Study design

Q1: What types of study designs
Aims:

• To design epidemiological study (studies) that will enable a Phase 3 trial to be undertaken, and to inform vaccine decision-making should a safe and effective vaccine become available
Before embarking on main epidemiological study

• Systematically collate and analyse and publish data already available
  • Comprehensive review of what we know about LF at the moment
• Also identify if there are existing serum banks or other resources that could be used to facilitate the main epi survey
Q1) Estimate the age-specific incidence of infection and disease (including the full range of severity) in well-defined populations

**Design summary: prospective cohort study with active follow-up**

1. Select a number of well defined high-risk populations, based on existing data on case loads that are relatively stable and served by well-defined health facilities

2. Recruit H-H (GPS) from these communities (note 1). Obtain baseline H-H data, demographics, risk status and knowledge and attitudes towards LF.

3. Obtain baseline serological status of participants

4. Follow-up for at least 1 year (possibly more)

5. During follow-up, actively case-fine. Home visits every 1-4 weeks (tbd). Those with Lass—like symptoms enter diagnosis algorithm
   - Testing using RDT, if available

6. At end of study (or perhaps at the end of each year), members of cohort are bled again to determine sero-incidence

7. Cases are asked about health-seeking behaviour
Q1) Notes

1. Public health information on how to reduce their risk of LF will be offered to these communities. Rodent control could/should also be offered
Q2) Determine age-specific seroprevalence of LASV across region

**Option 1**
- Conduct community-based seroprevalence studies in other areas
  - Select High-medium-low incidence districts, as based on case-data

**Option 2**
- Use existing serum banks, which could possibly include blood donors or antenatal screening samples (though this would be restricted by age and perhaps sex)

**Option 3**
- Identify sentinel hospitals across the region, and introduce Lassa testing as part of diagnostic work up for febrile cases
Q3) Identification of risk groups
Q4) Identification of risk factors and social and ecological drivers of incidence

Study 1: Case-control study

- Possibly a case-negative design
- Assess individual, H-H and community characteristics associated with being a confirmed case
- Conducted over different settings using (as far as possible) comparable methods

Study 2: Analysis of existing data

- Regression (including spatial regression analyses) to identify risk factors and how they may vary over time
- Requires analysis of a common standardised database (across all countries), and therefore common questionnaires (as far as possible) variables, etc.

- Option: collect data on prevalence of LASV in rodents, and rodent population during main cohort study (particularly if rodent control offered)
5) Documenting knowledge, behaviour and attitudes towards LF & LF vaccine in communities and HCW

• Study 1: health systems
  • Health systems research to be conducted to understand the extent to which referral patterns and local specimen transport systems/diagnostic processes can support whichever diagnostic/case definition threshold is chosen once the vaccine is developed

• Study 2: health seeking behaviour
  • Designed to understand how, when and why individuals seek/do not seek care
  • Mixture of quantitative and qualitative methods

• Study 3: Anthropological studies to explore local perceptions of LASV/vaccines to support community engagement strategies required for vaccine trials and subsequent roll out
Core elements to be standardised across sites

Questions

• Common standardised questionnaire to cover:
  • Basic demographics, H-H and environmental characteristics

• Common clinical variables and coding, to ensure that identical definitions of cases are used in each site

Data

• Standardised electronic data capture methods (tablets)
• Common database