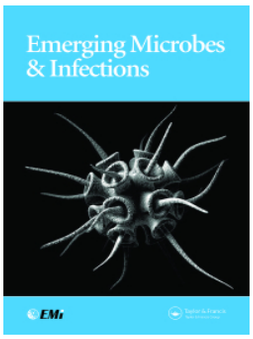

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Rodent control strategies and Lassa virus: some unexpected effects in Guinea, West Africa

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ABSTRACT

The Natal multimammate mouse (*Mastomys natalensis*) is the host of Lassa mammarenavirus, causing Lassa haemorrhagic fever in West Africa. As there is currently no operational vaccine and therapeutic drugs are limited, we explored rodent control as an alternative to prevent Lassa virus spillover in Upper Guinea, where the disease is highly endemic in rural areas. In a seven-year experiment, we distributed rodenticides for 10–30 days once a year and, in the last year, added intensive snap trapping for three months in all the houses of one village. We also captured rodents both before and after the intervention period to assess their effectiveness by examining alterations in trapping success and infection rates (Lassa virus RNA and IgG antibodies). We found that both interventions reduced the rodent population by 74–92% but swiftly rebounded to pre-treatment levels, even already six months after the last snap-trapping control. Furthermore, while we observed that chemical control modestly decreased Lassa virus infection rates annually (a reduction of 5% in seroprevalence per year), the intensive trapping unexpectedly led to a significantly higher infection rate (from a seroprevalence of 28% before to 67% after snap trapping control). After seven years, we conclude that annual chemical control, alone or with intensive trapping, is ineffective and sometimes counterproductive in preventing Lassa virus spillover in rural villages. These unexpected findings may result from density-dependent breeding compensation following culling and the survival of a small percentage of chronically infected rodents that may spread the virus to a new susceptible generation of mice.

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KEYWORDS Lassa virus; anticoagulant rodenticides; snap trapping; integrated pest management; *Mastomys natalensis*; Guinea; West Africa

Introduction

Wildlife reservoir culling is frequently suggested to prevent pathogen spillover to humans and livestock [1–3]. The success of this approach depends on three primary mechanisms: (i) reducing the contact rate between animals and humans/livestock, (ii) shortening the infectious period of animals, and (iii) lowering reservoir population densities below a transmission threshold [4,5]. For example, culling proved effective in eradicating bovine tuberculosis (TB) in swamp buffalo (*Bubalus bubalis*) and possums (*Trichosurus vulpecula*) [6,7]. However, various instances exist in which wildlife culling led to unforeseen outcomes in spillover dynamics. A well-known example is the culling of badgers (*Meles meles*) in the UK, which was associated with both increased and decreased incidences of bovine TB in cattle [8]. Unsuccessful culling efforts can result from failure to achieve population density transmission thresholds, or unanticipated behavioural, immunological and demographic responses within the target populations. For example, culling-induced changes in dispersal behaviour have been linked to an increase of rabies virus in vampire bats (*Desmodus rotundus*) and African swine fever in wild boars (*Sus scrofa*) [9,10]. Understanding the success or failure of culling programmes is imperative in refining wildlife disease control programmes and promoting alternative approaches like vaccination or breeding control.

Wildlife diseases are of concern worldwide, especially after the SARS-CoV-2 pandemic [11,12]. In West Africa, Lassa haemorrhagic fever (LF) is designated as a priority emerging infectious disease for research by the World Health Organization

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(WHO). The disease is caused by Lassa arenavirus (LASV), a member of the arenaviridae family (genus *Mammarenavirus*) [13]. While reported numbers range from 200,000–300,000 people with a fatality rate of 1–2% per year [14], these statistics are likely underestimated due to limited diagnostic capacities in the affected regions [15]. Furthermore, increased climate and land-use change threatens to exacerbate the LASV incidence, potentially expanding its geographic range [16]. Transmission to humans primarily occurs through direct or indirect contact with the virus' reservoir host, the Natal multimammate mouse (*Mastomys natalensis*) [17,18]. While recent studies suggest that also other rodents may serve as LASV reservoirs [19], *M. natalensis* is the predominant rodent found in West African households, especially in the absence of *Rattus rattus* [20,21]. The potential routes of rodent-to-human transmission encompass contaminated food, inhalation of infectious particles or direct contact with infected *M. natalensis* during hunting or consumption [22,23]. Human-to-human transmission is relatively infrequent, primarily occurring within hospital settings or among individuals from the same household [24].

Strategies for the control or prevention of LASV remain limited. In the context of LF treatment, ribavirin stands as the sole available drug, but its efficacy diminishes when administered too late [25]. LF vaccines hold the promise of significantly reducing the disease burden in endemic regions, but none have yet gained authorization for use. Nevertheless, ongoing progress towards a safe and effective vaccine is encouraging, with four vaccine candidates (NO-4500, MV-LASV, rVSVΔG-LASV-GPC, and EBS-LASV) currently in clinical evaluation, and five phase 1 and one phase 2 trials registered [26]. However, even if a good working vaccine would be available, the remote villages where LASV is endemic may face logistic challenges and vaccine hesitancy. Therefore, rodent culling is suggested as a sustainable alternative to prevent LASV spillover [25]. Its effectiveness is predicated on two independent assumptions: (i) the rodent-human contact rate is positively related to rodent population density, and (ii) LASV transmission within rodent populations correlates positively with rodent density [4]. While the first assumption is generally valid, it might not always hold true due to the complex interactions between humans and rodents (e.g. rodents might be eradicated in the houses, but hunted in the field for food) [27]. The second assumption stems from the fundamental characteristics of viral-host interactions, particularly the distinction between density vs frequency-dependent transmission [28]. In cases of density-dependent disease transmission, culling measures can effectively halt transmission when the host population density falls below a critical threshold. Conversely, frequency-dependent transmission indicates that pathogens may persist even at very low densities, necessitating either complete host eradication or host vaccination to achieve pathogen exctinction [5].

We recently investigated the impact of yearly rodent control on LASV transmission in rodents in six rural villages in Upper Guinea (i.e. we tested the second assumption) [29]. Our findings suggest that rodent control can indeed reduce LASV transmission in *M. natalensis* populations. However, the extent of this reduction proved to be rather modest (amounting to a mere 5% per year), even though we achieved an 80% reduction in the rodent population annually. Furthermore, the rapid resurgence of rodent numbers to pre-elimination levels raised concerns of a commensurate rebound in the LASV prevalence, which was clearly supported by simulations of a mathematical model. We concluded that periodic rodent control (e.g. annually) is an unsustainable strategy to curtail LASV spillover to humans. In contrast, our model simulations proposed that continuous density control may offer a more efficient means of eliminating LASV from the villages. For instance, our simulations indicated LASV extinction within four years' time if the rodent population was permanently reduced by 60%. Based on these results, we conducted an intensive snap-trapping experiment in one of the villages (Brissa) to explore the effectiveness of a combined strategy involving rodent culling through chemical control, followed by an intensive trapping regimen spanning three months. Here, we present the outcomes of this experiment and assess the cost-effectiveness of this integrated pest management approach in mitigating LASV spread within the rodent population.

Material and methods

Study site

We performed a seven-year rodent-control experiment in the village Brissa (10°13.010′ N; 10°41.326′ W), situated in the Faranah prefecture of Upper Guinea. The village was chosen based on its rather small population size of ±1500 inhabitants, its remote location from a paved road (which is accessible by a 45 min drive from Faranah), the abundant presence of *M. natalensis* in the houses (> 95% of captured rodents in the houses are *M. natalensis*) and the high LASV seroprevalence in the rodent population (±20%) [21]. Brissa embodies a typical village in the region, characterized by distinctive thatch-roof circular mud houses in Sudanese style [30]. These domiciles are mainly used as huts to sleep or as storehouses for safeguarding agricultural products and seeds [30]. In contrast, owners of metal-roofed structures typically

designate one of these rooms to sleep and another to safeguard their food from potential fire hazards. Rodent faeces are frequently encountered in or near the kitchen areas, on the floors of the sleeping rooms, and even within the bedding spaces [30]. Local rodent control practices are limited to acute poisons procured from the market and applied by individuals only. Some residents opt for alternatives to poison, such as Indomethacin, to prevent small children and domestic animals from unintended toxic effects. Additionally, a number of adults in the village keep cats or dogs as natural rodent hunters within their household. Notably, children in Brissa engage in rodent capture, either as a form of playing or as a food source [31].

Rodent control with anticoagulant rodenticide

From April 2014 to December 2018, we yearly distributed anticoagulant rodenticides (AR) (Bromadiolone and Difenacoum) in two baiting stations per room ($n = 400–704$ stations Coral, Ensystex Europe). Rodent control interventions were performed during the dry season (November to April each year), coinciding with the period when rodents seek refuge in the houses driven by the need for food and shelter [32]. The chemical treatment spanned 10 days during the first two years and extended to 30 days in the subsequent four years (Table S1). For the initial three years, we bought anticoagulants readily available in Conakry, opting for a 0.01% blend of wheat and bromadiolone in small sealed bags (titrated at 0.003% V. Lattard, pers. com. according to Fourel et al) [33]. For the next three years, we changed the rodenticide to avoid AR resistance and transitioned to 50 g cubes of Difenacoum at 0.005%, combined with paraffin as bait (Rodenthor bloc, Ensystex Europe). Our local control team, comprising villagers, collected any dead rodents they encountered outside of their burrows and subsequently incinerated them outside of the village in a designated area. Rodent bait consumption was monitored throughout the rodenticide application process during the third and fourth years. For a more comprehensive description of the rodenticide application setup, we refer to Sáez et al. 2018 [30]. Rodenticide efficacy was estimated by using the trapping success (TS) before and after treatment according to the following formula: 100 x (TS before – TS after)/TS before [34].

Intensive rodent control with snap trapping

From 17-Feb-2019 to 15-May-2019 (40 days after the last chemical control), we carried out an intensive control session using snap traps (Mini-Rex BellLaboratories Inc.). The traps were put in baiting stations to ensure the safety of children and domestic animals. Two baiting stations, each housing a single trap with mashed peanuts, were strategically positioned in all open houses of the village. Due to the progressive training of a field team (one Bachelor student, one village referent able to write and two field assistants) in the health and safety aspects of handling potentially infected rodents, we first distributed 200 traps on one quadrant of the village (denoted by the yellow dots in Supplementary Figure 1). One month later, an additional 640 traps were deployed (denoted by the red dots in Supplementary Figure 1) to cover the entirety of the village, resulting in a total of 840 traps. Each trap was geo-localized and subjected to daily inspection over a span of three months (88 days). We identified captured rodents morphologically before being incinerated outside of the village in a designated area.

Rodent sampling before and after chemical control operations

Trapping sessions were conducted both prior to and following chemical control, encompassing three consecutive trapping nights each time. In total, we distributed 120 Sherman live traps (Sherman Live Trap Co., Tallahassee, FL, USA) in pairs within 60 rooms across 42–50 randomly selected houses along a transect. Baiting was carried out in the evening, with a mixture of peanuts, dry fish and wheat flour, and checked the following morning. During the final trapping session, conducted in November 2019 (after the intensive snap trapping period), we conducted two successive three-night trapping sessions at two separate transects in the village, including the original one and a new one (Table S1). During all sessions, captured rodents were necropsied in situ, adhering to standardized biosafety procedures [35]. They were euthanized using isoflurane, morphologically identified, weighed, measured (length of head and body, tail, hind foot, and ear dimensions) and necropsied. Blood samples were drawn from the heart with a syringe and preserved under 2 different formats: whole blood in cryotubes and dried blood on filter paper (SEROBUVARD – LABOCEA, France), contained in small re-sealable zipper bags with desiccant silica. Organs (spleen and liver) were preserved in ethanol, while eyes were stored in 10% formalin.

Viral RNA, IgG detection and ELW estimation

For LASV screening, we followed the methodology as previously detailed in Mariën et al. 2020 [29]. In brief, viral RNA was extracted from the dried blood spots (DBS) using the QIAmp RNA Mini Kit (Qiagen,

Hilden, Germany) and subsequently tested with 2 PCRs: one targeting the glycoprotein, and one targeting the polymerase [36,37]. If positive, pooled samples were subdivided and retested individually with both RT-PCRs. The PCR products were Sanger sequenced, and only those sequences that unequivocally matched LASV using BLAST were considered positive. Here, we included the sequences obtained during 7 years between 2013 and 2019 and uploaded new ones on the GenBank server with the following accession numbers: PP079036-55 (See "this study" in supplementary Table S2). Detection of IgG antibodies against LASV was carried out through the use of in-house immunofluorescent assay slides (IFA) [29,38]. Whole blood samples were inactivated with Triton 1% diluted at 1:2, and then diluted at 1:10 with PBS before distribution on the IFA slides. In cases where whole blood was unavailable, we eluted blood spots from filter paper in PBS and 0.25% NH3. To ensure a higher degree of reliability and objectivity in our results, evaluation of the slides was conducted by two independent observers using a fluorescence microscope. Uncertain samples were re-evaluated on new IFA slides containing both infected and non-infected cells, with the serostatus being validated only if both results were congruent. To estimate the age of individuals, eye lens weight (ELW) was estimated, a metric known to increase with age independent of external factors [39]. Eye lenses were extracted using forceps, cleaned, dried for 2 h at 100°C, and then weighed to the nearest 0.1 mg [22].

Statistical analysis

To investigate the impact of the rodent control on the *M. natalensis* density, we employed a linear model with the number of captured *M. natalensis* as the response variable, and treatment status (before vs after chemical control) and year (continuous time) as explanatory fixed effects. The captured *M. natalensis* count served as a proxy for density, as the same number of traps was consistently used across the same duration of trapping nights.

For assessing the population recovery rate following interventions, we first examined the effect of chemical rodent control on ELW distribution, as a proxy for age distribution. This analysis involved a linear model with ELW as the response variable, and year (continuous time), treatment status (before vs after chemical control) and sex (male vs female) as explanatory fixed effects. Only the first six trapping sessions (chemical control) were considered in this analysis since a visual inspection (Figure 1B) revealed distinct ELW distribution patterns after intensive trapping control. Sex was included due to known differences in the lifespan of female and male *M. natalensis* [40]. A separate linear model was employed to assess the impact of intensive trapping control on ELW, comparing data from session 6 (before control) to data from session 7 (after intensive trapping). This model included ELW as a response variable and treatment status (before vs after intensive trapping control) and sex (male vs female) as explanatory fixed factors.

In addition, we aimed to evaluate if rodent control affects the rate at which susceptible individuals contract an infection. This rate was computed using age-specific seroprevalence data under the assumption of lifelong immunity after arenavirus infection in *M. natalensis* [41]. To estimate this rate and explore its potential influence by rodent control, we first fitted a generalized additive model (GAM) using LASV antibody status (positive or negative) as the response variable, and ELW and treatment status (before vs after chemical control) as explanatory variables, assuming a binomial distribution with logit-link function. Given the substantial disparity in ELW for trapping sessions with chemical versus snap trapping control, we decided to exclude data from trapping session 7 (snap trapping control) to test the relation between ELW and LASV seroprevalence and to use "year" as a fixed factor (and not continuous time). GAMs were chosen to account for the expected nonlinear response between seroprevalence patterns and ELW (decrease of maternal antibodies until 15 mg followed by an increase with age). Subsequently, a separate analysis was conducted to investigate the effect of rodent control on LASV infection rate over time. We employed a generalized linear model (GLM) with LASV antibody status (positive or negative) as the response variable, and ELW and year (categorical variable) as independent fixed factors. Animals with ELW below 15 mg (maternal antibodies) were excluded from this analysis, enabling the use of GLMs given the linear relation between ELW and serostatus. By examining the different years, any time effect on LASV infection rate was discernible within this model, while the influence of intensive trapping was assessed by evaluating the last year.

Finally, we employed a GAM to explore whether LASV RNA status in rodents (positive vs negative) was affected by age (ELW) and chemical control (before vs after chemical control). A smoother was applied for ELW due to the anticipated nonlinear relation between LASV RNA and age. Another separate GAM was used to evaluate the effect of snap trapping control (before vs after) on LASV RNA status, also including ELW as a smoothed fixed effect. For the latter analysis, we focused on comparing data from session 6 (before control) to data from session 7 (after intensive trapping).

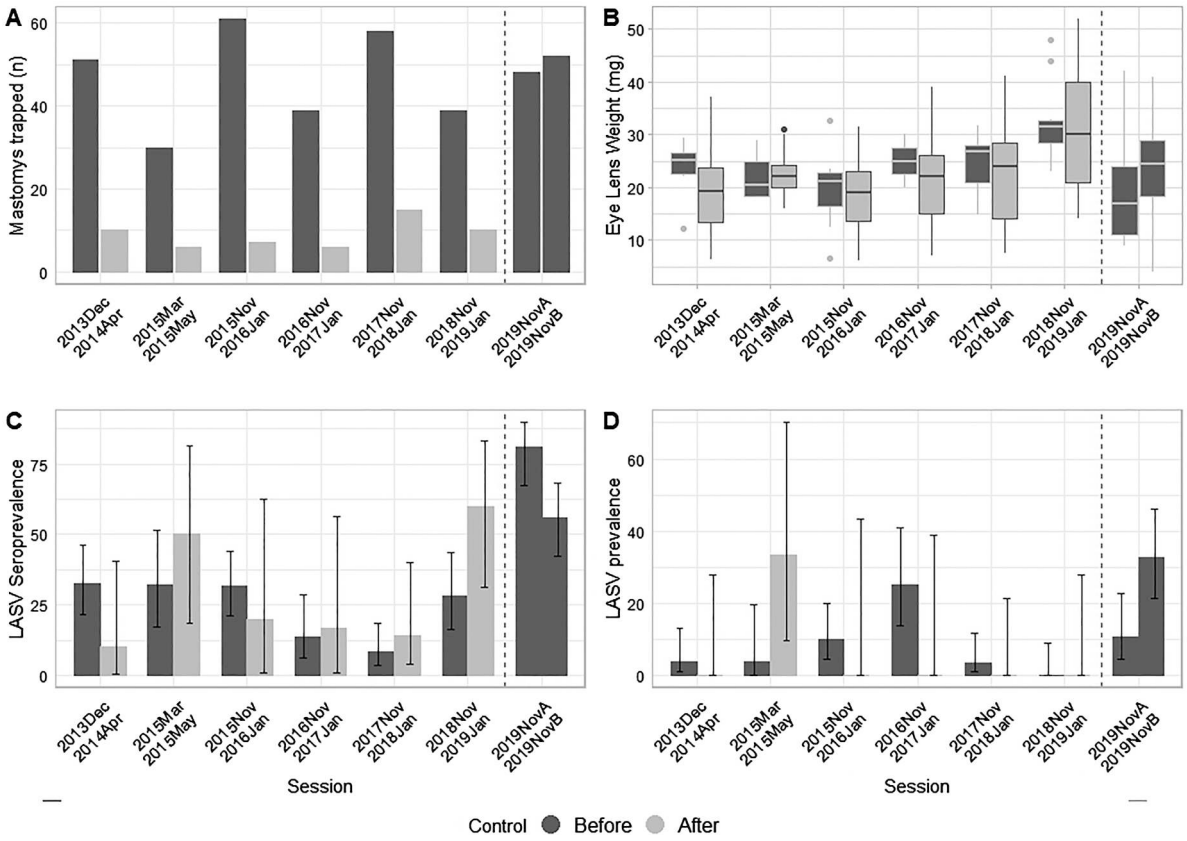

Figure 1. A) Number of *Mastomys natalensis* captured per 3-night trapping session in Brissa, both before and after rodenticide treatment. B) Boxplots illustrating the distribution of eye lens weights in captured *Mastomys natalensis* (a known proxy for age in mammals), categorized by trapping session before and after rodenticide treatment. C) Lassa seroprevalence (IgG) during trapping session, both before and after rodenticide treatment. D) Lassa prevalence (PCR) by session, both before and after rodenticide treatment. Bars denote 95% (binomial) confidence intervals on the (sero)prevalence estimates, with dark grey representing sessions before rodenticide treatment and light grey sessions after rodenticide treatment. The dotted lines signify the intensive snap-trapping session that took place between 17/02/2019 and 15/05/2019. X-labels indicate the start and end dates for each three-night trapping session. In November 2019, two separate 3-night trapping sessions were carried out, which have been labelled A and B.

We used the lm, glm and gam functions of the lme4 and MGCV packages (version 1.1–7) in the R statistical software version 4.2.2 [42,43]. Model refinement was performed by starting with fully parameterized models and sequentially excluding variables with the highest insignificant *p*-values or Akaike Information Criterion (AIC) values.

Results

Rodent control efficiency with rodenticide

From December 2013 to November 2019, we captured a total of 420 *M. natalensis*, with 369 live captures prior to chemical control and 51 captured post-intervention (Table S1). As anticipated, we observed a significant decline in *M. natalensis* captured during the sessions conducted after the rodenticide implementation measures ($\Delta AIC = 22$, $p < 0.0001$). Trapping success ranged from 5–14 captured *M. natalensis* after intervention to 25–60 prior to control. This variation in capture rate across sessions translated into a control efficiency that fluctuated from 74% to 92%, contingent on the session in question (see Figure 1A, Table 1). Interestingly, our analysis unveiled no significant fluctuations in rodent densities when comparing capture events labelled as "prior control" over time (Est = 0.77, $\Delta AIC = -2$, $p < 0.57$). This suggests that the *M. natalensis* populations in Brissa returned to their baseline densities one year following the introduction of chemical control, and even after five months of intensive snap trapping in 2019.

Rodent control efficiency with intensive snap trapping

From February to May 2019, a total of 2477 rodents were killed using snap traps (96.6% *M. natalensis*). Most of the rodent captures took place in the first week of initiating snap trap control, starting at a trapping efficiency of around 30%. Although the trapping efficiency progressively decreased as the study advanced, a constant number of rodents, amounting to ±2–5% of the traps deployed per night, were captured during the entire three-month study period.

Table 1. Overview of the different models used in this manuscript, their variables used and their selection parameters.

Model	Response	Explanatory	Estimate	ΔAIC	Pvalue
Linear	*Mastomys*	Year	0.77	−2.35*	0.57
	Number	Control (Before)	36.95	22.45	<0.001
Linear	ELW	Year	1.62	36.21	<0.001
	(sessions 1–6)	Control (Before)	−2.91	4.62	0.014
	Sex	Sex (male)	−3.12	8.96	0.0004
Linear	ELW	Snap trapping	−9.95	25.68	<0.001
	(session 6 vs 7)	Sex (male)	−1.96	−0.89*	0.249
GAM	LASV Ab	ELW	smoothed	10.78	0.006
	(session 1–6)	Control (Before)	−0.08	−1.73*	0.818
GLM	LASV Ab	ELW	0.0098	7.46	<0.001
	(all sessions)	Year	−2.2–1.5	45.37	<0.001
GAM	LASV RNA	ELW	smoothed	5.42	0.028
	(session 1–6)	Control (Before)	0.74	−1.52*	0.327
GAM	LASV RNA	ELW	smoothed	7.87	0.0065
	(session 6 vs 7)	Snap trapping	−2.29	10.12	0.0005

*Indicates that the model without the explanatory variable was preferred based on ΔAIC values. LASV Ab = Lassa virus antibody status; ELW = eye lens weight (proxy for age); AIC = Akaike Information Criterion.

This observed pattern held true for both trapping quadrants, involving 200 traps in the northeastern segment of the village and 640 traps situated in other parts of the village (Figure 2).

Effect of rodent control on age (Eye lens weight)

When comparing trapping sessions before and after chemical control, the ELW was significantly lower in sessions before versus after control (Est = −3.12, ΔAIC = 4.62, $p = 0.014$). Furthermore, ELW displayed a consistent increase over time (Est = 1.62, ΔAIC = 36.21, $p < 0.001$) (Figure 1B, Table 1). In contrast, when comparing the ELW of year session 6 (before chemical control) to year session 7 (after snap trapping control), we observed that the ELW significantly declined for *M. natalensis* following the trapping control (Est = −9.95, ΔAIC = 25.68, $p < 0.001$). We also found that males exhibited a lower ELW than females (Est = −3.12, ΔAIC = 8.96, $p = 0.0004$) when considering data from year 1–6.

Effect of rodent control on LASV infection rate (via serology and LASV PCR)

Among the 420 *M. natalensis* captured, we identified 42 (10%) as LASV-PCR positive, 145 (34%) as LASV seropositive (IgG) and 11 (3%) exhibited both PCR and antibody positivity (Figure 1C and D, Table S1). We found a significant non-linear (smoothed) relationship between LASV seroprevalence and ELW (edf = 3.35, ΔAIC = 10.78, $p = 0.006$). LASV seroprevalence first displayed a decrease up to an ELW of 15 mg, followed by a subsequent increase. This pattern

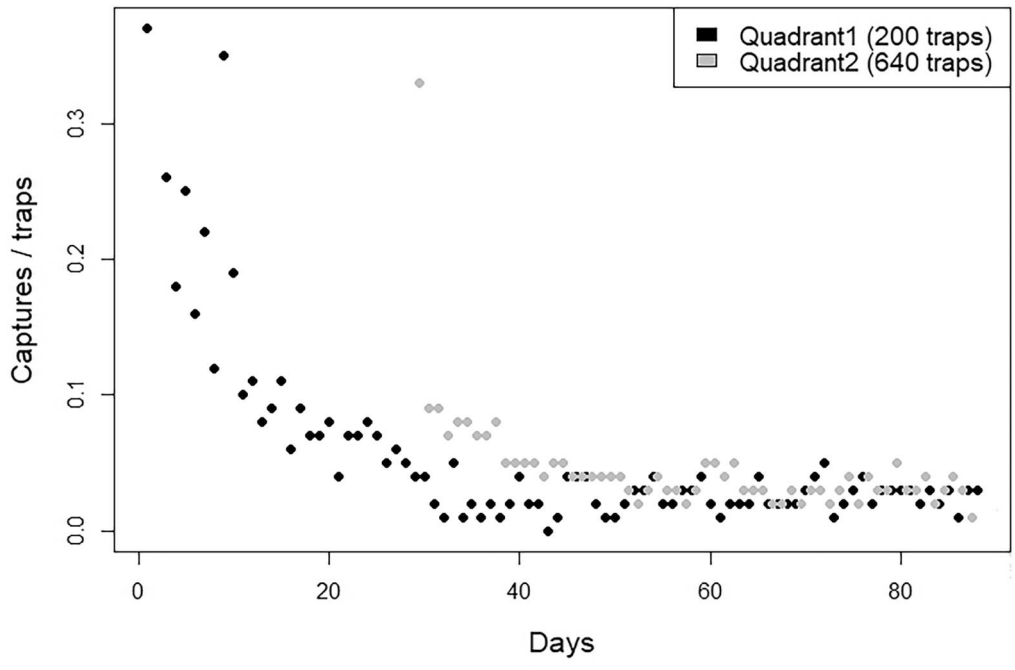

Figure 2. Proportion of closed traps with rodents over time (number of rodents divided by the total number of traps that were still open or closed without a capture). Black dots represent traps from the first line (200 traps) and grey dots from the second line (640 traps) in the village Brissa.

aligns with the concept that maternal antibodies decline following birth, while the infection probability increases with age due to horizontal transmission and exposure time. When considering the effect of age, LASV seroprevalence did not differ significantly between trapping sessions before and after chemical control (Est = −0.08, ΔAIC = −1.73, $p = 0.818$) (Figure 3, Table 1). However, the infection rate demonstrated significant variability among years (ΔAIC = 45.37, $p < 0.001$). While LASV transmission generally decreased over time when comparing trapping sessions before chemical control (year 2013–2018; est −0.38, ΔAIC = −10.38, $p < 0.0001$), it significantly increased during the final trapping session following the snap trapping control (Est = −1.5, ΔAIC = 45.37, $p = 0.0012$). Furthermore, we observed that a significantly higher proportion of *M. natalensis* tested LASV positive after intensive trapping (Est = −1.73, ΔAIC = 10.12, $p = 0.0005$) compared to the period before. Such an effect was not observed when comparing rodents before vs after chemical control (edf = 3.73, ΔAIC = −7.78, $p = 0.0065$).

Discussion

Our study aimed to assess the effectiveness of rodent culling as a means to reduce LASV spillover to humans. We observed that both chemical and intensive snap-trapping effectively reduced the rodent population by as much as 74–92%. However, it was striking to note that the rodent population swiftly rebounded to pre-treatment levels, with the intensive snap trapping method even achieving this within six months. Our findings also indicated that annual chemical control results in a modest decrease in LASV infection rates. However, it was unexpected to discover significantly higher infection rates following the intensive trapping period. After seven years of rigorous rodent control measures, we can conclude that annual chemical control, whether used independently or in combination with intensive trapping, is an ineffective strategy for achieving sustainable LASV control in rural villages. In certain cases, it may even yield counterproductive results.

The factor contributing to the failure was likely the absence of sustained rodent control measures during periods when we did not actively implement control measures ourselves. This lapse provided opportunities for rodent populations to rebound to pre-treatment levels quickly. Indeed, *M. natalensis* is known for its remarkable breeding capacity, characterized by prolific litter sizes of up to 20 pups every three weeks. For instance, in agriculture fields in Tanzania, its population can oscillate between as few as five and exceeding 350 individuals per hectare in typical years [27]. In Guinea, the rapid recolonization rate can be attributed to a combination of this formidable breeding capacity, increased survival due to lack of competitors and the rodents' ease of movement from the neighbouring fields to human dwellings [20,21,44]. The village of Brissa represents a mosaic of houses nestled amidst patches of agricultural fields and fallow land, which offers an ideal habitat to shelter for *M. natalensis*. This artificial sink-source metapopulation structure may also explain why we continued to capture *M. natalensis* in houses during the intensive trapping period, with 3–5% of the traps still yielding a catch, even after three months had elapsed.

Interestingly, our analysis of the ELW distribution suggested that the rodent population aged differently in response to various control methods. Specifically, after several rounds of chemical control, the rodent populations became older, while intensive trapping appeared to have the opposite effect. This observation aligns with other studies that also reported age-differential mortality following chemical control [45]. The effect can be explained by the assumption that older rodents tend to be more neophobic to rodenticides, as they already have their own established food sources [46]. This increased survival of older (reproductively active) *M. natalensis* could contribute to the population's recolonization capacity, as adults continue to reproduce and compensate for the substantial losses among the younger generation. Conversely, we expect that snap trapping is less age-discriminative, as the use of natural bait (such as peanuts) does not trigger neophobia in old adults, thus explaining the younger age classes observed during the last trapping session.

The latter result may also explain the increase in LASV infection rates during the final trapping session. Model simulations suggest that a pathogen's prevalence can indeed surge when density-dependent compensation, following culling, leads to an elevated birth rate. This occurs as immune adult animals are replaced by susceptible recruits [4,47,48]. This phenomenon has also been observed in other contexts, such as increased rabies transmission in vampire bats following culling, which was attributed to an influx of juveniles [49]. In addition, the snap-trapping may have disrupted existing social structures within the rodent population, potentially creating new interactions that facilitated transmission among the remaining *M. natalensis*. A similar disruption of social structures was suggested to increase *Leptospira interrogans* transmission in Norway rats [50]. Furthermore, while we still expect that LASV transmission in *M. natalensis* is density-dependent (based on the rodent's social behaviour), it is important to note that a small percentage of chronically infected animals can significantly reduce the transmission-density threshold, potentially leading to almost near eradication of the host population. Indeed, while most

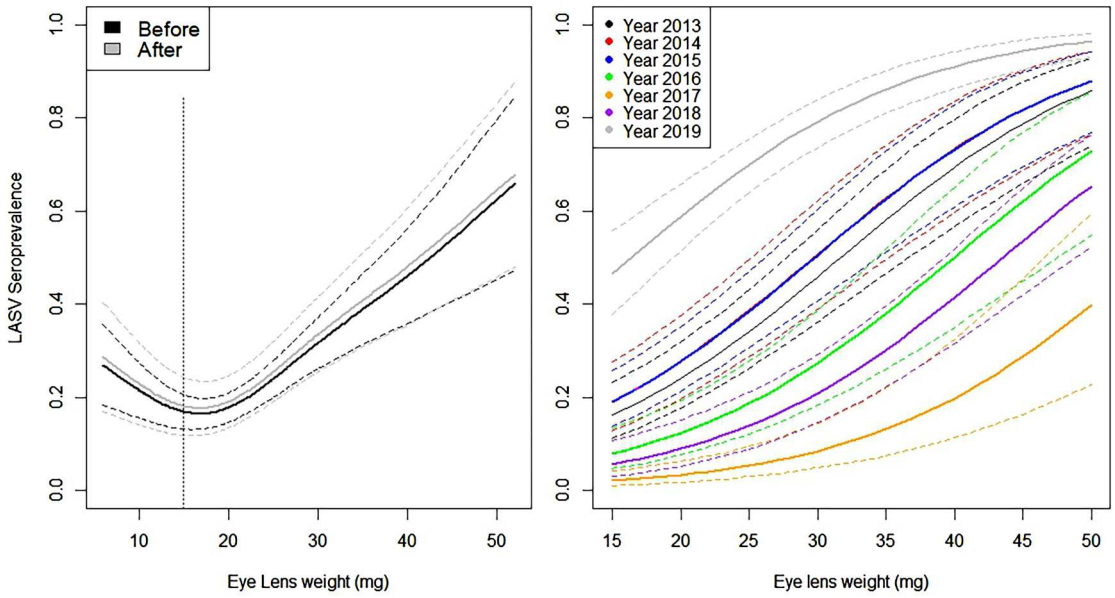

Figure 3. Infection rate of Lassa virus in the rodent population in Brissa, derived from age-specific seroprevalence data. *Left*: LASV seroprevalence depicted in function of eye lens weight for trapping sessions 1–6 (2013–2018). No difference in the infection rate was found when comparing trapping sessions before (black) and after chemical rodent control (grey). *Right*: Significant differences were found in the infection rate between years. Solid lines represent estimates derived from a generalized linear model with 95% confidence intervals (dotted lines).

M. natalensis are likely acutely infected with arenaviruses, we found that a small percentage of *M. natalensis* (5%) can also become chronically infected in the wild. These chronic infections are assumed to be a driving factor behind persistent arenaviruses infections in East Africa [28]. In summary, our findings suggest that the increased LASV transmission following intensive trapping control results from a complex interplay, which involves the survival of chronically infected rodents passing the virus to a susceptible juvenile population that readily moves between unoccupied houses and neighbouring fields.

We recommend that future rodent control strategies, aimed at reducing LASV spillover, focus on year-round management of *M. natalensis* populations. The success of these approaches will depend on the active participation of the communities and their ability to perceive direct benefits from the control measures[23,51]. In the case of Brissa, villagers readily embraced our control efforts due to the perceived nuisance caused by rodents, which destroy their harvest and disrupt their sleep [23]. While villagers who participated in the chemical control often complained about unpleasant odours resulting from rodent carcasses in burrows or corners of their houses, the intensive snap-trapping method was particularly well-received as they could witness immediate results. The latter approach also fostered a sense of triumph that garnered increased public support for the elimination programme. This sense of satisfaction aligns with observations made in similar campaigns in Uganda and Mozambique [52,53]. Furthermore, although snap traps may present a slightly higher upfront cost compared to rodenticides (Table S3), they offer substantial long-term advantages. These traps are durable and reusable, ultimately reducing costs over time [52]. From an ecological perspective, snap traps do not create problems related to secondary toxicity frequently observed in predators that consume poisoned rodents. In these villages, many kites and vultures prey on rodents which can inadvertently ingest the poison and suffer from secondary toxicity effects [54,55]. While outside snap trapping is discouraged due to its potential impact on other wild or domestic animals, fertility control offers a promising alternative for maintaining low rodent populations in the neighbouring fields [56]. This approach is not only considered to be less harmful than rodenticides but also to be more sustainable, as it prevents compensatory reproduction [57–59]. In addition to active rodent control, simple interventions (e.g. rodent proofing of houses or storing food in airtight containers) could also reduce rodent densities [60]. Future studies should investigate whether the suggested approach, involving community participation and year-round control methods, can effectively reduce the risk of LASV transmission risk to humans in a sustainable manner.

Ethics statement

All experiments were approved by the National Ethics Committee of Guinea (permit n° 12/CNERS/12 and129/CNERS/16), performed in collaboration with the local health authorities (Prefecture de Faranah) and in agreement with the village chiefs. Rodenticide

and traps were only placed in a house if permission was obtained from the individual house owner.

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Disclosure statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author statement

Conceived the study: JM, MS and EFC. Wrote the paper: JM. Performed the experiments: JM, MS, UB, MK, TR, BS, and EFC. Performed the statistical analyses: JM and AL. Supervised field and laboratory work: MS, MD, NM, and EFC. Funding acquisition: NM and EFC. All authors read and approved the final manuscript.

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