Incidence of Lassa fever disease and Lassa Virus infection in five West African countries: a prospective, multi-site, cohort study

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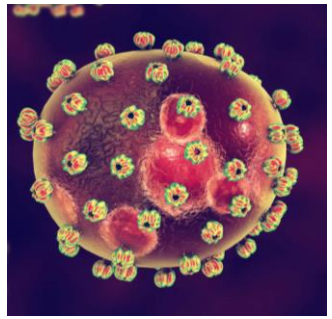
ASTMH 2024
16 November 2024

Lassa Fever Disease

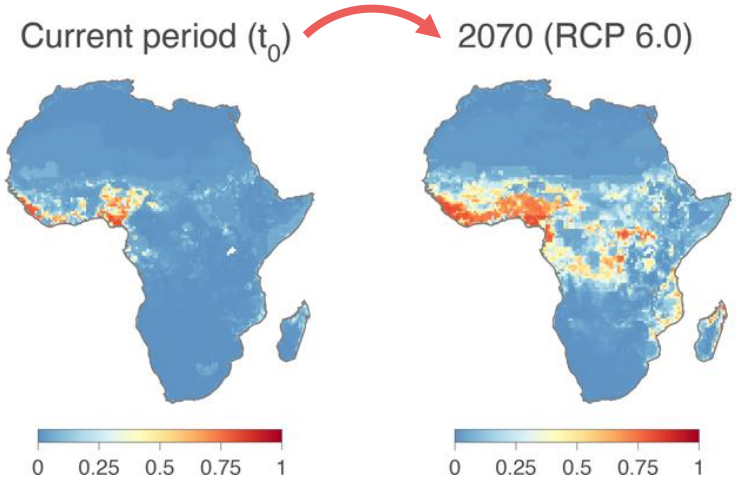
- Severe **haemorrhagic fever** caused by Lassa virus
- Transmission mainly from **rodent** (animal reservoir) but also **person-to-person** (nosocomial)
- Case management:
  - Mortality of **15-20% in hospitalized** patients and **30% in pregnant women** during last trimester[2]
  - Standard treatment: **ribavirin**
- **Endemic in West-Africa** & pandemic potential
  - CDC estimates **100k-300k cases** & **5 000 deaths** annually
- **No licensed vaccine**
  - **Priority pathogen** list for WHO's R&D Blueprint



Lassa virus

Mastomys natalensis[1]

Projection of human population at risk of LASV infection in 2070[3]



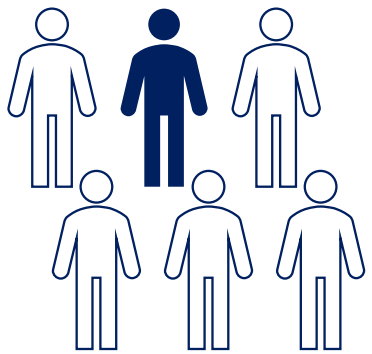
[1]Kelly et al. 2013 [2]Okogbenin et al. 2019 [3]Klitting et al. 2022

Lassa Vaccine Development

About 10 years & USD 100s of millions[1]

Pre-clinical	Phase 1 Safety	Phase 2 Immunogenicity	Phase 3 Efficacy	Regulatory approval
Completed	**Ongoing**	**Ongoing**	**Information needed**	

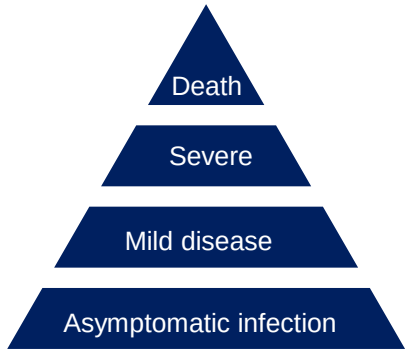
Incidence ?



Sero-protection ?

Risk groups ?

Severity ?



[1]Gouglas et al. 2018 *Lancet Global Health*

Primary Objectives of ENABLE

To assess the incidence rates of symptomatic **Lassa fever disease** & **Lassa virus infection** by country, age-group, etc.

20 000 participants

4 000 participants

3 000 participants

Baseline blood sample

LASV exposure (ELISA IgG)

− No

+ Yes

contacted every 2 weeks for 2 years

Fever? Symptoms?

Suspect case

RT-PCR+?

Symptomatic Lassa fever disease

visited every 6 months

0 6 12 18 24

− − + + +

Blood sample

Sero-conversion?

Lassa virus infection

Sites & Enrolment of Participants

3,014 HH

Refusal: 433 HH
65% due to blood sampling

20,898 pp (2581 HH)

No consent: 400 pp
45% due to blood sampling

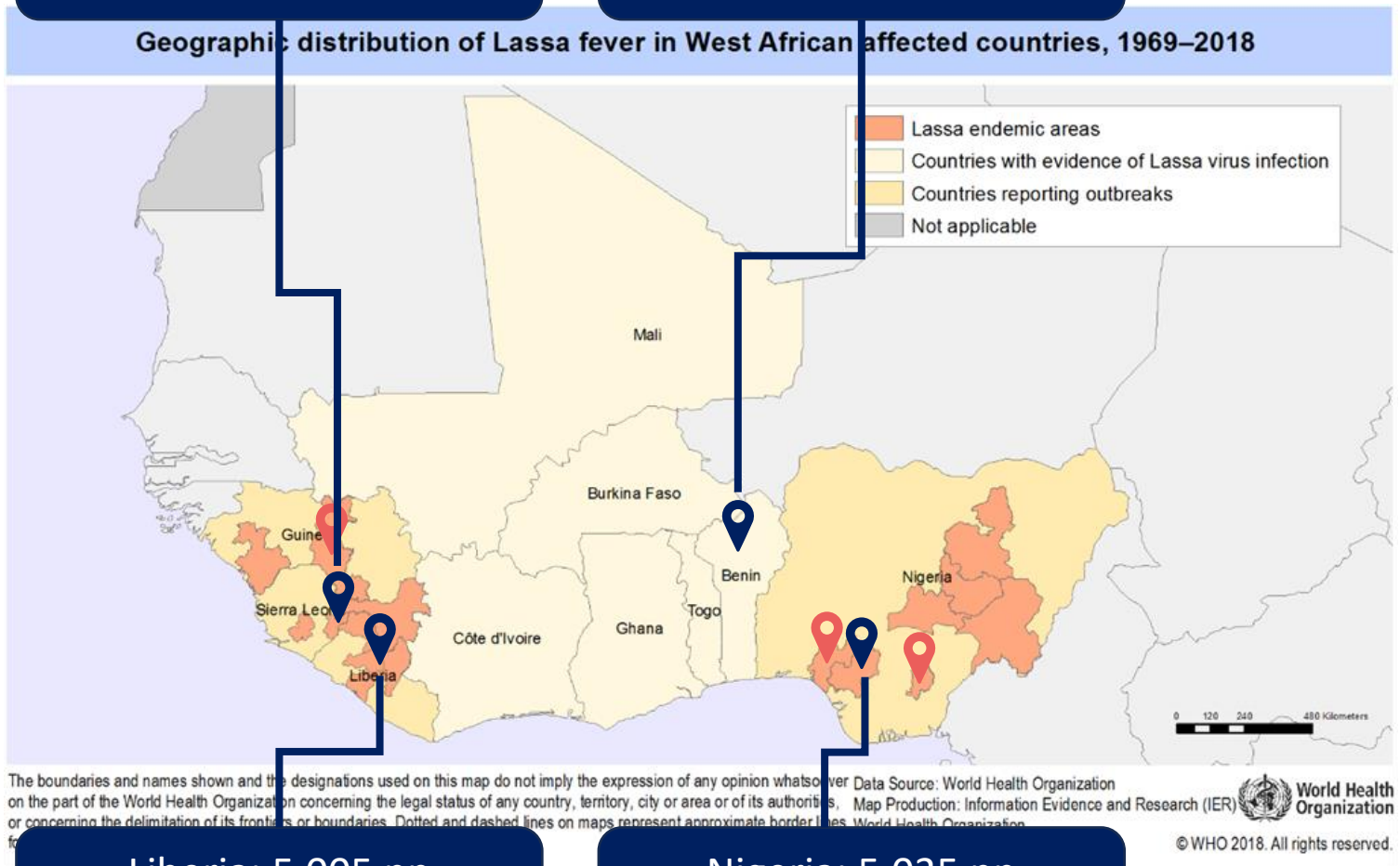
20,498 pp (2581 HH)

Not eligible: 326 pp
54% were < 2y-old

20,172 pp (2580 HH)

Sierra-Leone: 5,003 pp in 17 communities

Benin: 5,129 pp in 80 communities

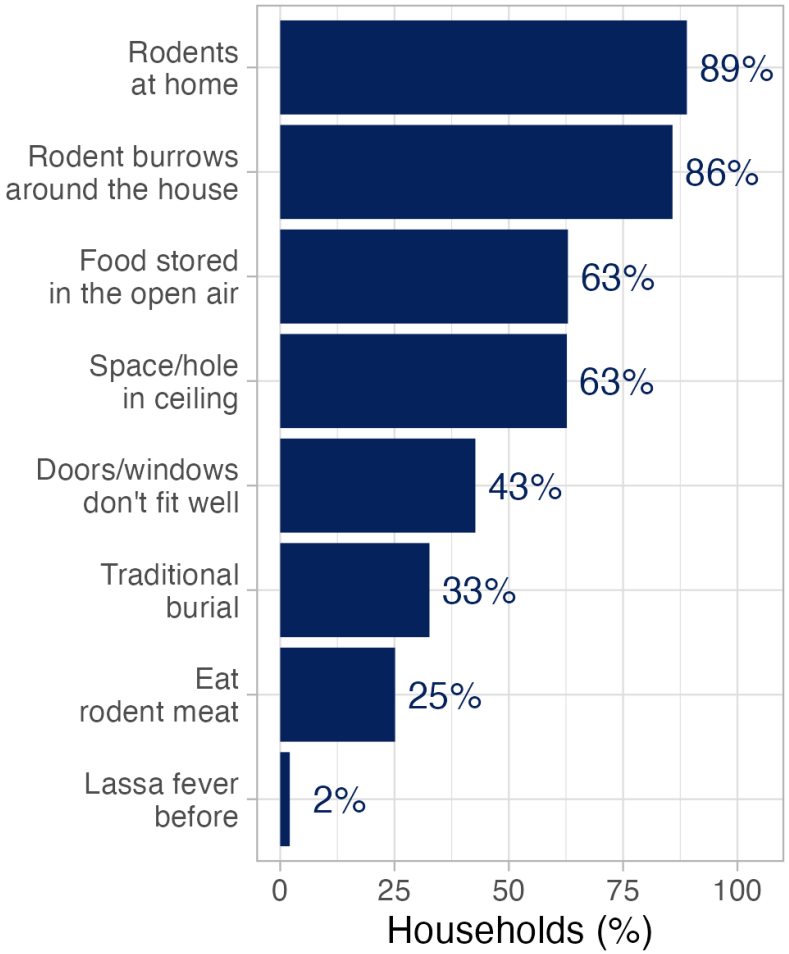


Liberia: 5,005 pp in 3 communities

Nigeria: 5,035 pp in 7 communities

Households & Participants Characteristics

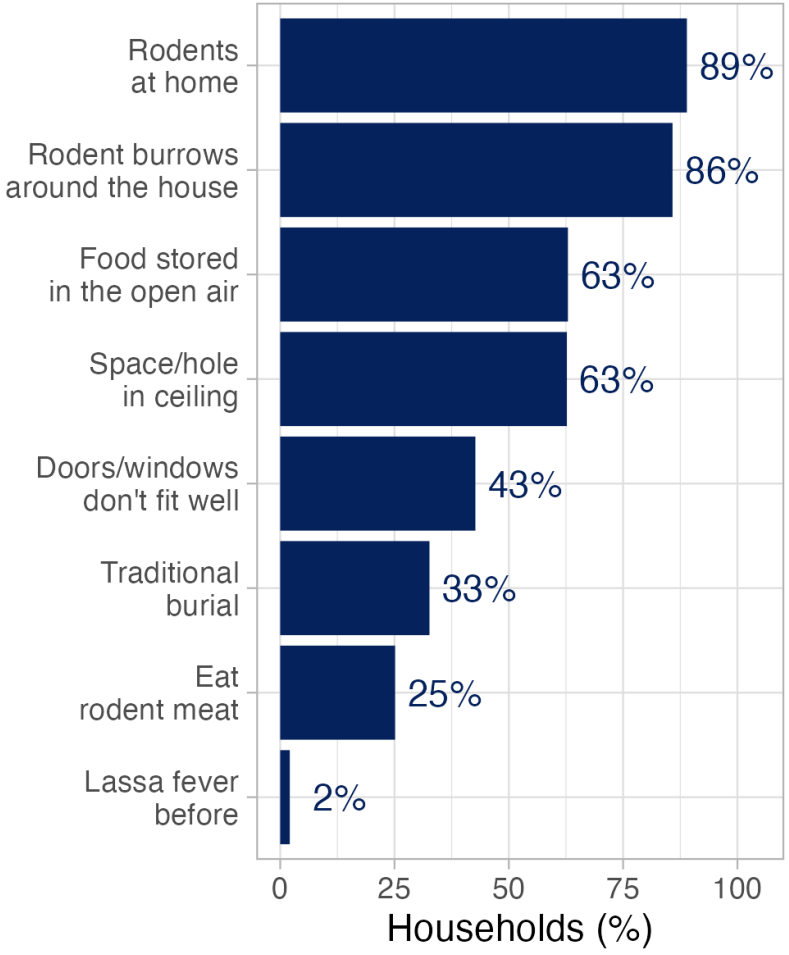
HH Risk Factors



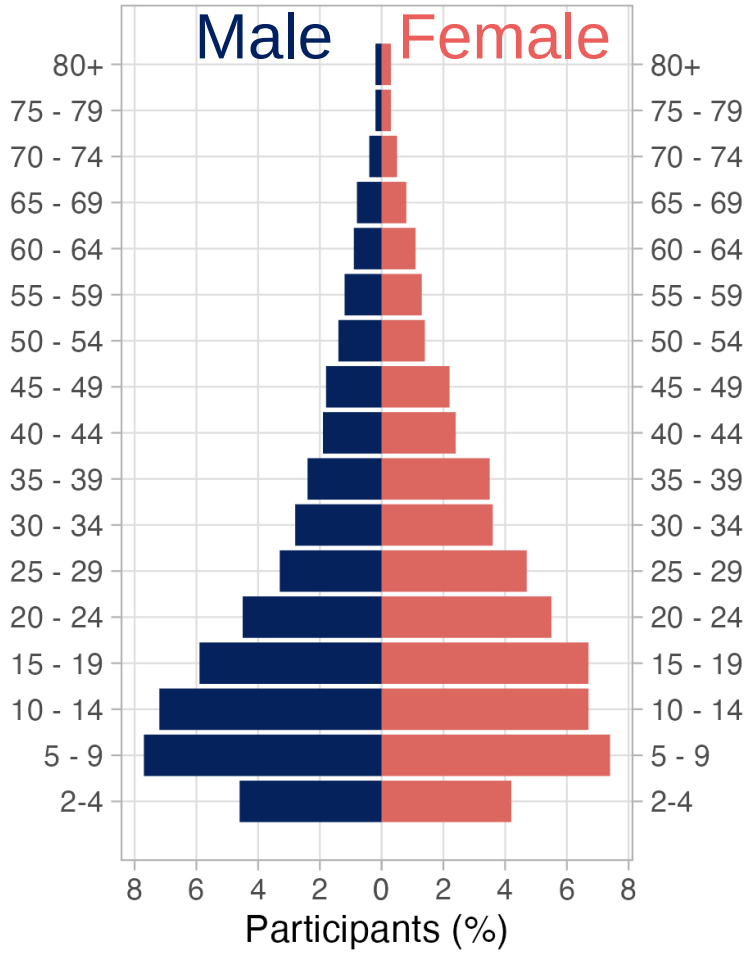
- **LF hotspot communities**
  - LIB & NGA: semi-urban
  - BEN & SLE: rural
- **HH size: 7 [5 - 10]**

Households & Participants Characteristics

HH Risk Factors



Age-Sex



- **Female: 53%**
- **Adults (18y+): 58%**
  - NGA & SLE ~60%
  - LIB & BEN ~50%
- **Kids <2y not eligible**

Households & Participants Characteristics

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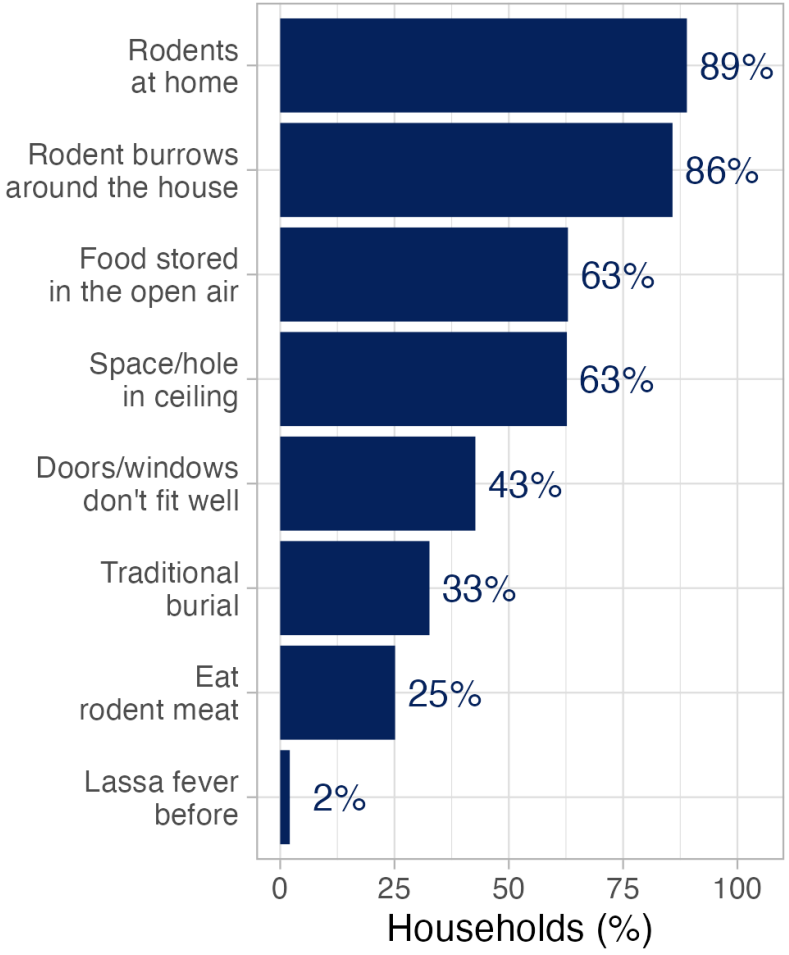

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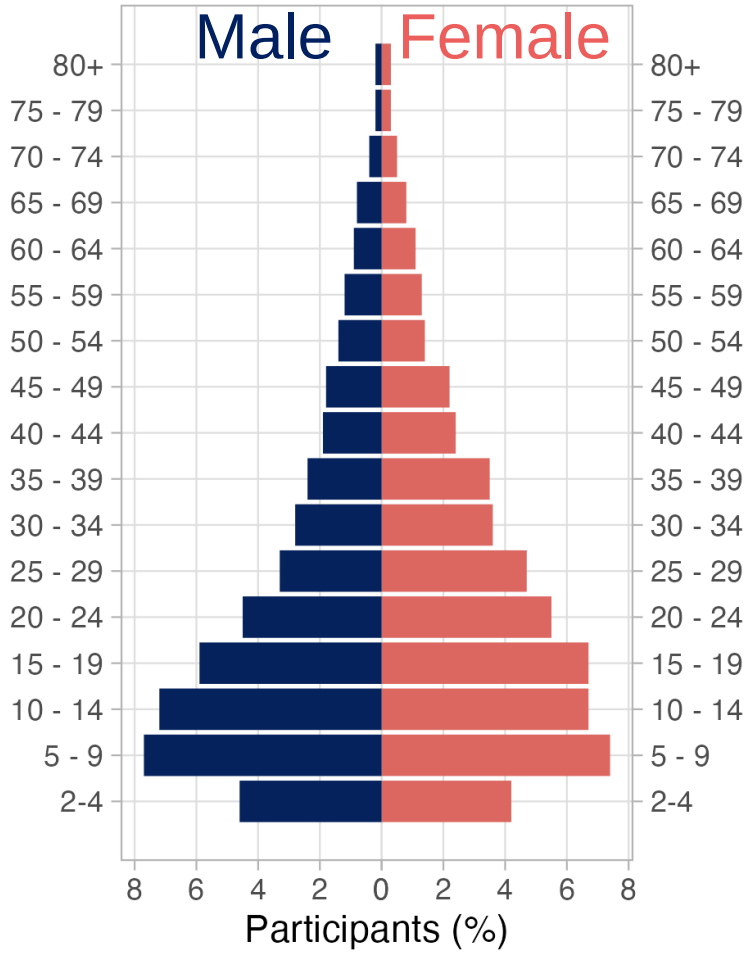
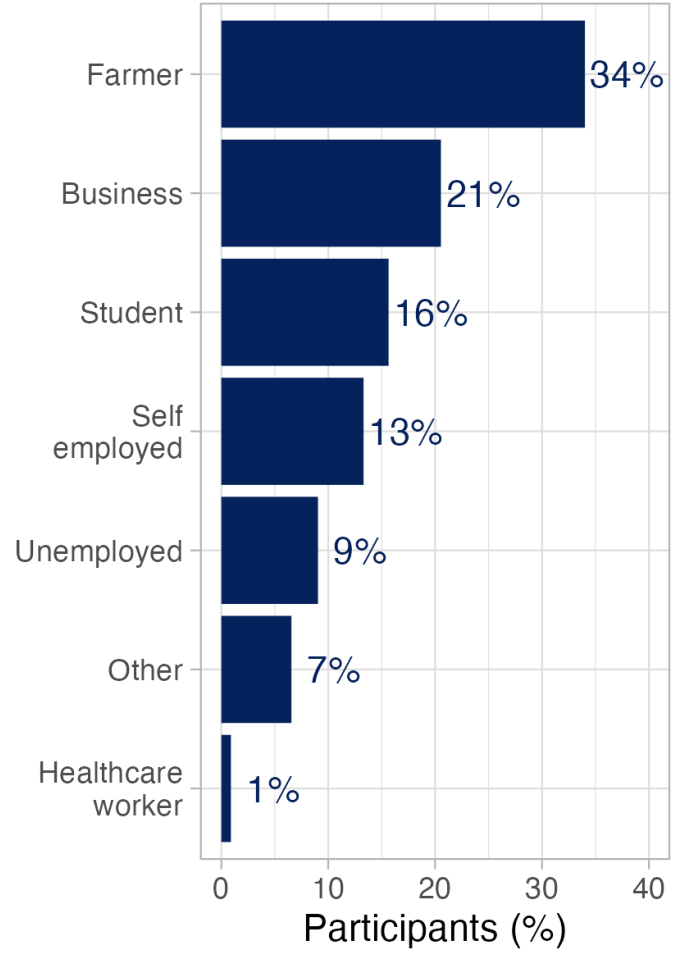


Occupation (18y+)



Follow-up of Participants

Contacts scheduled every 2 weeks for 24 months

>1 million

House visits

68%

NGA & SLE: ~50%, LIB & BEN: ~90%

Otherwise, contacts were made by phone

Participants contacted study team

12%

3,577 passive contacts by 2,400 participants, >99% health-related

Successful contact

98% [93% - 99%]

Median [Min - Max]

Participant responding

47%

BEN : 17%, LIB & SLE: ~50%, NGA: 70%

Most of the time it was the head of the household who responded for the other participants of their household

Early termination

4.1%

N = 834 participants
Moved away: 49%
Death: 23%
Lost-to-follow-up: 12%
Withdrawal: 12%

Lassa Fever Cases Assessment

Contacts made over 24m
~1 million
(100% of participants)

Fever episodes reported
9,028 episodes
5,458 participants (27%)

Field workers during follow-up visits of participants

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Acute Febrile Illness (AFI)
8,207 episodes
4,691 participants (23%)

Case definition for AFI

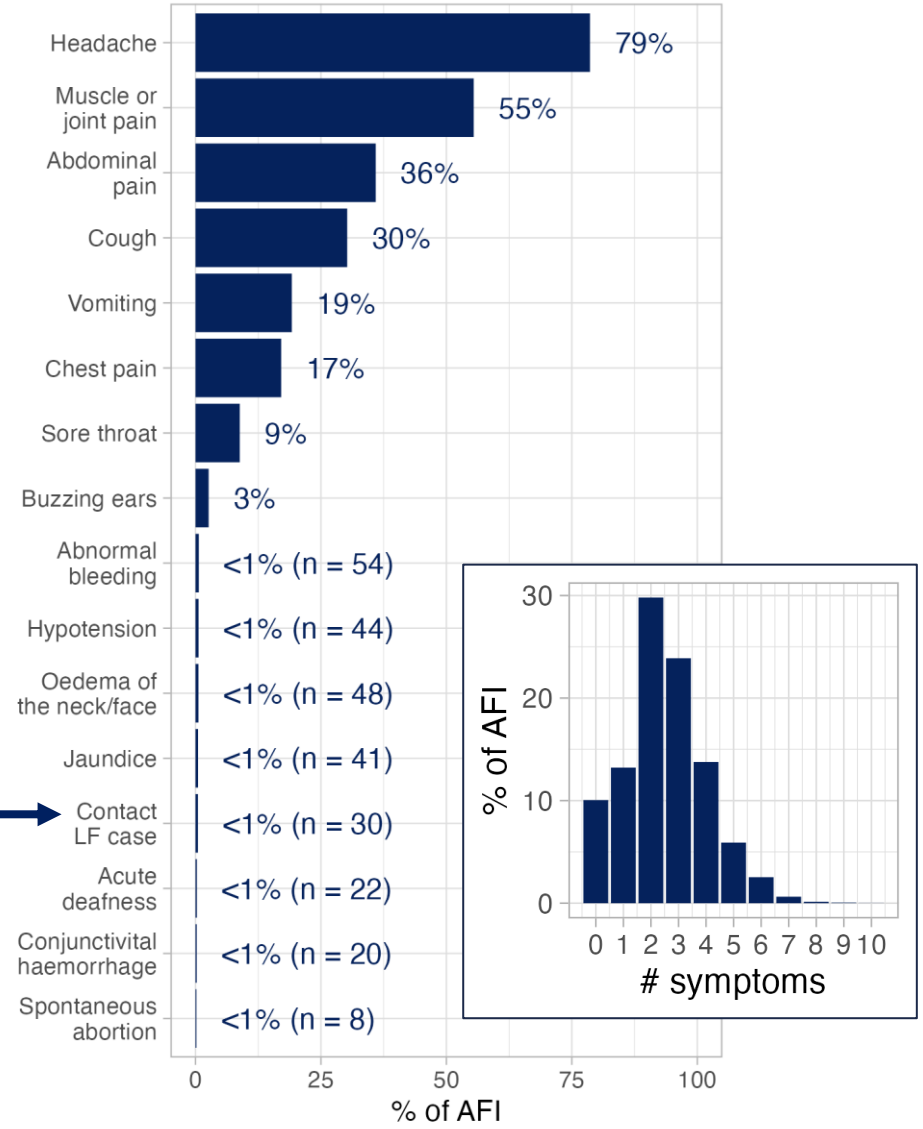
Self-reported fever of more than 48 hours duration

AND

One of the signs/symptoms

OR

A history of contact with a confirmed LF case



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Lassa Fever Cases
39 cases
0.2% of participants

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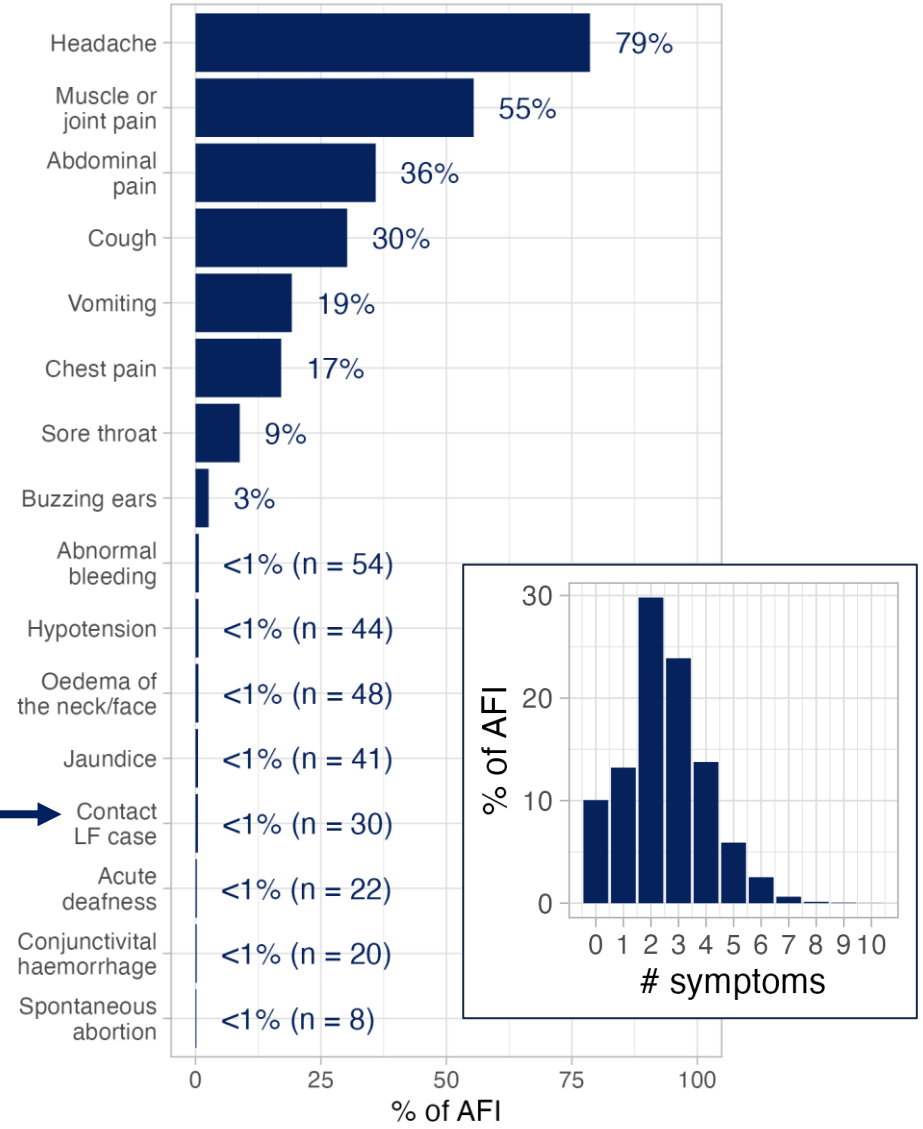
LASV-RT-PCR



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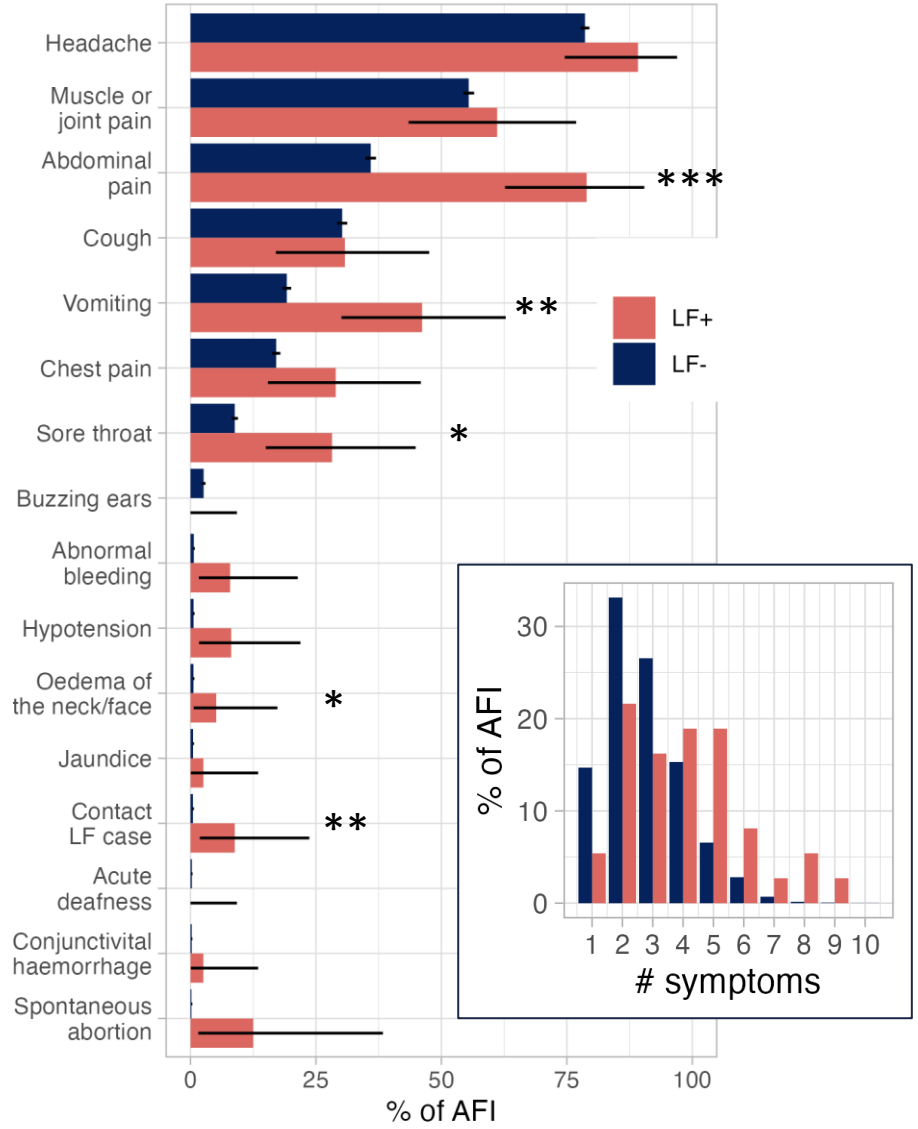
Abdominal pain, contact with LF cases, Vomiting, Sore throat are statistically significant **predictors of testing LF+.**

The **number of symptoms reported** was statistically significantly associated with **increasing odds of testing LF+** ($p<0.001$).

Multivariate mixed-effect logistic & Poisson regressions adjusting for country, age and sex.
*** $p<0.001$, ** $p<0.01$, * $p<0.05$

LASV-RT-PCR



Lassa Fever Cases (N=39)

	n/N (%)	Comment
Country		
Nigeria	23/39 (59%)	
Liberia	14/39 (36%)	
Benin	2/39 (5%)	
Sierra-Leone	0/39 (0%)	
Active FU	9/39 (23%)	During bi-weekly visit
Households	32	
Cases per HH	3 (1), 2 (5), 1 (26)	
Female	19/39 (49%)	
Pregnant	3/19 (16%)	2 miscarriages, 1 death
Deaths (CFR)	5/38[a] (13%)	9y, 15y, 18y, 46y, 71y

[a]1 left against medical advice;

Twin delivery via C/S conducted by Prof Okogbenin at ISTH Irrua, of our first Lassa positive participant

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	n/N (%)	Comment
Age groups		
2-4 y	3/39 (8%)	All in Liberia
5-17 y	19/39 (49%)	
18+ y	17/39 (43%)	
Had LF before	0/39 (0%)	
Contact with LF case	3/34[b] (9%)	2/3 from same HH
Malaria RDT+	17/39 (44%)	
SNHL at discharge	9/28[c] (32%)	No SNHL in Liberia at hospitalisation nor 4 months later
Persistent at 4m	5/9 (55%)	
Resolved at 4m	4/9 (45%)	
Delayed at 4m	5/18 (28%)	Hearing loss not performed in Benin

[a]1 left against medical advice; [b]missing information for 5 patients; [c] no hearing test in the 5 patients who died, missing in 6 other.

Incidence Rates (pooled analysis)

Acute Febrile Illness

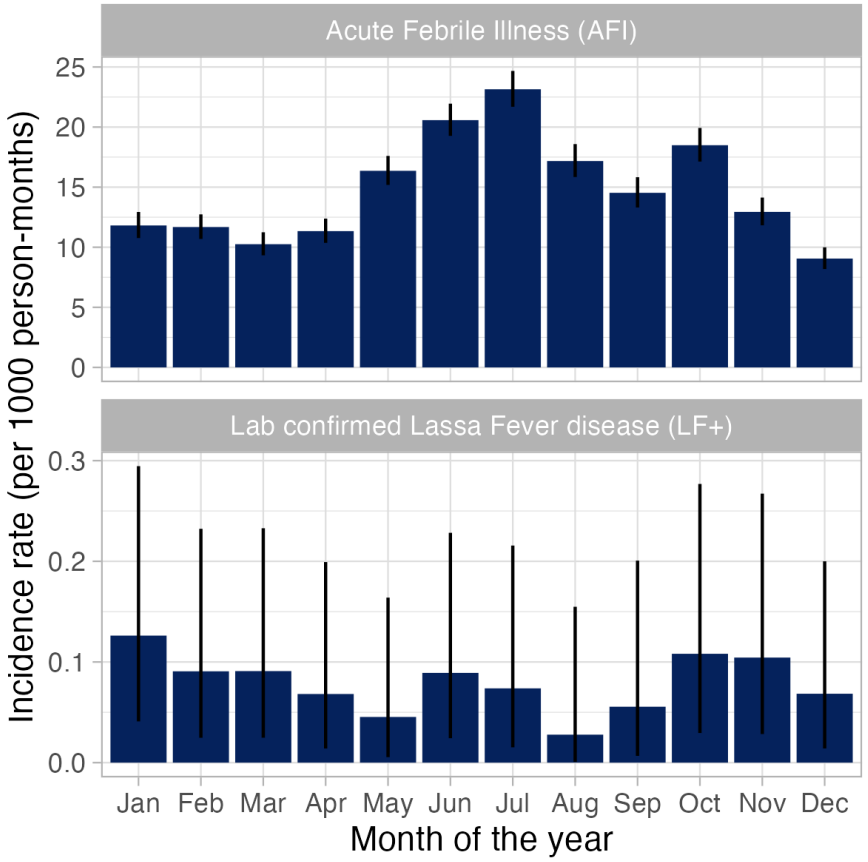
200 [200 – 210]

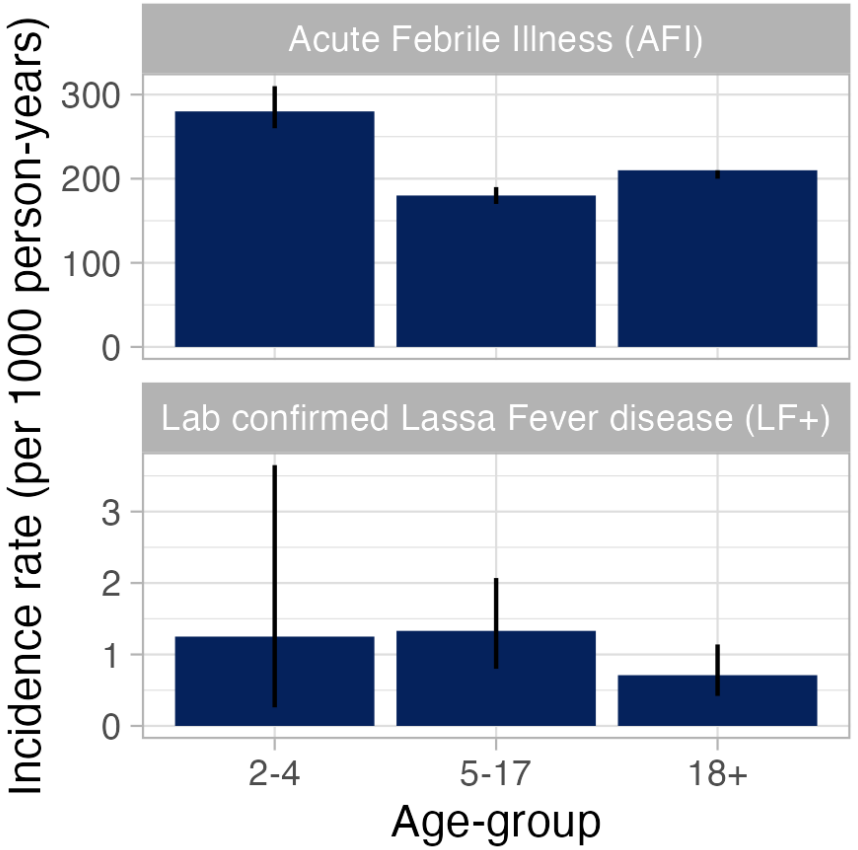
per 1000 p-years

Lassa Fever disease

0.96 [0.68 – 1.32]

per 1000 p-years



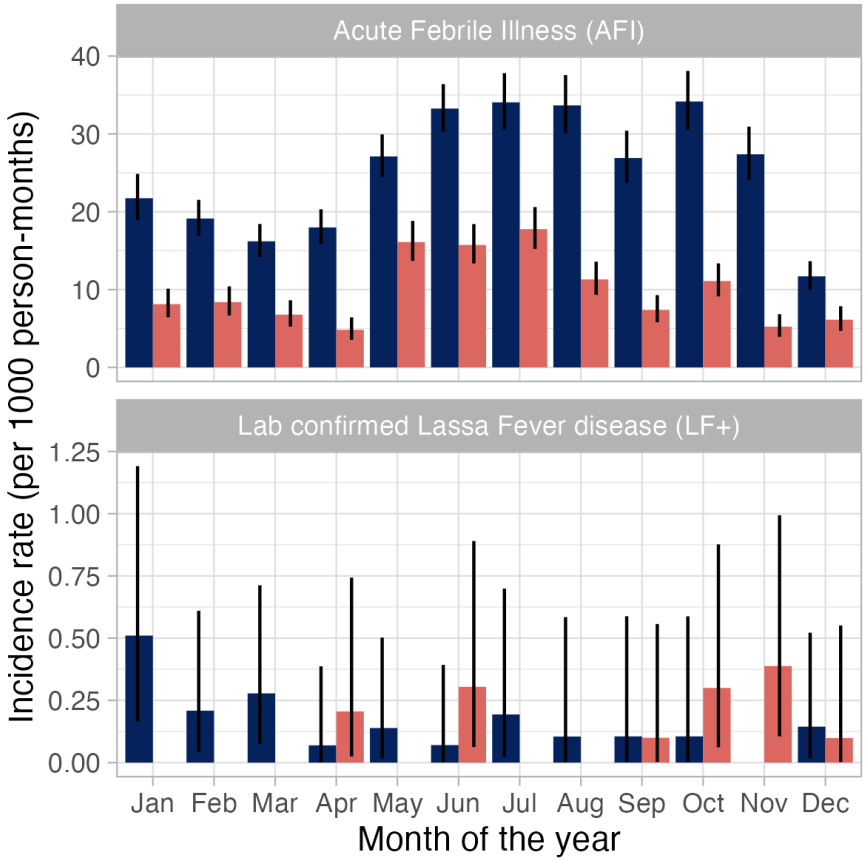


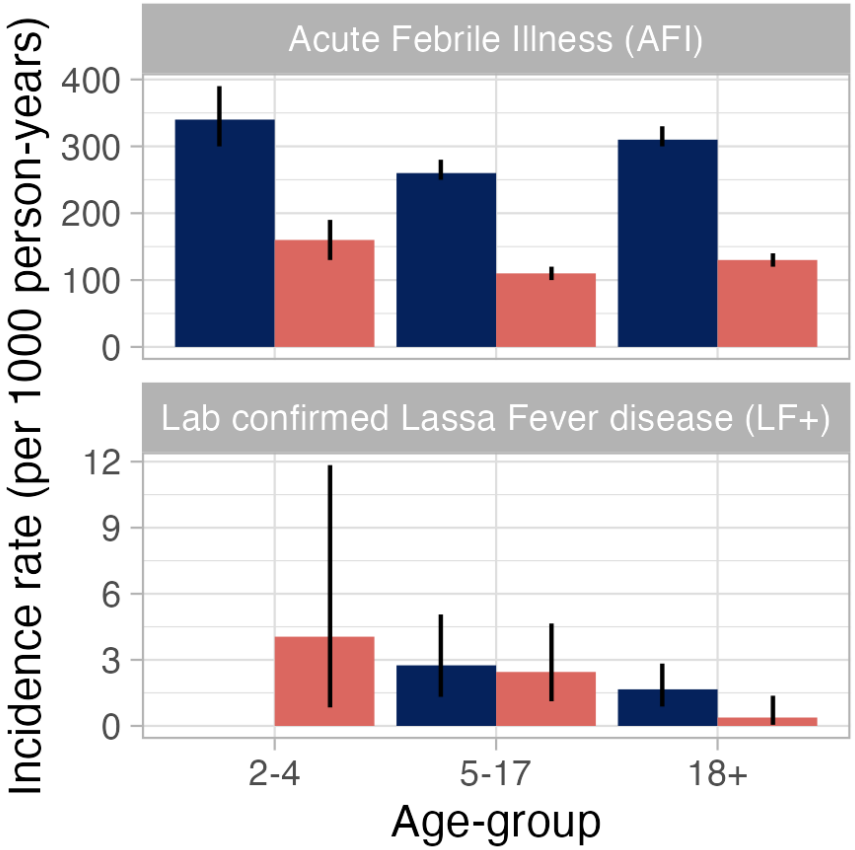
- **Incidence of AFI was highest during the malaria season (May - October) and highest in children under 5.**
- **Incidence of LF throughout the year, slightly higher during the dry season (October - March) and higher in children than adults.**

Incidence Rates (NGA vs LIB)

Acute Febrile Illness
NGA: 300 [290 – 310]
LIB: 120 [120 – 130]
per 1000 p-years

Lassa Fever disease
NGA: 1.9 [1.2 – 2.85]
LIB: 1.45 [0.79 – 2.43]
per 1000 p-years





- **Incidence of AFI was higher in Nigeria than Liberia, but similar time and age trends.**
- **The incidence of LF was highest at the beginning of the year (January-March) in Nigeria and at the end of the year in Liberia (October-November). No LF incidence observed in children under 5 in Nigeria.**

Conclusion

- First large-scale epidemiological study to measure **incidence of Lassa fever disease** and LASV infection in West Africa
  - **Feasibility**: high retention and follow-up of 20k participants
  - **Hotspot communities**: results cannot be generalised to the whole of West Africa
- **Inform** the design of Phase 3 **vaccine trials**
  - Incidence of ~1/1000 p-years means **large trials** (10k to 100k participants)
  - **Children** seems at greater risk than adults and **should be included** in vaccine trials if proved safe and immunogenic (Phase 1 and 2)
- **ENABLE 1.5** started in October (5 sites x 1000 participants x 1 year)
  - **More sensitive LF suspected case definition**: more LF+ cases detected?
  - **Age-stratified sampling**: better comparison between children/adults and between countries

Partners & acknowledgements

Enable Lassa Research Programme partner institutions

- Fondation pour la Recherche Scientifique (FORS)
- University of Parakou
- Benin Ministère de la Santé
- Conseil National de Lutte contre le VIH/Sida, la Tuberculose, le Paludisme, les Infections Sexuellement Transmissibles et les Épidémies (CNLS-TP)
- Institut de Recherche Clinique du Bénin (IRCB)
- Université Gamal Abdel Nasser de Conakry (UGANC)
- Faranah Regional Hospital
- Phebe Hospital
- National Institute of Public Health Liberia (NPHIL)
- Nigeria Centre for Disease Control (NCDC)
- Irrua Specialist Teaching Hospital (ISTH)
- Alex Ekwueme Federal University Teaching Hospital Abakaliki (AEFUTHA)
- Federal Medical Center – Owo (FMCO)
- African Field Epidemiology Network (AFENET)
- Redeemer's University (RUN)
- Kenema Government Hospital
- International AIDS Vaccine Initiative (IAVI)
- Tulane University
- University of North Carolina (UNC)
- Institute of Tropical Medicine - University of Tübingen (ITM-EKUT)
- Centre de Recherches Médicales de Lambaréné (CERMEL)
- Robert Koch Institut (RKI)
- UK Public Health and Rapid Support Team (UK-PHRST)
- University of Laval
- P95
- Margan Clinical Research Organization (MMARCRO)
- Epicentre
- Bernhard-Nocht-Institut für Tropenmedizin (BNITM)

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- Prof Adebola Olayinka (Nigeria Centre for Disease Control)
- Dr Jefferson Sibley (Phebe Hospital)

Special thanks to our many programme stakeholders and advisors for their continued support.

This programme is funded by the Coalition for Epidemic Preparedness Innovations (CEPI).

Thank you to our participants

and to you for your attention