# Transmission Workpackage: Progress to Date

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SPEAK India

Setting the Post-Elimination Agenda for Kala-azar in India

# Project overview

- Aim: to determine the feasibility and potential scalability of xenomonitoring as a passive surveillance tool for VL to be used in a post-elimination setting
- Objectives:
    1. Optimise and carry out field-testing of a metacyclic-specific assay for *L. donovani* detection in *P. argentipes* to determine the proportion of caught sandflies infected with metacyclic specific promastigotes
    2. Determine the best practice for sampling *P. argentipes* in terms of surveillance of *L. donovani* transmission potential
    3. Determine the cost effectiveness, feasibility and scalability of xenomonitoring as a surveillance mechanism
    4. Utilise generated data to improve VL transmission models
    5. Utilise generated data to inform the development of guidelines for VL transmission endpoint assessment

# Project structure

- Four phases:
  1. Pilot study to compare the effectiveness of CDC light traps, mechanical vacuum aspirators and Prokopacks in collecting female *P. argentipes*
  2. Optimisation of the metacyclic-specific assay for *L. donovani* detection in *P. argentipes*
  3. Xenomonitoring
  4. Analysis and model development

# Pilot study

- **Aim:** to determine the optimal method of capturing female *P. argentipes* sandflies, for use in a visceral leishmaniasis xenomonitoring programme
- Samples will be retained for metacyclic-specific PCR analysis and inclusion in xenomonitoring study
- Three collection methods:

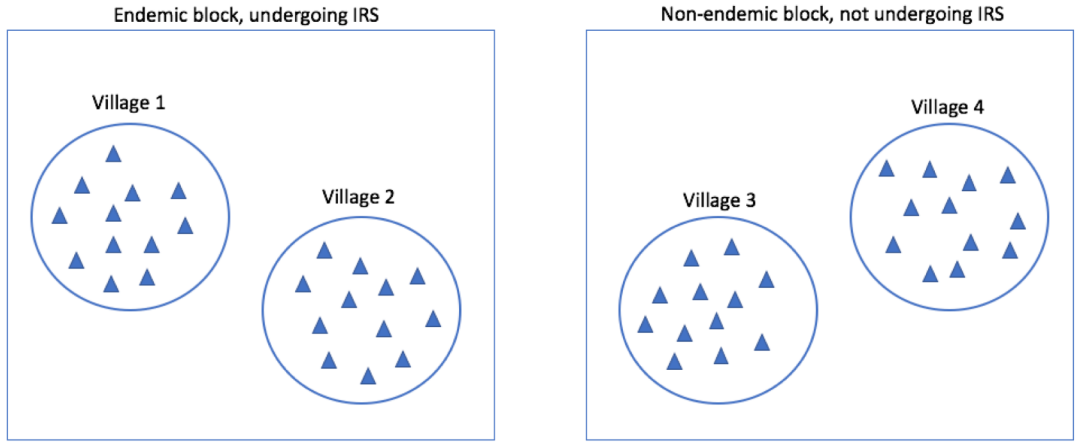
Mechanical vacuum aspirators

CDC light traps

Prokopack

# Pilot study: sample size

- Study sites: 24 households in a non-endemic block of Nalanda district that has not undergone IRS in the past three years; 24 households in an endemic block of Saran district that are currently undergoing IRS




- Number of trap nights required per treatment group calculated based on unpublished Kalanet data

| Effect size | Trap nights required |
|---|---|
| 1.0 | 166 |
| 1.25 | 106 |
| 1.5 | 74 |

- Eight replicates of each method per day for two consecutive days in one of the study blocks (four replicates/village/day), across 20 days in May

# Pilot study

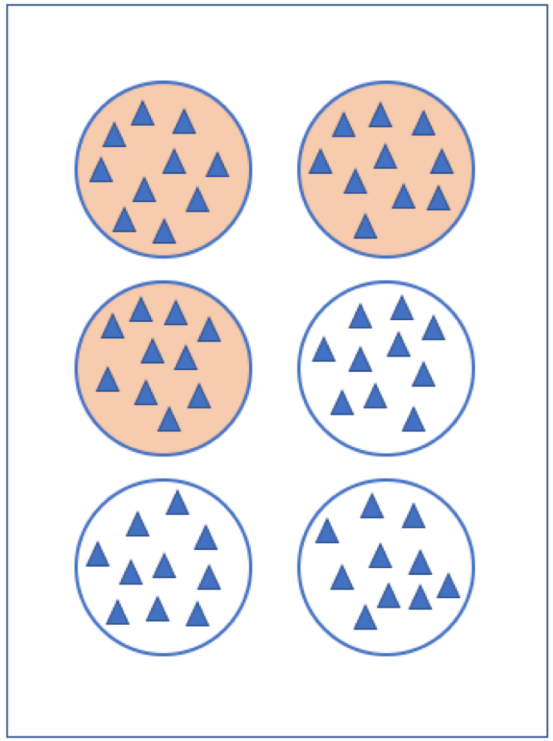
- Collection methods will be rotated between households on a daily basis, following a Latin Square design balanced for carryover effects

| | D1 | D2 | D5 | D6 | D9 | D10 | D13 | D14 | D17 | D18 |
|---|---|---|---|---|---|---|---|---|---|---|
| V1H1 | C | P | M | M | P | C | C | P | M | M |
| V1H2 | P | M | C | C | M | P | P | M | C | C |
| V1H3 | M | C | P | P | C | M | M | C | P | P |
| V1H4 | C | P | M | M | P | C | C | P | M | M |
| V1H5 | P | M | C | C | M | P | P | M | C | C |
| V1H6 | M | C | P | P | C | M | M | C | P | P |
| V1H7 | C | P | M | M | P | C | C | P | M | M |
| V1H8 | P | M | C | C | M | P | P | M | C | C |
| V1H9 | M | C | P | P | C | M | M | C | P | P |
| V1H10 | C | P | M | M | P | C | C | P | M | M |
| V1H11 | P | M | C | C | M | P | P | M | C | C |
| V1H12 | M | C | P | P | C | M | M | C | P | P |

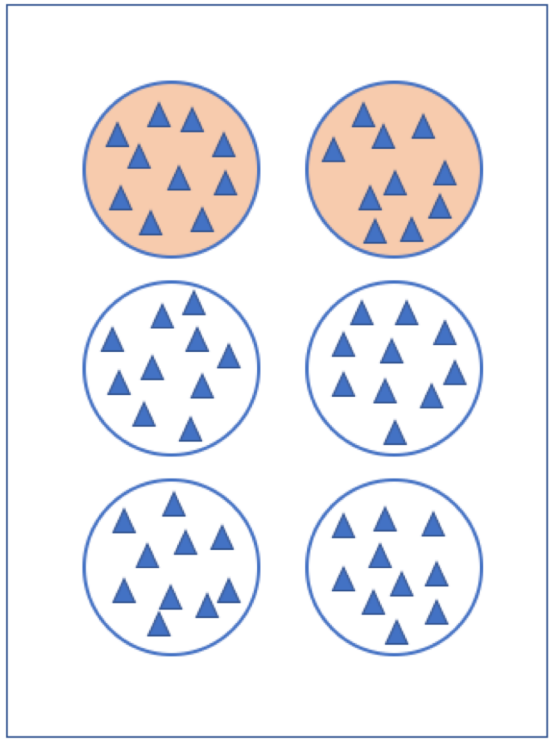
- Additional measures:
  - Soil temperature, pH value, sunlight intensity and moisture recorded daily within a 1m radius of each house
  - Ambient temperature and humidity recorded daily in 6 households/village
  - Qualitative survey to determine aspects of each method householders found disruptive or unpleasant, and collection method preference, if any

# Xenomonitoring

- Sampling method and protocol will be finalised based on the results of the pilot study
- 12 villages, 10 households/village will be selected. 5 villages (3 endemic, Saran district; 2 non-endemic, Muzaffarpur district) will overlap with sero-surveillance project sites



VL endemic villages



VL non-endemic villages

# Xenomonitoring

- 2 replicates will be carried out per month for 1 year, one under strict research conditions and one solely by RMRI-trained field workers, to give an indication of both the theoretical and operational feasibility of xenomonitoring
  - Analysis will account for both inter- and intra-collector variations

| Jul 2018 | | | | | | |
|---|---|---|---|---|---|---|
| S | M | T | W | T | F | S |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 8 | 9 | 10 | 11 | 12 | 13 | 14 |
| 15 | 16 | 17 | 18 | 19 | 20 | 21 |
| 22 | 23 | 24 | 25 | 26 | 27 | 28 |
| 29 | 30 | 31 | | | | |
| | | | | | | |

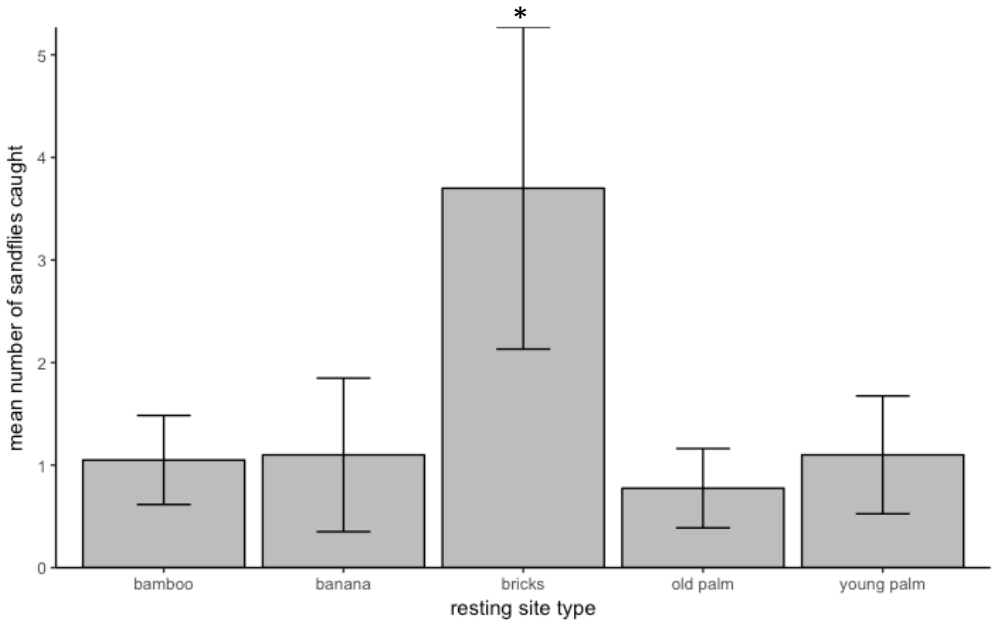
- Sample size calculation will be refined based on the results of the pilot study, as it currently assumes:
  - Capture rates will be similar to Kalanet trial
  - Approximately 2.53% of female *P. argentipes* will be infected with *L. donovani* (based on the average proportion of positive individually tested samples from previous studies in Bihar

# Progress

- September 2017: HMSC approval granted by the Ministry of Health and Family Welfare
- October 2017: Institutional ethical approval granted by RMRI
- September – October 2017: Preliminary testing of mechanical vacuum aspirator in field conditions

# Preliminary study results

- Effectiveness of mechanical vacuum aspirators assessed through outdoor sampling of 20 sites over 10 days (200 collections total) in one village in Nalanda district
  - 5 different vegetation types sampled; bamboo stands, banana trees, short/rough palms, tall/smooth palms, and brick stacks
  - 309 sandflies captured, 83.8% *P. argentipes*, 36.3% female
  - Samples remained alive and in-tact following aspiration




# Progress

- January 2018: LSHTM-RMRI contract prepared and delivered to RMRI for approval
- January 2018: Open Data Kit (ODK) set up for qualitative data collection
- February 2018: Two pilot study villages in Nalanda district (Bihar) and two in Saran district (Bihar) selected for pilot study
- February 2018: Xenomonitoring site selection meeting and village visit with members of the surveillance workpackage at KAMRC Muzaffarpur
- March 2018: Pilot study protocol finalised
- March 2018: Procurement of lab and field equipment

# Progress

- April 2018: Pilot study recruitment of 48 households in Nalanda and Saran districts completed
- April 2018: LSHTM-RMRI contract approved and signed by RMRI
- April 2018: Research Assistant appointed to work at LSHTM on metacyclic-specific assay development

# Data collection & results timeline

- Include point indicating prelim results will be available in time for COR NTD

| | May '18 | Jun '18 | Jul '18 | Aug '18 | Sept '18 | Oct '18 | Nov '18 | Dec '18 | Jan '19 | Feb '19 | Mar '19 | Apr '19 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pilot study | | | | | | | | | | | | |
| Xenomonitoring | | | | | | | | | | | | |

Pilot study results available

Preliminary xenomonitoring results

Conclusion of field collections

# Summary of outputs

| Pilot study | Xenomonitoring |
|---|---|
| Optimal sampling framework for *P. argentipes* | Entomological inoculation rate |
| Proportion of *P. argentipes* resting indoors v. outdoors | Critical infection thresholds |
| Relationship between microclimate and *P. argentipes* emergence | Prevalence of *L. donovani* infection and infectiousness |
| | *P. argentipes* seasonality |
| | Operational feasibility & scalability of xenomonitoring |
| | Cost effectiveness |
| | Metacyclic-specific PCR assay |

# Questions & Comments