRMS wrote the first draft. The final version of this manuscript was reviewed and approved by all authors.

Declaration of interests

AC serves as the senior statistician for the LEAP4WA consortium, which is doing a phase 2b pilot efficacy study of the rVSVΔG-LASV-GPC vaccine against Lassa virus in healthy adults, adolescents, and children in west Africa. All other authors declare no competing interests.

Data sharing

All data used in this study are publicly available. The code and minimum dataset required to reproduce the results are available at www.github.com/drmsmith/lassaRiskVac.

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References

1 Andersen KG, Shapiro BJ, Matranga CB, et al, and the Viral Hemorrhagic Fever Consortium. Clinical sequencing uncovers origins and evolution of Lassa virus. *Cell* 2015; **162:** 738–50.

2 Kafetzopoulou LE, Pullan ST, Lemey P, et al. Metagenomic sequencing at the epicenter of the Nigeria 2018 Lassa fever outbreak. *Science* 2019; **363:** 74–77.

3 Siddle KJ, Eromon P, Barnes KG, et al. Genomic analysis of Lassa virus during an increase in cases in Nigeria in 2018. *N Engl J Med* 2018; **379:** 1745–53.

4 Richmond JK, Baglole DJ. Lassa fever: epidemiology, clinical features, and social consequences. *BMJ* 2003; **327:** 1271–75.

5 Basinski AJ, Fichet-Calvet E, Sjodin AR, et al. Bridging the gap: using reservoir ecology and human serosurveys to estimate Lassa virus spillover in West Africa. *PLoS Comput Biol* 2021; **17:** e1008811.

6 McCormick JB, Webb PA, Krebs JW, Johnson KM, Smith ES. A prospective study of the epidemiology and ecology of Lassa fever. *J Infect Dis* 1987; **155:** 437–44.

7 Smith DRM, Turner J, Fahr P, et al. Health and economic impacts of Lassa vaccination campaigns in West Africa. *Nat Med* 2024; **30:** 3568–77.

8 Sulis G, Peebles A, Basta NE. Lassa fever vaccine candidates: a scoping review of vaccine clinical trials. *Trop Med Int Health* 2023; **28:** 420–31.

9 Tschismarov R, Van Damme P, Germain C, et al. Immunogenicity, safety, and tolerability of a recombinant measles-vectored Lassa fever vaccine: a randomised, placebo-controlled, first-in-human trial. *Lancet* 2023; **401:** 1267–76.

10 Chen W. A Phase 1, randomized, recipient- and observer-blinded, dose-escalation study to evaluate the safety, reactogenicity, and immunogenicity of two doses of rabies-vectored monovalent Lassa fever vaccine (LASSARAB) administered with 3D-(6-Acyl) PHAD-SE (aphad-SE) adjuvant in healthy adults. ClinicalTrials.gov ID: NCT0654709. https://clinicaltrials.gov/study/NCT06546709 (accessed Nov 21, 2024).

11 Coalition for Epidemic Preparedness Innovations. Participants in Nigeria vaccinated in first-ever phase 2 Lassa fever vaccine clinical trial. CEPI, April 2, 2024. https://cepi.net/participants-nigeria-vaccinated-first-ever-phase-2-lassa-fever-vaccine-clinical-trial (accessed Dec 1, 2024).

12 Ochalek J, Lomas J, Claxton K. Estimating health opportunity costs in low-income and middle-income countries: a novel approach and evidence from cross-country data. *BMJ Glob Health* 2018; **3:** e000964.

13 Camacho A, Ndiaye A, Amevoin Y, Mousset M. Enable interim analysis: preliminary results (data as of 24 October 2022). CEPI, 2022. https://cdn.who.int/media/docs/default-source/blue-print/day1_session1_7_anton-camacho_lassa-vaccine-meeting_nigeria.pdf?sfvrsn=60534f12_3 (accessed Sept 12, 2024).

14 Nigeria Centre for Disease Control and Prevention. Lassa Fever Situation Report, Epi Week 25: 17th–23rd June 2024. NCDC, 2024. https://ncdc.gov.ng/ncdc.gov.ng/diseases/sitreps/?cat=5&name=An%20update%20of%20Lassa%20fever%20outbreak%20in%20Nigeria (accessed Sept 12, 2024).

15 Duvignaud A, Jaspard M, Etafo IC, et al, and the LASCOPE study group. Lassa fever outcomes and prognostic factors in Nigeria (LASCOPE): a prospective cohort study. *Lancet Glob Health* 2021; **9:** e469–78.

16 Kayem ND, Benson C, Aye CYL, et al. Lassa fever in pregnancy: a systematic review and meta-analysis. *Trans R Soc Trop Med Hyg* 2020; **114:** 385–96.

17 WHO. Geographic distribution of Lassa fever in West African affected countries (1969–2023). World Health Organization, 2024. https://www.who.int/health-topics/lassa-fever (accessed Sept 1, 2024).

18 UN Department of Economic and Social Affairs Population Division. Data from: population by single age – both sexes. UN, 2024. https://population.un.org/wpp/downloads?folder=Standard%20Projections&group=Population (accessed Nov 26, 2025).

19 UN Department of Economic and Social Affairs Population Division. Data from: births, by age of mother. UN, 2024. https://population.un.org/wpp/downloads?folder=Standard%20Projections&group=Fertility (accessed Nov 26, 2025)

20 WorldPop. Age and sex structures/Constrained individual countries 2020. WorldPop. https://hub.worldpop.org/geodata/listing?id=87 (accessed Feb 20, 2023).

21 Penfold S, Adegnika AA, Asogun D, et al, and the Enable Protocol authorship group. A prospective, multi-site, cohort study to estimate incidence of infection and disease due to Lassa fever virus in West African countries (the Enable Lassa research programme)—study protocol. *PLoS One* 2023; **18:** e0283643.

22 Duvignaud A, Etafo IC, Jaspard M, et al. Presentation and Outcomes of Lassa Fever in Children in Nigeria: A Prospective Cohort Study (LASCOPE). *J Pediatric Infect Dis Soc* 2024; **13:** 513–22.

23 Ficenec SC, Schieffelin JS, Emmett SD. A Review of Hearing Loss Associated with Zika, Ebola, and Lassa Fever. *Am J Trop Med Hyg* 2019; **101:** 484–90.

24 Cummins D, McCormick JB, Bennett D, et al. Acute sensorineural deafness in Lassa fever. *JAMA* 1990; **264:** 2093–96.

25 WHO. WHO target product profile for Lassa virus vaccine. World Health Organization, June, 2017. https://www.who.int/publications/m/item/who-target-product-profile-for-lassa-virus-vaccine (accessed Sept 1, 2024).

26 Angell B, Sanuade O, Adetifa IMO, et al. Population health outcomes in Nigeria compared with other west African countries, 1998–2019: a systematic analysis for the Global Burden of Disease Study. *Lancet* 2022; **399:** 1117–29.

27 Garry RF. Lassa fever—the road ahead. *Nat Rev Microbiol* 2023; **21:** 87–96.

28 Phillips J, Millum J. Valuing Stillbirths. *Bioethics* 2015; **29:** 413–23.

29 Doohan P, Jorgensen D, Naidoo TM, et al, and the Pathogen Epidemiology Review Group. Lassa fever outbreaks, mathematical models, and disease parameters: a systematic review and meta-analysis. *Lancet Glob Health* 2024; **12:** e1962–72.

30 Moore SM, Raphael E, Guerrero SM, Dean NE, Stoddard ST. Estimation of Lassa fever incidence rates in West Africa: development of a modeling framework to inform vaccine trial design. *PLoS Negl Trop Dis* 2025; **19**: e0012751.