Evidence snapshot: a cluster randomized trial in Northern Mozambique

Background

The Mopeia District of Zambezia Province in Mozambique has a high malaria burden despite a history of high access to standard long-lasting insecticide-treated nets (LLIN). Additionally, the primary vector in Mopeia, *Anopheles funestus*, is resistant to pyrethroids – the type of insecticide that is used on standard LLINs. In this high transmission context, a two-year cluster-randomized trial was set up to evaluate the impact of indoor residual spray (IRS) with a 3rd Generation IRS (3GIRS) product[‡] when combined with LLINs.

Study design

An enumeration exercise conducted during June and July of 2016 identified 139,286 total residents across 194 villages. Identified villages were delineated into clusters and stratified by size (combining some villages in close proximity and the same spray status), resulting in 168 clusters that were randomized 1:1 into either the IRS or non-IRS study arm. In the **non-IRS study arm**, clusters received standard LLINs; in the **IRS study arm**, clusters received IRS with a microencapsulated formulation of pirimiphos-methyl (Actellic®300CS) in addition to standard LLINs. A total of 86 clusters (43 IRS, 43 non-IRS) were selected for participation in the active cohort component of the study in which 18 children from each cluster ages 6-59 months at the time of enrollment (1,535 total children) were followed monthly to assess malaria incidence at the community level in the two study arms. The routine health centre reporting system was also strengthened to assess malaria incidence by passive case detection. Two cross sectional studies conducted in April 2017 and April 2018 measured malaria prevalence at the community level. Entomological data including mosquito densities, sporozoite rates, resistance status, and indoor to outdoor biting ratios were also collected from both sprayed and non-sprayed areas.
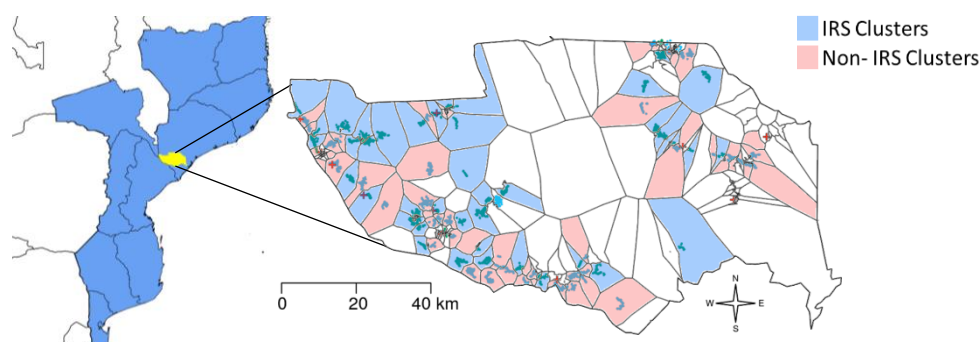

Figure 1. Mozambique map highlighting Zambezia Province and IRS and Non-IRS study clusters.


Left: Members of the entomological team hang indoor CDC light traps to monitor indoor host-seeking *Anopheles* mosquito densities. (Photo Credit: J Wagman, PATH) Right: Members read the results of a rapid diagnostic test performed on a cohort member to test for malaria (Photo Credit: B Savaio, PATH).

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Epidemiological impact of 3GIRS in Mozambique

Children in the IRS arm experienced a significantly lower incidence of malaria compared to the non-IRS arm throughout the study period. Using monthly rapid diagnostic tests, a total of 5,758 cases were identified in the non-IRS cohort versus 4,801 cases in the IRS cohort, resulting in an Incidence Risk Ratio of 0.82 (95% CI: 0.79, 0.86, p-value <0.001). Based on this **18% reduction in malaria infections**, it is estimated that roughly 20,000 malaria infections were averted in children under five years of age living in IRS clusters during the study period.
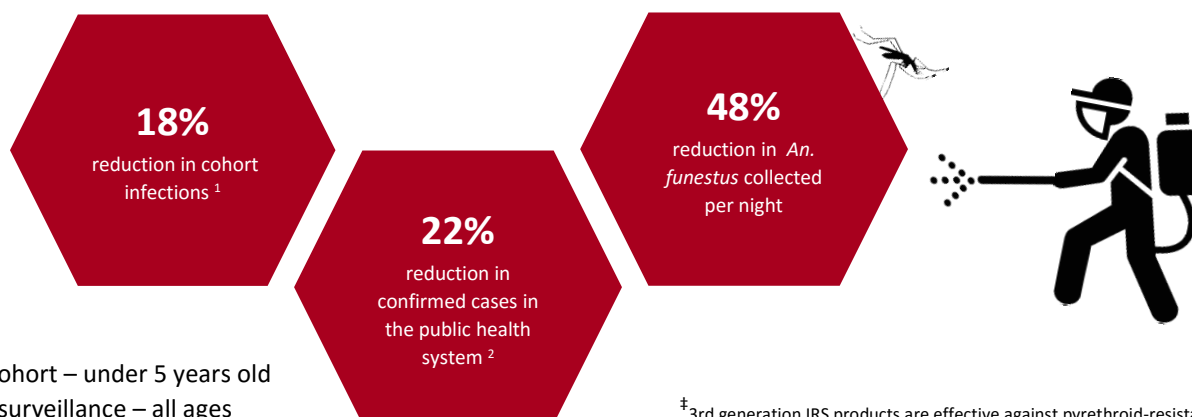

Monthly Cohort Incidence By Spray Status (ITT)
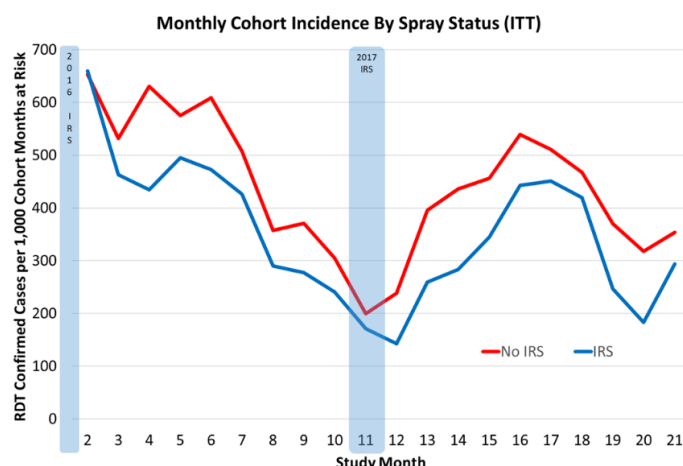
Entomological impact of 3GIRS in Mozambique

Monthly trends in the average number of mosquitos collected per trap night were higher in IRS clusters during the baseline months of September and October 2016. After IRS implementation, this trend reversed dramatically, after which the overall IRR for *An. funestus* s.l. was 0.52 (CI$_{95}$: 0.41 – 0.67; p<0.001) – indicating a significant reduction of 48% (CI$_{95}$: 33% – 59%) in the average number of mosquitoes collected per night over the entire duration of the study. Note that data from three months are missing: specimens and data from January and February 2017 were lost in an insectary fire, and collections from April 2018 were not performed.

CDCLT Collections: Average *An. funestus* s.l. collected per night
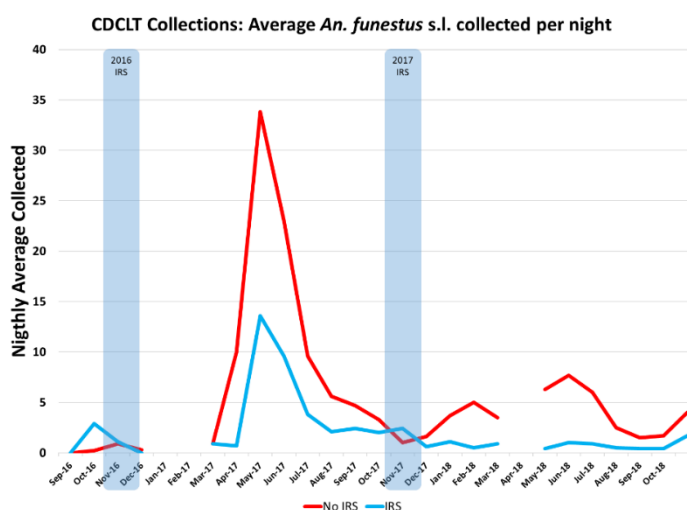
In a highly endemic district of Mozambique, where LLIN access is high and vectors are resistant to pyrethroids, **3GIRS implementation provided significant additional impact - reducing both malaria incidence and vector densities.**

18%
reduction in cohort infections [1]

22%
reduction in confirmed cases in the public health system [2]

48%
reduction in *An. funestus* collected per night

[1] Active cohort – under 5 years old
[2] Passive surveillance – all ages

[‡] 3rd generation IRS products are effective against pyrethroid-resistant vectors and have a residual efficacy of at least 6 months.