LB-5532

# A cluster randomized trial to measure the impact of indoor residual spraying with a third-generation indoor residual spray (3GIRS) product in combination with long-lasting insecticidal nets in Zambezia, Mozambique


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## Introduction

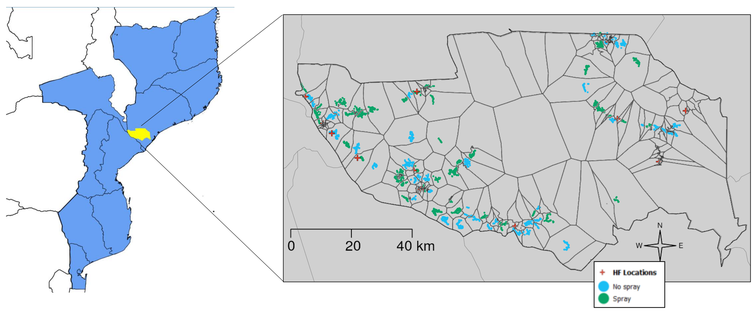
The Mopeia District of Zambezia Province in Mozambique has a high malaria burden despite documented high long-lasting insecticide-treated nets (LLIN) access.

In this context, a two-year, two-armed cluster-randomized trial is ongoing to determine the impact of indoor residual spray (IRS) when combined with LLINs. One study arm is receiving standard LLINs only and the other is receiving IRS with a microencapsulated formulation of pirimiphos-methyl (Actellic®300CS) in addition to LLINs.

The epidemiological and entomological impact and cost-effectiveness of adding IRS to LLINs are being evaluated over two years through active case detection in a cohort of 1548 children followed monthly, enhanced passive surveillance, two annual cross-sectional surveys, continuous entomological surveillance, and prospective monitoring of intervention and malaria-associated costs.

Here, preliminary interim results comparing a key surveillance indicators from the LLIN and LLIN+IRS study arms are presented.

## Study Location



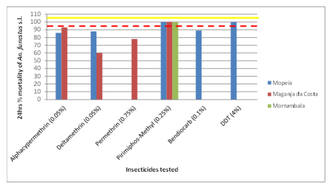

**Mopeia District**

- 7, 614 km$^2$
- 160,000 total population
- 30,000 children under 5 years old (U5)
- U5 malaria prevalence = 54% (2012)
- 1 District Hospital and 13 local Health Facilities
- >50% of households own at least 1 LLIN in 2015

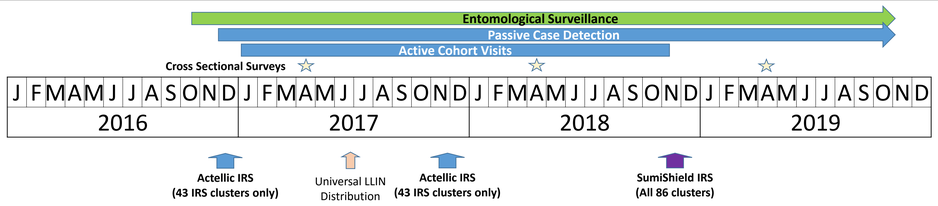
**Clusters established at the village level**

- Clusters stratified by number of households (Large (>125), Med (71 - 125), Small (<70))
- Randomized 1:1 to receive IRS (Spray) or No-IRS (No spray) with Actellic in 2016 and 2017. All clusters to receive SumiShield in 2018 (see timeline)

*An. funestus* s.l., the dominant vector species in Mopeia, demonstrated resistance (<90% mortality in WHO tube tests) to pyrethroids and bendiocarb in 2018



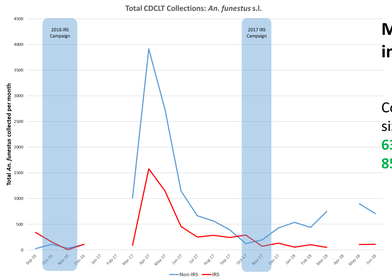

### Study Timeline




The study is expected to continue for a 3rd year after the decision to spray SumiShield® 50WG (clothianidin) in all villages in Mopeia in 2018. The study team will continue entomological collections, passive case detection, and will perform a 3rd parasite prevalence survey to determine the effects of this rotation strategy on previously sprayed (Actellic) clusters as well as spray naïve clusters.

## Interim Results

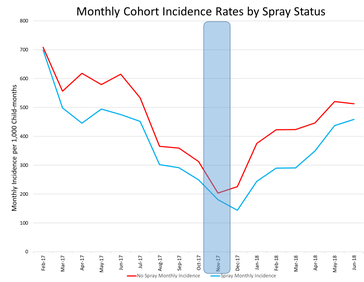
### Entomological Surveillance




**Monthly trends in total *An. funestus* specimens collected in CDCLTs, by IRS status.**

Considering the months January – June, IRS was associated with a sizable cumulative reduction in *An. funestus* densities:
**63% reduction in 2017 (year 1)**
**85% reduction in 2018 (year 2)**

### Active Cohort Surveillance



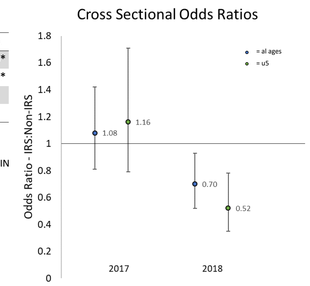

**Active Case Detection: Preliminary summary based on spray status only**

**17-month cumulative rate ratio: 0.81 (0.77 – 0.84)**
**Crude Protective Efficacy: 19.4%**
**Cohort Infections Prevented: 1,105**
**Total Infections Prevented (all IRS clusters): 16,235**

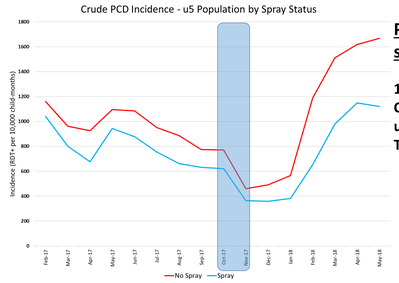
### Cross-Sectional Surveys

| | 2017 | | | 2018 | | |
|---|---|---|---|---|---|---|
| | No Spray | Spray | OR | No Spray | Spray | OR |
| RDT+ (overall) | 191 (42.5%) | 164 (44.4%) | 1.08 | 173(42.6%) | 131 (34.1%) | 0.70* |
| RDT+ (u5) | 86 (47.3%) | 96 (52.7%) | 1.16 | 122 (63.2%) | 92 (47.2%) | 0.52* |
| Possess nets [1] | 255 (56.9%) | 184 (49.9%) | - | 356 (94.1%) | 374 (95.2%) | - |
| Used nets [2] | 66% | 59% | - | 75% | 83% | - |

[1] From the cross-sectional survey question: does this household have at least 1 LLIN?
[2] From the active cohort household visit survey question: did the cohort member sleep under an LLIN last night?
* Odds Ratio (OR) is significantly different than 1.0, p<0.001




### Passive Health Facility Surveillance




**Passive Case Detection: Preliminary summary based on spray status only**

**17-month cumulative rate ratio: 0.75 (0.73 – 0.87)**
**Crude Protective Efficacy: 25%**
**u5 cases averted at health facilities: 4,806**
**Total u5 cases Prevented (all IRS clusters): 6,920**

## Discussion

- Preliminary analysis of interim results from this cluster randomized trial show that case data from routine health systems reflect the same trends seen in infection data from the active cohort – a significant reduction in malaria incidence of approximately 20% to 25% in IRS vs. non-IRS clusters
- The effect has persisted for two years but health facility routine data suggests that the impact on case reduction may be amplified in year two after a universal LLIN distribution campaign in mid 2017
- Similarly, cross sectional survey data showed no impact of IRS 5 months after the first spray campaign, but indicates a significant reduction in malaria infection prevalence in year two (5 months after the second spray campaign)
- Results are also supported by reductions in vector abundance and biting rates in IRS clusters vs. non-IRS clusters
- Final, in-depth analyses are forthcoming and will aim to understand the incremental benefit of IRS on top of LLINs in a high prevalence setting. Formal analysis will utilize models to account for the effects of clustering, stratification, and random effects.

## Project Partners


*The NgenIRS (Next Generation IRS) project is a partnership, led by IVCC, that includes the US President's Malaria Initiative, Abt Associates, and PATH. NgenIRS works in close collaboration with leading insecticide manufacturers, national malaria control programs, the Global Fund, and other stakeholders to save lives and protect health by reducing transmission of malaria through affordable indoor residual spraying of long lasting, non-pyrethroid insecticides. It is funded by UNITAID. For more information please visit http://www.ivcc.com/ngenirs or email David McGuire (david.mcguire@ivcc.com).



**References**

[1] Chaccour, et al. 2018. BMJ Glob Health;3(1):e000610