Understanding Risk Factors Related to Lassa Fever in Ebonyi, Bauchi, and Plateau States, Nigeria

Desk Review

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Acronyms

EOC	Emergency Operation Center
FMARD	Federal Ministry of Agriculture and Rural Development
FMEnv	Federal Ministry of Environment
GHSA	Global Health Security Agenda
HCW	Health Care Worker
IMS	Incident Management System
IPC	Infection Prevention Control
LF	Lassa Fever
LFTWG	Lassa Fever Technical Working Group
LGA	Local Government Area
MDA	Ministries, Departments, and Agencies
MOH	Ministry of Health
NCDC	Nigeria Centre for Disease Control
PHEOC	Public Health Emergency Operation Centre
PPE	Personal Protective Equipment
PZD	Priority Zoonotic Disease
RCCE	Risk Communication and Community Engagement
SBC	Social and Behavior Change
TWG	Technical Working Group
USAID	United States Agency for International Development
WHO	World Health Organization

Background

Emerging and endemic zoonotic diseases represent critical threats not only to the health of animals and humans but also to global health security. With increases in global migration, international trade, and environmental challenges such as climate change, interactions between humans and animals have become more prevalent. Globally, zoonoses are responsible for approximately 2.5 billion cases of human illnesses and 2.7 million human deaths worldwide every year (Salyer et al., 2017). In Nigeria, endemic diseases such as anthrax, zoonotic tuberculosis, and rabies are widespread, especially among livestock keepers. The country has also experienced epidemics of zoonotic origin such as Ebola virus disease, avian influenza, and Lassa fever (LF) more frequently in the past few years (Nigeria One Health Strategic Plan, 2019). To successfully control these epidemic-prone diseases, the Nigerian government used a One Health approach in which multiple sectors plan, communicate, and work together to achieve better public health outcomes for the human, animal, and environment sectors.

The implementation of the One Health approach in Nigeria includes building the capacity of medical doctors, veterinarians, laboratory scientists, and environmental scientists, especially regarding outbreak control and research. Additionally, recognizing the need to work across sectors for the timely prevention and control of zoonoses and other public health emergencies, the federal government has institutionalized the One Health approach in its various ministries, departments, and agencies (Nigeria One Health Strategic Plan, 2019). This action is in line with the Global Health Security Agenda (GHSA), of which Nigeria is member country.[1] As a member country, Nigeria committed to a complete evaluation of its health security capacity and to planning and mobilizing resources to address the gaps identified. This commitment led to the joint external evaluation, which was conducted in June 2017, to assess Nigeria's readiness and capacity to prevent, detect, and respond to public health threats.

Key findings from the joint external evaluation indicated the need to (1) identify the highest priority zoonotic diseases (PZDs) in Nigeria; (2) strengthen laboratory capacity; (3) establish intersectoral collaboration for emergency response, especially between human and animal health (environmental sectors and security agencies), and (4) enhance and sustain the Integrated Disease Surveillance and Response at all levels (federal, state, local government area [LGA], health facilities) (Nigeria One Health Strategic Plan, 2019).

To identify the highest PZDs in Nigeria, the Nigerian government held a multisectoral zoonotic disease workshop in July 2017. Through the workshop, 12 PZDs were identified as focal diseases for funding support. They include rabies, avian influenza, Ebola, swine influenza, anthrax, tuberculosis, African trypanosomiasis, LF, *Escherichia coli* O157, brucellosis, monkeypox, and yellow fever (with the last two having a resurgence in the past few years). Through consultation meetings with the Nigeria Centre for Disease Control's (NCDC's) risk communication technical working group (TWG), owing to its resurgence

[1] Global Health Security Agenda: https://ghsagenda.org

and the frequent nature of its outbreaks, LF was identified as the focus priority disease for this desk review and United States Agency for International Development (USAID) Nigeria's GHSA efforts.

The objectives of this desk review are the following:

1. To understand LF by answering the following questions:
    a. What is it?
    b. Why is it a zoonotic disease?
    c. How is it transmitted?
    d. What are its peak times?
2. To understand how Nigeria prepares for LF at the national and state levels
    a. How does the One Health approach inform LF prevention and control interventions at the community level?
3. To understand the knowledge, attitudes, and practices around LF and risk communication and community engagement (RCCE) by considering the following:
    a. What are existing LF knowledge, attitudes, and practices?
    b. What are LF prevention and control communication strategies at the community level?
4. To identify gaps around risk communication to inform recommendations for Breakthrough ACTION-Nigeria programming

Breakthrough ACTION-Nigeria

Breakthrough ACTION-Nigeria is a USAID flagship integrated social and behavior change (SBC) and risk communication project under the prime implementation of Johns Hopkins Center for Communication Programs from 2017 to 2022. Its goal is to increase the practice of priority health behaviors in the areas of malaria; maternal, newborn, and child health, including nutrition; family planning/reproductive health; tuberculosis; and priority zoonotic diseases at the national and subnational levels in collaboration with the relevant USAID implementing partners. The project also works with federal and state Ministry of Health programs, departments, and agencies to improve their SBC capacity and coordination.

The three intermediate results toward achieving this goal are the following:

- Improved individual and social determinants of health to facilitate individual and household adoption of priority behaviors
- Strengthened monitoring, coordination, and quality of SBC across U.S. government investments
- Strengthened public sector systems for oversight and coordination of SBC at the national and subnational levels

Breakthrough ACTION-Nigeria works at the national level and in 12 states and the Federal Capital Territory. In fiscal year 2021, Breakthrough ACTION-Nigeria GHSA activities are focused in three states: Ebonyi, Bauchi, and Plateau. This desk review will focus on LF in these three states.

Nigeria Global Health Security Agenda Program

USAID/Nigeria through Breakthrough ACTION is supporting a program to increase the capacity of Nigerian institutions and partners to effectively address high-risk behaviors associated with the PZDs identified in Nigeria. The Nigeria GHSA program focuses on the World Health Organization's (WHO's) International Health Regulations core capacity for risk communication and IHR coordination.

Breakthrough ACTION is working with USAID and in partnership with the government of Nigeria, One Health stakeholders, and GHSA partners to improve risk communication capacity and address behaviors associated with preventing and/or controlling selected high-priority diseases, such as LF.

Risk communication is an integral part of any emergency response. It is the real-time exchange of information, advice, and opinions between experts, community leaders, or officials and the people who are at risk to support understanding and adoption of protective behavior. SBC communication uses strategies that are based on behavioral science to positively influence knowledge, attitudes, and social norms among individuals, institutions, and communities.

Methods

This desk review provides a review of the literature of risk factors and SBC interventions related to LF in Nigeria. The literature reviewed encompasses gray literature, including the 2019 and 2020 NCDC's LF surveillance reports, technical reports, and peer-reviewed articles. Peer-reviewed articles were accessed through Google Scholar and PubMed with inclusion criteria for LF, LF cases in Nigeria, risk and prevention factors and interventions related to LF in Nigeria, and publication dates from 2010 to 2021. This search was conducted between October 2020 and May 2021. This desk review also includes insights from a series of informal interviews with the NCDC's LF risk communication focal person, Mr. Chimezie Anueyiagu, the Emergency Preparedness and Response Officer, Mr. Emmanuel Benyeogor, and the head of the NCDC's Risk Communication Unit, Dr. Yahya Disu.

The following table summarizes the various articles used to inform the review based on the risk factors for LF infection, interventions implemented, and the barriers to eradication of the disease in Nigeria, as identified by the respective authors.

Desk Review Articles

REFERENCE	DISEASE	SOURCE TYPE	POPULATIONS	RISK FACTORS IDENTIFIED	INTERVENTIONS	BARRIERS
Adebayo et al., 2015	LF	Peer-reviewed article	Nigeria (Ebonyi, Nasarawa, and Plateau States)	• Low to non-adherence to infection control and prevention guidelines when dealing with an infectious disease outbreak	A cross-sectional study was conducted using a standardized, self-administered questionnaire, which enquired about the risk perception, knowledge, attitude, and health-seeking behavior towards Lassa fever among health care workers	N/A
Ajayi et al., 2013	LF	Peer-reviewed article	Nigeria	• Eating rats or poorly stored/rat-infested food • Nosocomial infection due to slow identification of suspected cases and exposure to bodily fluids of infected patients during surgery	Analysis of an LF outbreak	• Lack of laboratory capacity for quick diagnosis confirmation, which is addressed through empirical treatment (ribavirin) while waiting for results. • Financial and logistical challenges in confirming cases • Lack of adequate personal protective equipment (PPE) supplies for health

REFERENCE	DISEASE	SOURCE TYPE	POPULATIONS	RISK FACTORS IDENTIFIED	INTERVENTIONS	BARRIERS
						care workers (HCWs) • Inadequate knowledge among community and HCWs • Inability to trace origin of infection • Lack of epidemic preparedness
Akhmetzhanov et al., 2019	LF	Peer-reviewed article	Nigeria	• Rainfall pattern: strongly negatively correlated with LF incidence • Rodents migrate to within proximity to human settlements to breed and hibernate during the dry season, increasing rodent-human contact rate and consequently increasing the probability of acquiring LF.	N/A	N/A

REFERENCE	DISEASE	SOURCE TYPE	POPULATIONS	RISK FACTORS IDENTIFIED	INTERVENTIONS	BARRIERS
Bagcchi, 2020	LF	Peer-reviewed journal article	Nigeria	Increased human-rodent contact facilitated by • General worsening of environmental sanitation • Explosion in the populations of the *Mastomys* rodents.	N/A	N/A
Bonwitt et al., 2016	LF	Peer-reviewed article	Sierra Leone	• Human consumption of rodents	N/A	N/A
Dzingirai et al., 2017	Zoonotic diseases	Peer-reviewed article	Africa	• Rodent consumption, rural agriculture (exposure in fields) • Poverty and food insecurity • Long-term cultivation and cohabitation of humans and animals in these environments	N/A	• Weakness of the government and economy contributing to health system failures • Colonialism and neocolonialism
Ekweume and Asogwa, 2018	LF	Peer-reviewed article	Ebonyi State, Nigeria	School children's consumption of:	Survey methodology to investigate impact of social media in handling	

REFERENCE	DISEASE	SOURCE TYPE	POPULATIONS	RISK FACTORS IDENTIFIED	INTERVENTIONS	BARRIERS
				• Rodents (rat hunting) • Rodent feces/urine-infested garri	of 2018 LF outbreak in Ebonyi State	
Federal Republic of Nigeria, 2019	Zoonotic diseases	Strategic Health Plan	Nigeria	Increased human population growth results in: • Increased need for food (need for farming and animals as sources of food) • Human encroachment on ecosystems that are at high risk for disease transmission, closer integration with animals/wildlife, and rapid urbanization	N/A	N/A
Iroezindu et al., 2015	LF, Ebola	Peer-reviewed article	Nigeria	• Direct exposure to infected rats' excreta • Person-to-person transmission	N/A	• Failure of HCWs to use appropriate PPE • Absence of viral hemorrhagic fever isolation units

REFERENCE	DISEASE	SOURCE TYPE	POPULATIONS	RISK FACTORS IDENTIFIED	INTERVENTIONS	BARRIERS
						• Lack of nearby facilities for laboratory diagnosis • Availability of ribavirin on demand for treatment
Ijarotimi et al., 2018	LF	Peer-reviewed article	Nigeria	• Contact with contaminated excreta from infected rodents • Human contact with bodily fluids of infected person • Nosocomial infection due to lack of infection control measures in hospitals	N/A	N/A
Kumoji et al., 2018	Priority zoonotic diseases	Literature review	West Africa	• Rural poverty • Human handling of rats	N/A	N/A
Oladeinde et al. 2014	LF	Peer-reviewed article	Nigeria	• Poverty • Overcrowding • Rat consumption	Study aiming at assessing public awareness of LF in Edo State, Nigeria	• No knowledge of vehicle of transmission of LF

REFERENCE	DISEASE	SOURCE TYPE	POPULATIONS	RISK FACTORS IDENTIFIED	INTERVENTIONS	BARRIERS
				• Poor sanitary conditions • Living in rural areas • Existing misconceptions around modes of transmission of LF		• Low to non-existent knowledge about LF prevention methods
Otitoju et al., 2019	Vector-borne diseases	Peer-reviewed article	Nigeria	• Desertification due to increased ambient temperature, altered precipitation, and climatic variability, which alters the geographical range and seasonality of transmission of many vector-borne diseases	• Investigates the impact of bush burning on the environment, health, and economy of Nigeria; also highlights the effects of bush burning on global warming, climate change, habitat destruction, loss of biodiversity, increased erosion, and the resurgence of vector-borne diseases	N/A
Oyeniran and Chia, 2020	COVID-19	Peer-reviewed article	Nigeria	N/A to LF	Emergency collection review of Nigeria's response to COVID-19 pandemic	• Public engagement and compliance with regulations

REFERENCE	DISEASE	SOURCE TYPE	POPULATIONS	RISK FACTORS IDENTIFIED	INTERVENTIONS	BARRIERS
Salyer et al., 2017	Zoonotic diseases	Peer-reviewed article	Thailand, Kenya, Ethiopia, Azerbaijan, Cameroon, South Africa, and the Democratic Republic of the Congo	N/A to LF	N/A	N/A
Tambo et al., 2018	LF	Peer-reviewed article	Nigeria	• Poverty • Spread by human-rodent contact with infected rodents' feces or urine • Inhaling contaminated dust, eating contaminated food, or coming into contact with the fluids of an infected person (dead or alive)	N/A	N/A
Tobin et al. 2014	LF	Peer-reviewed article	Nigeria (Edo State)	• Poor hygiene practices • Low knowledge of disease	Multistage sampling with 421 respondents	N/A

REFERENCE	DISEASE	SOURCE TYPE	POPULATIONS	RISK FACTORS IDENTIFIED	INTERVENTIONS	BARRIERS
				transmission and prevention • Too much general information about LF which is leading to confusion		
Usuwa et al., 2020	LF	Peer-reviewed article	Nigeria Albakaliki LGA, Ebonyi State respondents aged 18 years and above in affected communities	• High LF incidence during the dry season (November–April) when outbreaks often occur.	Cross-sectional study of knowledge and risk perception	• Poor knowledge of LF among the respondents and the high proportion of low perceived benefit of LF infection preventive practices show a gap in the content and acceptance of LF risk communication information in the state despite the high level of perceived threat of LF and self-efficacy towards LF preventive practices.

REFERENCE	DISEASE	SOURCE TYPE	POPULATIONS	RISK FACTORS IDENTIFIED	INTERVENTIONS	BARRIERS
Wogu et al., 2020	LF	Peer-reviewed article	Nigeria	• High fatality rate from outbreaks due to the prevalence of unhealthy sanitary and environmental behaviors that increase the risk of LF. For example, people (particularly children) living in rural areas eat rodents, which are the primary carriers of LF.	Literature review to show reportage of LF outbreaks	N/A
Wogu, 2018	LF	Peer-reviewed article	Nigeria Ebonyi State rural communities	• Poor sanitation, Overcrowding • Inadequate resources to manage cases • Lengthy dry season • Weak health system • Poor public information program • Poor epidemic preparedness	Investigates the impact of media campaign on the prevention and spread of LF in Ebonyi State	• Results of analysis reveal that the media campaign has rural reach but has little or no impact.

Results

The results of this desk review are organized based on the objectives above. It establishes a clear contextual understanding of the biology and epidemiology behind LF in Nigeria. It then focuses on knowledge, attitude, and practices around LF and LF RCCE strategies. States other than Ebonyi, Bauchi, and Plateau were highlighted when data in the three states were scarce.

Context and Epidemiology

LF is a hemorrhagic viral fever with a rodent host, *Mastomys natalensis*. It is endemic in parts of West Africa. In Nigeria, LF is referred to as a disease of poverty and has emerged as a disease with severe outbreak potential and as a public health threat in the country (Tambo et al., 2018). The primary transmission of LF to humans occurs through direct or indirect contact with rodent body fluids such as urine, feces, saliva, or blood. Secondary human-to-human transmission occurs through contact with bodily fluids or objects in the household or in health care facilities that have been contaminated (Dzingirai et al., 2017). Human-to-human transmission can also take place through aerosol secretions from sneezing, sputum, stool, urine, blood, and seminal fluid (Inegbenebor et al., 2010). There is no vaccine, and prevention is based on improved hygiene practices, including safe food storage, rodent proofing, and infection control practices (Bonwitt et al., 2016).

The incubation period of LF ranges from 6 to 21 days. The onset of the disease, when it is asymptomatic, is usually gradual, starting with fever, general weakness, and malaise. When symptomatic, symptoms include headache, sore throat, muscle pain, chest pain, nausea, vomiting, diarrhea, cough, and abdominal pain. Misdiagnosis is usually common at this stage because the symptoms can be attributed to other common febrile illnesses such as influenza, malaria, and typhoid. In fatal cases, death usually occurs within 14 days of symptom onset. The disease is especially severe late in pregnancy, with maternal death and/or fetal loss occurring is more than 80% of cases during the third trimester (WHO, 2017)[2].

In Nigeria, the annual peak of human cases is usually observed during the dry season (December to April), following the reproductive cycle of the *Mastomys* rats in the rainy season (May to June). The breeding season for the rodents starts about two months after the end of the rainy season (November). At that time, newborn offspring, and a scarcity of food on the ground force mature rodents to approach human-occupied areas, which may lead to a rise in the contact frequency between humans and infected rodents. This high-exposure frequency persists until the rainy season starts again the following year, at which point the rodents migrate back to the ground and the incidence of human cases of LF declines.

[2] World Health Organization: 2017 Lassa fever fact sheet. https://www.who.int/en/news-room/fact-sheets/detail/lassa-fever

These findings highlight the importance of seasonal ecology of animal hosts in explaining the seasonality of LF epidemics (Akhmetzhanov et al., 2019). In addition to seasonal ecology, it is important to recognize that rats are a delicacy in certain remote areas of Nigeria, with some overlap with our three states. A person can become infected with LF by eating a sick rat and can subsequently infect others who come in contact with their bodily fluids.

Environmental challenges such as climate change can help explain the resurgence of LF; in particular, a link exists between global warming and booms in rat populations. Warmer temperatures lengthen the agricultural season, and rodents are known to breed more in warmer weather and to have easy access to food. In addition, the scarcity of food and bush burning in Nigeria during the dry season pushes rodents to seek food. Therefore, the more rodents produced in the rainy season, the more rodents searching for food in the dry season, which leads to more contact between humans and rodents (Akhmetzhanov et al., 2019). Recurring bush burning has gradually become the norm in many northern states in Nigeria, which overlap with two of the states in this desk review—Plateau and Bauchi (Otitoju et al., 2019).

Bush burning involves using fire to clear uncultivated land of weeds and grasses. In Nigeria, most farmers use this practice as an easy and convenient way to prepare for the planting season, and more than half of bush burning in the country is deliberate (Otitoju et al., 2019). Bush burning has an impact on the atmosphere, the environment, and the climates (specifically global warming). Moreover, bush burning leads to deforestation, which also has a negative impact on the natural habitats of many animals, including rodents, which therefore increases the proximity of rodents to human populations (Akhmetzhanov et al., 2019). Human populations are also expanding in size and geographic range globally.

With Nigeria being the seventh most populous country on the planet, with an estimated population of 200 million, factors such as unplanned urbanization, population explosion in the cities and urban areas, indiscriminate refuse disposal, poor personal hygiene, and overcrowding facilitate contact between humans and rodents (Wogu et al., 2018).

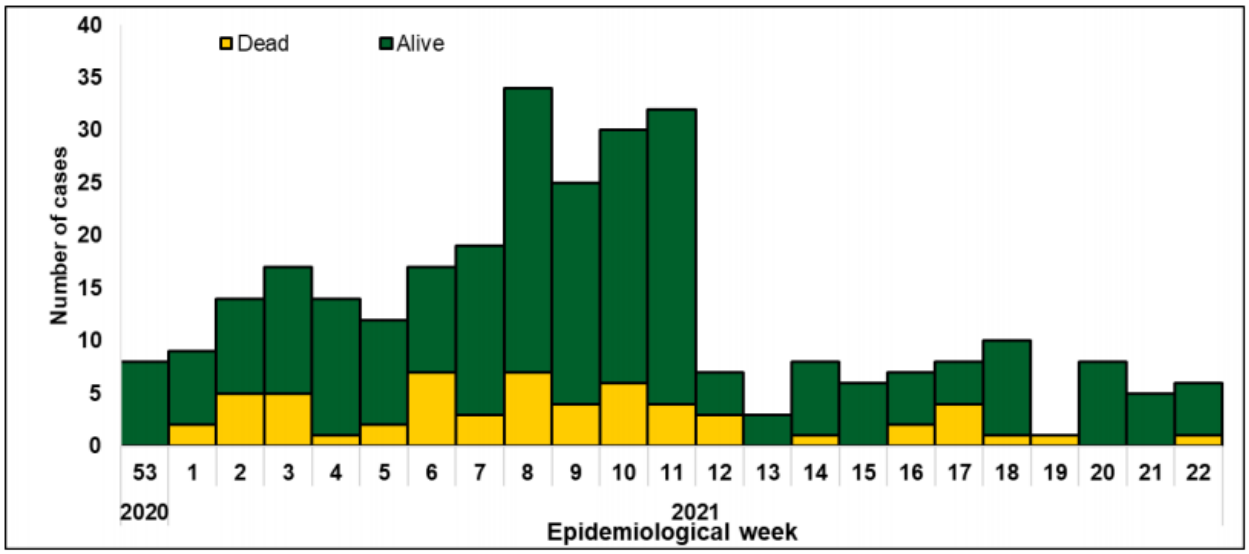
Surveillance, Reporting, and Resurgence of LF in Nigeria

Nigeria has experienced a resurgence of LF in the past few years, characterized by regular outbreaks with an increasing number of suspected cases, dry season peaks, and high morbidity (Bagcchi, 2020). LF data are managed and shared with the public by the Nigeria Centre for Disease Control (NCDC) through weekly epidemiological situation reports.

From January 1, 2021, through June 6, 2021 (Figure 1), the NCDC reported 292 laboratory-confirmed cases of LF and 59 deaths due to the disease (case fatality ratio of 20.2%). This is lower than the same time period in 2020, when NCDC reported 1,021 confirmed cases and 212 deaths from LF (case fatality

ratio of 20.8%). For both 2020 and 2021, heightened LF cases are most notable during the months of January to March.[3]

Figure 1: Epidemic Curve of Confirmed LF Cases From January 2021 (Week 1) to June 2021 (Week 22)[3]



In its most recent weekly report, NCDC indicates that the confirmed cases were reported across 14 states of Nigeria. Seventy-nine percent of the reported cases were from the states of Edo (44%), Ondo (29%), Taraba (6%), Ebonyi (5.8%), Bauchi (3.4%), and Plateau (2.8%). Elevated cases in Edo and Ondo states are consistent with the previous year's statistics as well, with novel cases seen in Taraba, a neighboring state of Plateau.[3]

Figure 2: Confirmed LF Cases by States in Nigeria From June 2021 (week 22)[3]

[3] NCDC Situational Reports: https://ncdc.gov.ng/diseases/sitreps/?cat=5&name=An%20update%20of%20Lassa%20fever%20outbreak%20in%20Nigeria

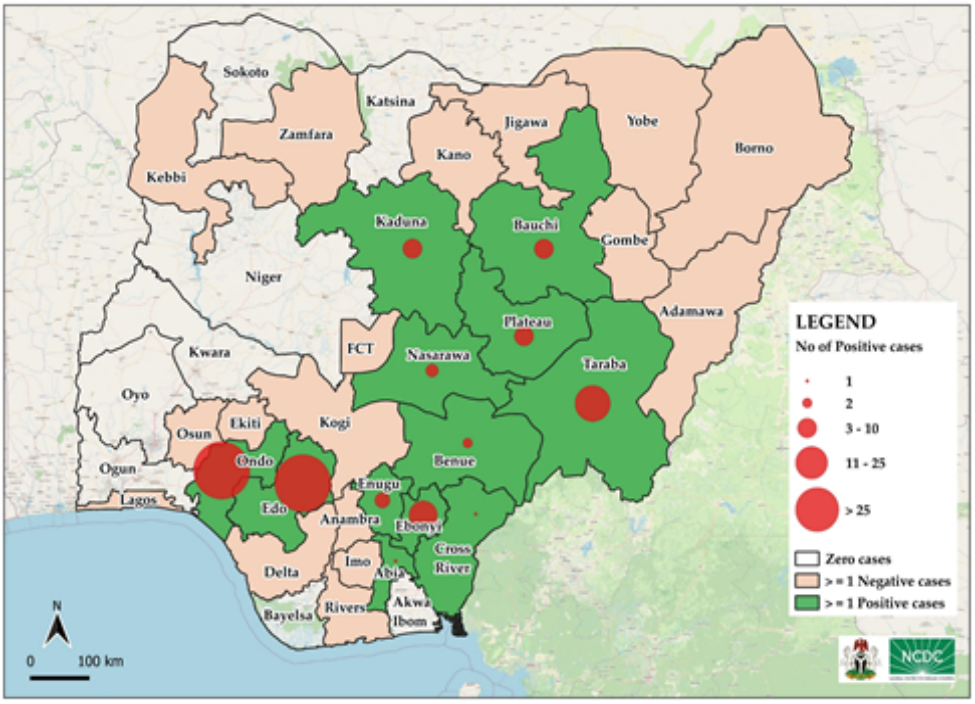


Table 3: LF Trends in Bauchi state, Nigeria, During 2019–2021[4]

SUSPECTED CASES			CONFIRMED POSITIVE CASES			DEATHS IN CONFIRMED CASES			CASE FATALITY RATE (CFR %)		
2019	**2020**	**2021**	**2019**	**2020**	**2021**	**2019**	**2020**	**2021**	**2019**	**2020**	**2021**
150	418	61	57[5]	53[5]	6[5]	9	19	2	20.5	48.00	20.0

Table 4: LF Trends in Ebonyi State, Nigeria, During 2019–2021[6]

SUSPECTED CASES			CONFIRMED POSITIVE CASES			DEATHS IN CONFIRMED CASES			CASE FATALITY RATE (CFR %)		
2019	**2020**	**2021**	**2019**	**2020**	**2021**	**2019**	**2020**	**2021**	**2019**	**2020**	**2021**
No data	372	99	57	81	12	No data	23	2	35.0	31.00	11.00

Table 5: LF Trends in Plateau State, Nigeria, During 2019–2021[5]

[4] NCDC Situational Report: https://ncdc.gov.ng/diseases/sitreps/?cat=5&name=An%20update%20of%20Lassa%20fever%20outbreak%20in%20Nigeria

[5] From email correspondence with NCDC

[6] NCDC Situational Report: https://ncdc.gov.ng/diseases/sitreps/?cat=5&name=An%20update%20of%20Lassa%20fever%20outbreak%20in%20Nigeria

SUSPECTED CASES			CONFIRMED POSITIVE CASES			DEATHS IN CONFIRMED CASES			CASE FATALITY RATE (CFR %)		
2019	**2020**	**2021**	**2019**	**2020**	**2021**	**2019**	**2020**	**2021**	**2019**	**2020**	**2021**
No data	188	18	36	33	6	No data	8	0	30.0	29.00	0.00

Men and women between the ages of 21 and 30 years old have been the most affected by the outbreak in the current year, with slightly more women than men.[5] The literature lacks an explanation as to why this difference exists in Nigeria, but studies in other countries such as Sierra Leone allude to reasons of occupational risk factors particularly in agriculture (Dzingirai et al., 2017).

Coordination of LF Response at the National and State Levels

There are current research activities around an LF vaccine in the world. Various candidates including live-attenuated, vesicular stomatitis virus vectored, and plasmid DNA vaccines are being assessed through animal trials. Currently, the most promising candidate is the DNA vaccine INO-4500, which is the only candidate that has entered Phase 1b clinical trials and was administered to the first human participants at Noguchi Memorial Institute for Medical Research in Ghana. Phase 1b will enroll 220 participants, who will receive two doses, 28 days apart. Outcomes from this phase will inform dosage recommendations for Phase 2 clinical trials, which will be conducted across West Africa[7].

In the absence of an LF vaccine, NCDC uses prevention, detection, and response as public health strategies to respond to the frequent outbreaks of LF nationally and in all affected states[8] (Bagcchi, 2020). To lead and coordinate responses to any health outbreaks and emergencies, NCDC established national emergency operations centers (EOCs) at the federal and state levels. An EOC is a physical building where an incident management system (IMS) is activated during a public health emergency. The IMS is activated to improve information sharing as well as joint programming (planning, implementation, monitoring, and evaluation) towards improved management during identified public health emergencies.

The NCDC Public Health Emergency Operations Center (PHEOC) started in 2018 because of the Cerebrospinal Meningitis (CSM) outbreak in 2017. Before the establishment of the PHEOC, about seven states had the Polio EOC set up with funding from the Bill and Melinda Gates Foundation and other stakeholders. Between 2018 and 2021, thirty-one (31) PHEOCs have been established. In the process of establishing an EOC, 2 categories of staff are trained which are the core staff and the surge staff at the state level. The core staff makes up the core team of the state epidemiologist while the surge staff includes every other person that should be involved in a response during an outbreak.

[7] European Pharmaceutical Review, 2021: https://www.europeanpharmaceuticalreview.com/news/144089/patient-dosed-with-first-lassa-fever-vaccine-to-reach-human-trials/
[8] WHO Lassa Fever Webpage: https://www.who.int/emergencies/disease-outbreak-news/item/2020-DON245

The IMS included several pillars of action such as surveillance, laboratory, RCCE, infection prevention control (IPC), case management, and safety. Moreover, each state has an IMS with pillars particular to the health challenges of the state. For instance, a state might add a health security pillar and others might not if health security is not an issue. Each specific disease has an IMS activated. For instance, in the case of LF, the technical persons that work when an IMS is activated are called the incident management team. When an IMS is dormant, it becomes a technical working group (TWG) at both the state and national levels. In essence, the LFTWG is the same as the LF IMS, but TWG is when the IMS is dormant. In periods of non-emergencies, the TWGs are both the state and national levels focus on developing strategies and staying abreast of changes in the specific health area to inform future decision and readiness of the country before the next outbreak.

The LFTWG is very active at the national level but less regulated at the state level. At the national level, the LFTWG manages routine LF data from the state disease surveillance and notification officers, convening all the necessary pillars on a regular basis and implementing risk communication activities. It also strengthens LF surveillance, diagnosis, and treatment, and prepares for the next LF emergency. With the peak season of LF usually occurring from December to April, the LFTWG starts planning a response in June based on lessons learned from the previous LF season. The LFTWG also develops guidelines for appropriate case management and IPC measures that are then disseminated to all EOCs in the affected states during an LF outbreak. Before determining whether there is a LF outbreak or not and activating an IMS, a risk assessment is conducted at both the state and national level looking at six different criteria. They are 1) Geography and environment (the nature of the environment), 2) Severity of the outbreak, 3) Capacity of the state to cope, 4) Spread of the disease, 5) Political and media interest, and 6) International significance.

Given the results of the risk assessment, the IMS enters one of three modes of activation as further explained in Figure 6: 1) Watch Mode (Level 1) meaning that the risk is low, 2) Alert Mode (Level 2) meaning that the risk is medium, and 3) Response Mode (Level 3) meaning that the risk is high. Moreover, Level 1 means that the outbreak is within a contained area either in a unit, within a ward, LGA etc. The state alone handles the outbreak at this level. At Level 2, the NCDC IMS steps in to support the state and coordinate efforts. In this case the state is still leading the response but with external support from the NCDC. Finally at Level 3, the NCDC takes over the response as the state is overwhelmed. However, leadership still lies with the state because it is the state's government territory.

The IMS brings together an interdisciplinary, multi-partner technical team to ensure a well-coordinated response and swift control of the outbreak. It also brings members of all the various pillars together to develop a response plan with guidelines that are then communicated to the respective state EOCs. Strengthening the operationalization of state-level EOCs is a key priority of the NCDC 2017–2021 Strategy and Implementation plan[9]. Strategic conversations are ongoing regarding the establishment of

[9] NCDC 2017-2021 Strategic and Implementation Plan: https://ncdc.gov.ng/themes/common/files/establishment/fdaa94605dcb87478f9b12002ff7eeb7.pdf

EOCs at the LGA level to support response during an outbreak. However, the question remains about whether the LGA EOCs should be led by states or the NCDC. For a decentralized response and proper ownership of the system, the NCDC prefers these to be led by states. To inform this decision, the recommendation is for the NCDC to pilot this approach in two or three LGAs and use lessons learned to arrive at a strategic decision.

The country's experience with the COVID-19 pandemic outbreak provides a recent example of how the IMS gets activated. During the COVID-19 response, the IMS was activated similarly using the steps described above. First, the national ICC, also called the National Incident Coordination Center, was activated to support response to the outbreak. The IMS, established in 2017 by NCDC, was responsible for central coordination of data collection, analysis, dissemination, operations, and logistics, and support of the state-level IMS, all of which were also subsequently activated.[10] The global severity and publicity of the pandemic highlighted the issues of inadequate resources, capacity, and coordination among the state IMS, but it also provided an opportunity for improvement through increased support from NCDC and partners such as the African Union, the African CDC, and WHO.[11]

Before the first COVID-19 case was identified in the country, the COVID19 TWG prepared by sharing the disease case definition to HCWs, disseminating information on prevention measures, establishing five laboratories for testing, and gearing up the incident management system that provides coordination between the national and state-level IMS. After the first case was confirmed in late February 2020, the IMS was activated at level 3, which is the highest level in a health emergency (Figure 6). This was followed by the activation of state-level IMS, and the addition of two testing laboratories in two major cities, bringing the total number of laboratories to seven. The main tasks of the state-level IMS were to coordinate response activities of risk communication, health care preparedness, heightened surveillance of entry points, expansion of laboratory testing facilities, and self-isolation and mass gathering guidelines (Oyeniran & Chia, 2020).

Fifteen rapid response teams were also deployed, and the 2004 Quarantine Act was revised to include COVID-19 Regulations 2020 to restrict population movement and the subsequent spread of the virus in high-prone states (Oyeniran & Chia, 2020). State IMS were responsible for epidemiological, surveillance, case management, laboratory, and ports of entry data collection, as well as communication and public messaging. Prioritization of COVID-19 efforts coupled with several resource limitations led to interruptions of other operations and programs including immunization, nutrition, tuberculosis, measles, and acute febrile illness (such as LF) response at some state-level IMS, while other states reported that there were no changes in any pre-established program due to the pandemic.[12]

[10] Public Health EOC Guidance: https://www.epidemic-em.org/case-studies/nigeria/

[11] Nature Medicine: https://www.nature.com/articles/d41591-020-00004-2

[12] Public Health EOC Guidance: https://www.epidemic-em.org/case-studies/nigeria/

Figure 6: Nigeria PHEOC Level of Activation and Grading Criteria[13]

Response Levels – Nigeria PHEOC	
Level	**Assessed Foreseeable Risk and Actions**
1 (Green)	1. Public health impact including public interest is limited to one state, however it exceeds what is determined to be routine work. The response can be managed at a state level. 2. The command and control (EOC) of the incident will be locally focused, and the coordination will be from the State EOC. 3. It requires onsite NCDC support by a Rapid Response Team but incident leadership is from the state. 4. External partners will be invited to provide support at state level. 5. NCDC will monitor this through the Incident Coordination Centre and will receive Situation Reports (SitReps) provided by the state team.
2 (Orange)	1. This is either an escalation of a level 1 event or event could also be designated as a level 2 event from the start. 2. Public health impact including public interest or concern could expand beyond the affected State. 3. The public health implications of the incident or public anxiety go beyond affected LG / State. 4. A National Incident Management Team is set up with specific terms of reference guided by National leadership. 5. An Incident Manager is appointed at NCDC to provide coordination and overview from the national level providing support to state. 6. The response may involve inter-agency and a larger external partner support. 7. The Incident Manager will issue briefing notes to be cascaded via the EOC's daily / weekly activity report and / or briefing to ensure that all parts of the response organization are aware of the incident and its management.
3 (Red)	1. The impact of the incident has significant national and / or international implications. 2. Public health impact including public interest or concern for the national population is severe. 3. Full central EOC coordination, enhanced extended surveillance is required through NCDC. 4. A level 3 response requires national / federal level direction or leadership, resource mobilisation and ensures national coordination while providing a more proportionate response to the threat to the public. 5. Requires a significant interaction with MDAs at the national level. 6. The response will involve inter-agency liaison and will require significant NCDC and partners / international resources.

COVID-19 highlighted the coordination and capacity strengthening strengths and opportunities of each state's EOC that affect their response to all outbreaks, including LF. For example, confirmed LF cases are referred to designated treatment centers following optimized standard of care protocols. Nigeria currently has six laboratories with capacity to test for LF infection. However, with the recent COVID-19 pandemic, the federal government has increased the number of COVID-19 laboratories to cover all states in Nigeria. These testing centers will also be used to test for LF during the next outbreak. In addition to testing centers, surveillance activities include the use of the WHO Rapid Case Management Form[14] to enhance active case finding and allow investigation teams to ensure all relevant information is recorded.

Knowledge, Attitude, and Practices

In February 2020, research conducted in affected communities in Ebonyi state found a high level of knowledge about LF among community members. However, among the 326 study respondents, the authors found that knowledge of LF symptoms and risk factors was poor despite high levels of awareness of the disease in the state. Moreover, respondents had better knowledge of risk factors of the disease compared with its symptoms, which could hinder the early identification of suspected cases.

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[13] Handbook for Public Health Emergency Operations Center Operations and Management Brazzaville: WHO Regional Office for Africa; 2021. License: CC BY-NC-SA 3.0 IGO. Cataloguing-in-Publication (CIP) data. https://www.afro.who.int/publications/handbook-public-health-emergency-operations-center-operations-and-management

[14] WHO disease investigation forms: https://www.who.int/emergencies/outbreak-toolkit/data-collection-standards/disease-case-investigation-forms

Finally, a third of the respondents in the study reported being unlikely to accept a person who had been treated for LF, which shows some degree of stigmatization that could delay presentation for treatment of LF (Usuwa et al., 2020).

Regarding risk perception, most respondents had a high perception of susceptibility and severity if they do not carry out preventive practices but a low perception of benefits of LF preventative practices. Respondents wrongly perceived benefits of self-medication (which delays testing and case finding), bush burning (which drives rodents from bushes to residents' homes), and open air drying of food (which increases exposure to rodents' feces and urine) (Usuwa et al., 2020). Common misconceptions about sleeping under bed nets and using herbal medicine being effective prevention measures also contributed to decreased perception of susceptibility in a study by Oladeinde et al. (2014). A sizable number (7.4%) of respondents self-reported never hearing about LF, and of those aware of the disease, more than half did not know how to prevent it or how it was transmitted. While some respondents identified rat consumption as a mode of transmission, others assumed that LF was transmitted by mosquito bites and/or dog bites (Oladeinde et al., 2014).

Challenges also arise from community practices of rodent consumption, which Tobin et al. (2014) found to explain a high risk of rodent contact for 45.8% of respondents in their study. Among study respondents, other risk factors for contracting LF included poor knowledge of the disease (76.6% of respondents) and poor hygiene practices (33.7%). Other practices identified in Edo State included consumption of food contaminated by rodent excrement, poor food production, traditional autopsies of infected bodies, and drinking infected water as part of traditional burial practices (Inegbenebor et al., 2010).

Among HCWs, overall knowledge of the epidemiology, clinical features, and precautions in care for patients with LF is low. In their study of HCWs in Ondo state, Ijarotimi et al. (2018) found that less than half of respondents had good knowledge of LF, with registered nurses scoring the highest compared with health assistants, trainees, and community health extension workers. However, Adebayo et al. (2015) found high knowledge of LF among doctors and nurses in tertiary facilities specialized in caring for LF cases. Risk factors in health facilities include lack of isolation rooms, adequate PPE, and qualified health personnel, particularly at the primary and secondary levels. Ijarotimi et al. (2018) also found poor practice of infection prevention control measures regardless of the level of the facility.

These results can be contextualized with knowledge, attitude, and practices identified in Sierra Leone, where LF incidence in the eastern region is reported to be the highest in the world. A study by Bonwitt et al. (2016) in Sierra Leone indicated both high awareness of LF as a serious and fatal disease and high knowledge of symptoms and the special burial practices required. However, no respondents in the study were aware of the exact carrier of LF and 62% of respondents did not associate LF with animals. Of those that identified LF as animal borne, misconceptions about which rodent species to avoid were common (Bonwitt et al., 2016). Dzingirai et al. (2017) found that perceived risk of transmission from the correct LF-carrying rodent species *M. natalensis* was zero. In some communities in Sierra Leone, rat

consumption was argued to be necessary for a balanced diet, while in others it was associated with poverty and therefore highly stigmatized. Agricultural work in mounded fields and gardens was also identified as a major risk factor for transmission of LF.

RCCE Strategies

With LF being transmitted through human contact with rodent contaminated food or items, a One Health approach that addresses this animal-human-environment linkage is appropriate to address this epidemic disease (Tambo et al., 2018). Nigeria's One Health Strategic Plan, coordinated by NCDC prioritizes risk communication and intersectoral collaboration to facilitate surveillance data sharing, reports, transfers of laboratory specimens, and intervention planning and programming between the Federal Ministry of Agriculture and Rural Development (FMARD), the Federal Ministry of Environment (FMEnv), and the Federal the Ministry of Health at the national, state, and local government levels.

The mission of the 2019–2023 strategic plan is to "build a strategic, dynamic, and functional platform that advances human, animal, and environmental health through multidisciplinary and intersectoral collaboration."[15] The plan is based on five themes: surveillance and laboratory, training and research, governance and leadership, resource mobilization, and communication. The thematic goal of communication is to increase awareness of One Health for all stakeholders, including communities and the general public. This is closely related to the concept of RCCE. The five pillars of RCCE strategy are captured in the NCDC's One Health strategy through fostering collaboration between researchers and policy makers to develop and implement trainings, enabling communication and advocacy to improve public awareness through mass media, conferences, workshops, and town hall meetings with community stakeholders to disseminate culturally and linguistically appropriate messaging.

RCCE strategies specifically around LF are not new in Nigeria. In the absence of an LF vaccine, RCCE strategies are even more important. They involve the dissemination of messages through television, radio, print, and social media led by NCDC and other local and international entities. Moreover, traditional methods of communication, such as mobilization through religious leaders and HCWs, are also often used. Current examples of RCCE include sensitization and awareness campaigns to sensitize community members (Figure 7) and HCWs (Figure 8) on the cause of LF, symptoms of LF, and prevention methods.

Mass media reporting is crucial before and during an epidemic to share timely and correct information about a health emergency in addition to increasing preparedness of communities to respond. Owing to a lack of data from Bauchi and Plateau States, data from Ebonyi are highlighted. In Ebonyi state, state government and nongovernmental organizations (including faith-based organizations) (Wogu et al., 2020) used television and radio stations, newspapers, posters, banners, and HCWs to sensitize rural

[15] Nigeria's One Health Strategic Plan: https://onehealthinitiative.com/publication/ncdc-nigeria-one-health-strategic-plan-2019-2023/

populations in the state. Messaging focused on discouraging consumption of potentially rat-contaminated food, identifying LF symptoms, and transmission routes (Ajayi et al., 2013). Ekweume and Asogwa (2020) also reported that during the 2018 outbreak, the State Ministry of Health identified four health behavior change measures: always covering meals and foodstuff, avoiding bush burning, killing rats as soon as they are sighted, and avoiding travel to peak case areas.

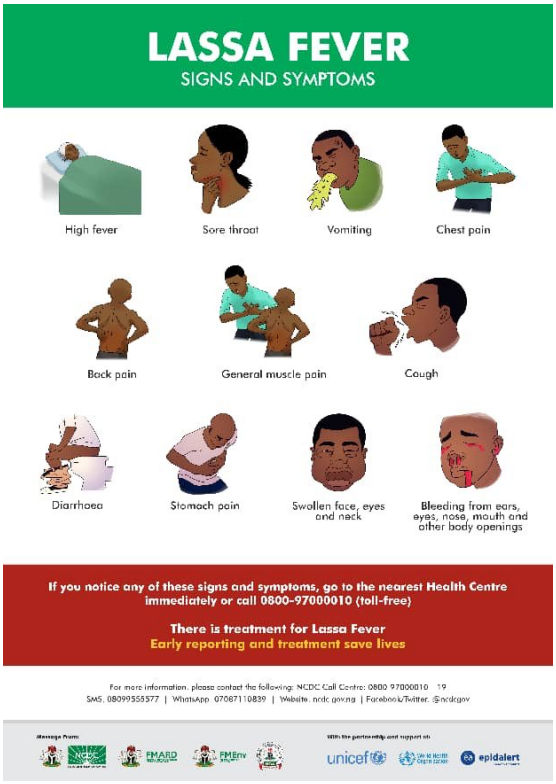
According to the impact evaluation conducted by Wogu et al. (2018), such sensitization activities indicated high awareness of LF in Ebonyi state, with radio and TV programs being identified as the main sources of information. However, respondents had low appropriate knowledge of LF symptoms in addition to low appropriate knowledge of the required personal and family hygiene practices and the health behaviors needed to prevent the spread of LF (regular hand washing, covering food [cooked and uncooked], and maintaining a clean home). The authors found that the lack of appropriate content in the awareness campaigns led to low adoption of preventative health behaviors in rural communities in Ebonyi state in addition to low use of curative health services. Moreover, challenges around network connection, when broadcasts were aired, and people's indifference contributed to the low adoption of preventative behaviors. Mass media was also used in southwestern Ogun State, with varying levels of success, particularly among people living in rural areas. Wogu et al. (2020) suggested that these findings may be associated with illiteracy and a lack of access to the internet or other forms of mass media. The authors indicated that the lack of awareness of prevention methods and rats as a vector of LF negatively affects the success of campaigns attempting to combat the spread of the disease.

Social media use also contributed to a high level of awareness about LF outbreaks in Ebonyi State. Ekweume and Asogwa (2020) found that about 74% of the 500 respondents in their study identified social media as the first place they got information about the outbreak, with only 0.7% of respondents receiving their information from the state Ministry of Health (MOH). The state MOH also disseminated information on the outbreak through their own social media platforms. Of all platforms, Facebook was regarded as the most significant source of information, followed by WhatsApp. Most respondents self-reported that awareness through social media influenced their health habits and that they shared information about the disease with their contacts. The MOH also provides toll-free numbers for community members to facilitate active surveillance and updates. Ajayi et al. (2013) noted that during the epidemic outbreak of early 2012, HCWs in the community received algorithm training to identify alert and suspected cases and refer them to the hospital facilities through the Ebonyi State MOH task-force committee, which facilitated transportation of cases to the Federal Teaching Hospital Abakaliki.

Person-to-person communication is also facilitated by community and religious leaders who are mobilized and trained to educate people within their areas and provide appropriate safe referral information to the closest hospital. Community HCWs have been trained on how to identify and refer alert cases to the hospital. The Ebonyi MOH then arranges for transport of suspected cases to the local hospital for evaluation, where HCWs use algorithms to diagnose cases (Ajayi et al., 2013). Within the hospital, infection control and surveillance teams conduct contact tracing, risk assessment, administering of postexposure prophylaxis, and decontamination of the environment (Iroezindu et al.,

2015). However, a cross-sectional study conducted among HCWs in Owo and Ose LGAs in Ondo state found that the LF surveillance system is slow to react at the beginning and during a pandemic, which causes slow laboratory reports and communication challenges between the different bodies coordinating the response. Delayed laboratory results, timely risk communication, and the low knowledge of health facility staff increase opportunities for infection of staff, potential wrong diagnosis of LF in patients, and more community spread of the disease.

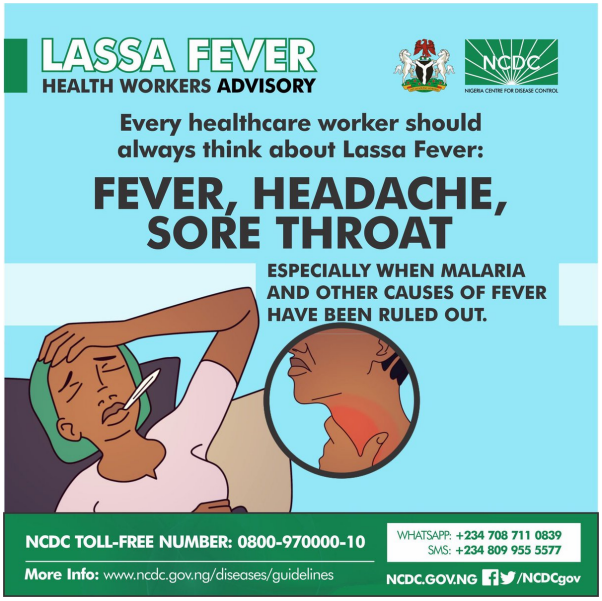
Figure 7: NCDC LF Public Health Advisory Poster— "Lassa Fever Signs and Symptoms"[16]



[16] NCDC Lassa Fever Health Advisory for the general public: https://twitter.com/NCDCgov/status/1214533415648796672?s=20

Figure 8: NCDC LF Public Health Advisory poster— "How to Prevent Lassa Fever"[17]

Figure 9: NCDC LF Health Workers Advisory Poster on Symptoms[18]



[17] NCDC Lassa Fever Health Advisory for the general public: https://twitter.com/NCDCgov/status/1214533415648796672?s=20

[18] NCDC Twitter Post on Lassa Fever: https://twitter.com/NCDCgov/status/1223628442773737477?s=20

Figure 10: NCDC LF Health Workers Advisory Poster on Suspicion[19]

Recommendations

Based on the findings above, key recommendations include using diverse methods of communication with the general public, strengthening data sharing at the state and national levels, and increasing knowledge of IPC strategies among HCWs.

Various methods of communication include the use of the same media channels but with target content incorporating LF symptoms, required preventative health behaviors, curative measures, and especially information on testing and treatment centers. Improved knowledge around LF symptoms for both community members and HCWs will lead to early identification of suspected cases, which reduces the chances of greater spread if isolation begins immediately (Figure 7). Including simple and short calls to action lines in messages will help remind community members not only of how to prevent LF and respond to observed symptoms but also the communal effort needed to keep individuals and communities safe. Audience segmentation can be appropriate in this instance because it can contribute to a higher effectiveness of the messages by taking into consideration the variations in perceived risk of contracting LF for various communities (rural vs. urban).

Messages to the general public should also stress the importance of preventive measures that aim to contain seasonal epidemics of LF. This can be envisioned as an eradication campaign, especially in rural areas with agronomic activities and in public markets in urban areas, which frequently attract rodents. Preventive measures may also include improved hygiene practices, safeguarding food from rodents during the nighttime, or designing educational campaigns that raise awareness of LF pathogenicity

[19] NCDC Twitter Post on Lassa Fever: https://ncdc.gov.ng/news/212/lassa-fever-healthcare-worker-advisory

(Figure 8). The implementation of such programs would be expected to lead to a decline in LF cases in the near future.

In addition to the strong efforts to raise awareness through mass media, there is a need for more structured partnerships with key stakeholders in the community. Identifying and working with key community influencers such as religious and community leaders and social and affinity groups will create a better understanding of the misconceptions and misinformation around LF and the barriers to behavior change. Through education and training of the identified community influencers, stigma around LF can be addressed, which could lead to earlier identification of suspected cases and reduce the size of the outbreaks

Given the recurring nature of LF outbreaks and challenges such as climate change, messages should also include safer agricultural practices, such as avoiding bush burning. At the national level, systematic policies to address climate change should be reviewed and revised using a One Health approach through inclusion of other cadres of health professionals such as veterinarians. In the meantime, enforcement of the existing government policies should be strengthened to regulate bush burning. In addition, community education should be provided on how bush burning affects the environment and soil fertility, and possible alternatives such as reforestation and safe herbicide use should be promoted (Otitoju et al., 2019). Closer collaboration between NCDC, FMARD, and FMEnv will be necessary to understand the threats of climate change on human and animal health in Nigeria to decrease the annual toll of LF outbreaks.

HCWs should be aware of the necessary IPC measures (basic hand hygiene, respiratory hygiene, and use of PPE) needed to avoid nosocomial infections. They should maintain a high awareness and suspicion of cases by identifying symptoms and ordering testing early (Figures 9 and 10). Increased training on proper hygiene practices around suspected LF cases, provision of and enforcement of use of needed PPE supplies, and hospital infrastructure for viral hemorrhagic fevers (purposed isolation units) will decrease the occurrence of nosocomial infections for both staff and other patients.

Limitations of the Desk Review

There are a few limitations to this desk review. Finding sources on LF interventions specific to the primary states mentioned in the background section was challenging. National level data were more readily available than information at the state and LGA level. LF data were scarce in Plateau and Bauchi States, so the desk review focused primarily on examples from Ebonyi State, where numerous interventions and evaluation studies have been conducted. Examples from other countries were also relied upon to identify similarities and gaps. Missing information was also supplemented through informal interviews with representatives from NCDC at the national level. Multiple meetings were also organized between Breakthrough ACTION-Nigeria staff and the disease surveillance and notification officers at the LGA level in the states in question.

Summary and Conclusions

LF is a re-emerging disease of epidemic proportions in West Africa. In Nigeria, poverty is the main driving factor. Consumption of rodents, rodent-related exposures during rural farming, seasonal ecology, and poor hygiene practices are all risk factors for transmission. Trends in surveillance data show that cases remain high during the dry season from December to March, while the case fatality rate remains steady at around 20 percent. Nigeria's response to disease outbreaks is through coordination between the state and national PHEOCs that manage deployment of rapid response teams.

Through this literature review, we found that while awareness of LF is high among community members, knowledge about risk factors, symptoms, and perceived benefits of preventative measures is low. Risk perception is also affected by misconceptions of the disease host and methods of transmission, which contributes to the continuation of community practices of rodent consumption and bush burning. Poverty and food insecurity are also barriers to preventive behaviors.

The animal-human-environment condition of the disease justifies the use of a One Health approach with an emphasis on RCCE. Mass media is the most common RCCE method currently utilized, particularly in Ebonyi state. Person-to-person community engagement efforts involve community and religious leaders and community HCWs receiving training to increase awareness on identifying symptoms.

Recommendations for Breakthrough ACTION Nigeria, to address LF in Nigeria focus on strengthening ongoing RCCE efforts through targeted messaging that is specific, measurable, and modifiable. Methods of mass media and social media as cues to action should continue, along with audience segmentation and greater collaboration with community stakeholders and other implementing partners. Given the seasonality of the LF outbreaks, RCCE efforts should be geared towards preparing national and state governing bodies through advocacy and capacity building activities for a more proactive response ahead of a LF outbreak. Finally, addressing the systemic challenges of climate change and sustainable agricultural practices require closer collaboration between NCDC, FMARD, and FMEnv.

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