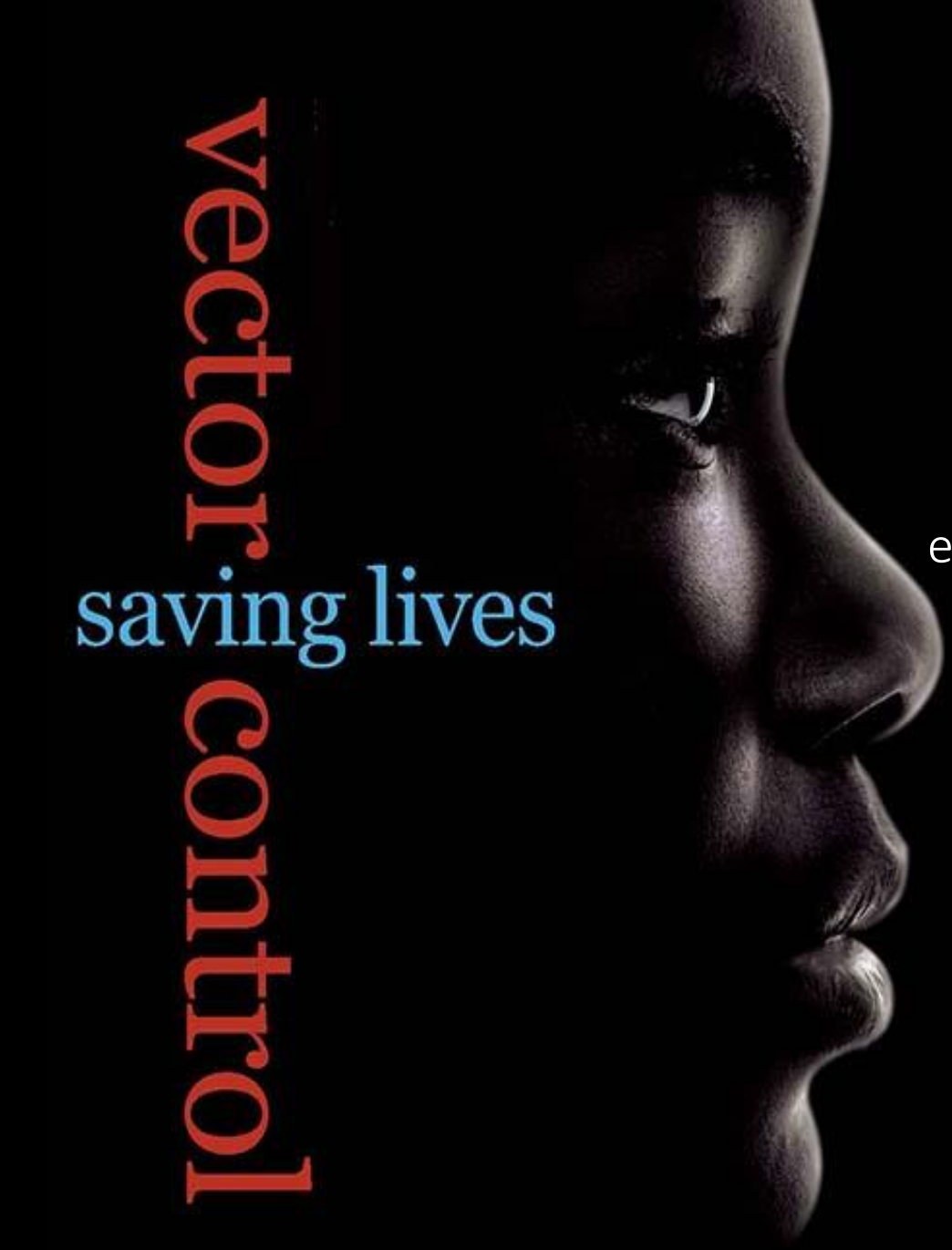


Next generation IRS Project

Developing an evidence base showing the impact and cost effectiveness of 3GIRS: Progress, challenges, and dissemination

MIM 2018

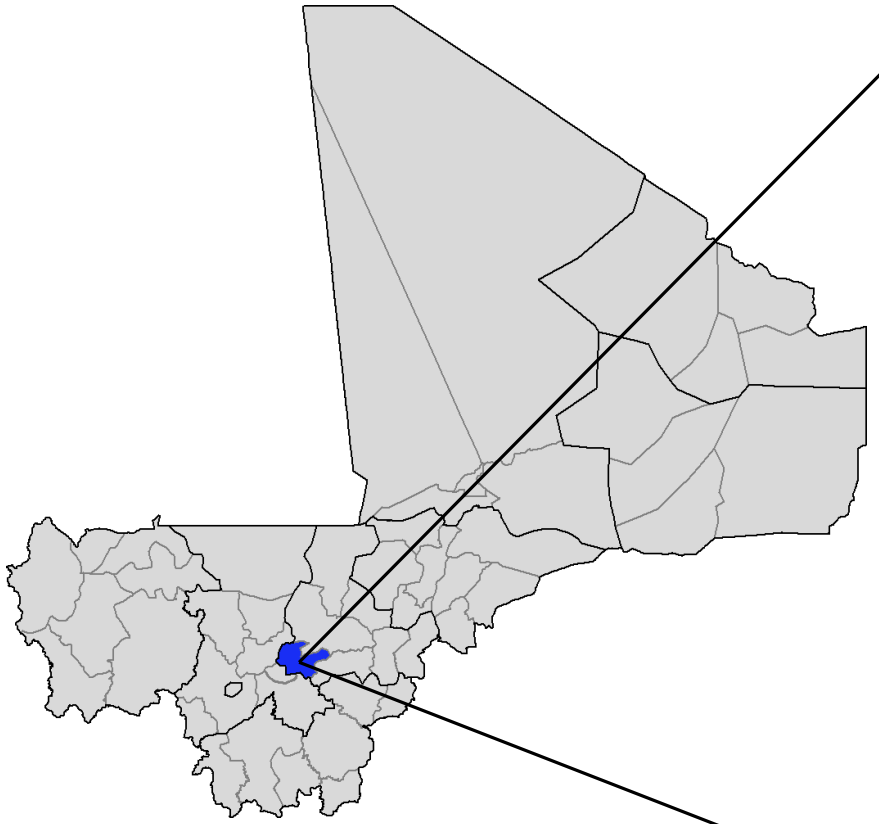
Fransisco Saute & Molly Robertson

IVCC NgenIRS

Building an evidence base - why

- Cost-effectiveness compared to, or incrementally in combination with, other interventions:
  - LLINS
  - New vector control tools
  - MDA/SMC
  - Quality of Case Management (passive, active)
- Effectiveness of IRS in different transmission settings over time and space
- Benefits and ideal monitoring and evaluation of interventions to inform decision-making
- Use of evidence for targeting of IRS
- Creating mechanisms to estimate need to drive demand (decision-making)

NgenIRS Impact Analysis – Critical Data Needs



Intervention Data	Epidemiology Data
IRS	Suspected Cases (Fever)
Insecticide	RDTs Performed
Coverage	RDTs Positive (Confirmed Cases)
Duration of Efficacy	Severe Malaria Cases
LLINs	Malaria Deaths
Net Type	All Cause Deaths
Coverage	**Entomology Data**
Usage Rates	Vector ID & Distribution
Efficacy/Durability	Entomological Inoculation Rates
Case Management	Insecticide Susceptibility
Quality of diagnosis	Feeding/Resting behaviors
Quality of treatment	**Demographic Data**
Other Interventions	Total Population
Mass Test & Treat	Demographic Characteristics
SMC	Behavioral Characteristics
IPTp	**Climate Data**
Vaccine	Rainfall
Etc	Temp

The better the data **resolution**, the stronger the analysis (e.g. IRS implementation data by village can be very useful if Epi data is aggregated to that level.)

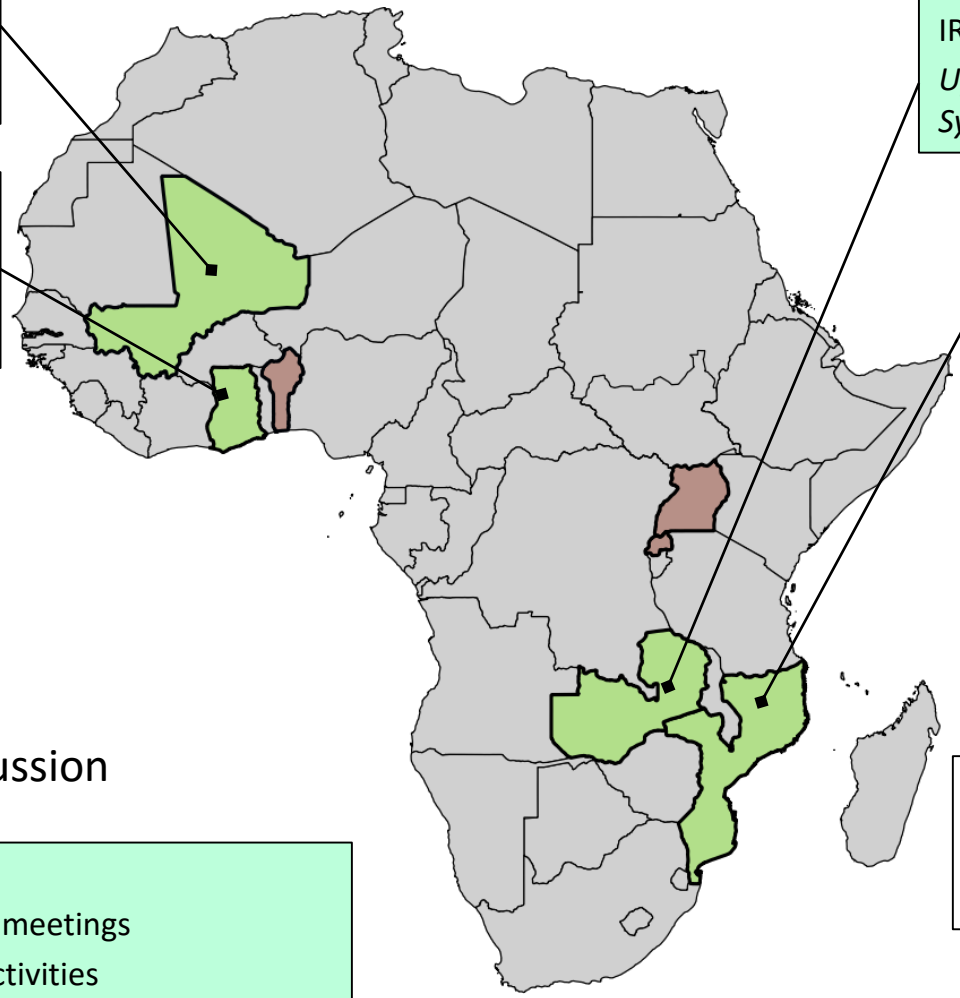
Building an evidence base

Mali: Observational analysis of impact of IRS (including 3GIRS) from 2012-2014 in Segou

Upcoming analysis of introduction of IRS in Mopti and of SumiShield

Ghana: Observational analysis of the impact of 3GIRS in Northern Ghana

Upcoming analysis of previously unsprayed areas and introduction of SumiShield in 2018.



Zambia: Retrospective evaluation of the effectiveness of IRS with Actellic on malaria transmission

Upcoming analysis of SumiShield by NMEC and possible Sylando trial.

Mozambique: Prospective CRT to measure the health impact and cost-effectiveness of 3GIRS combined with LLINs and impact of SumiShield

Epidemiological results to be presented at the 2018 MIM

VectorLink synergies: ongoing discussion

Global Standards:
- Costing Framework
- Standardized IRS M&E

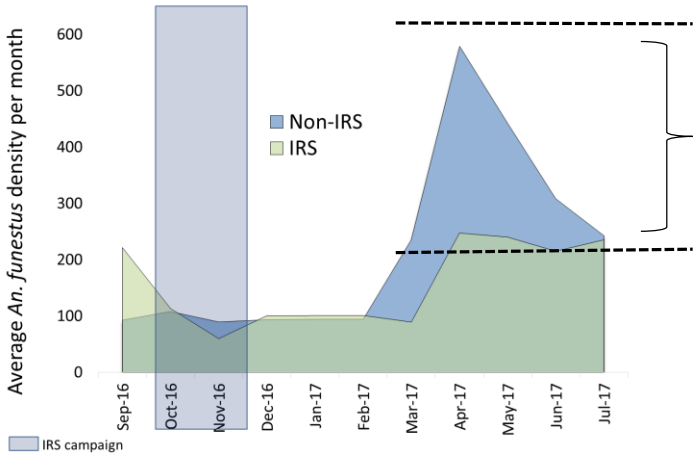
Decision-making:
- Evidence review meetings
- Dissemination activities
- Synthesis of decision-making processes

In discussions:

Burkina Faso: Observational analysis of SumiShield

Malawi: Observational analysis of Actellic

Building an evidence base

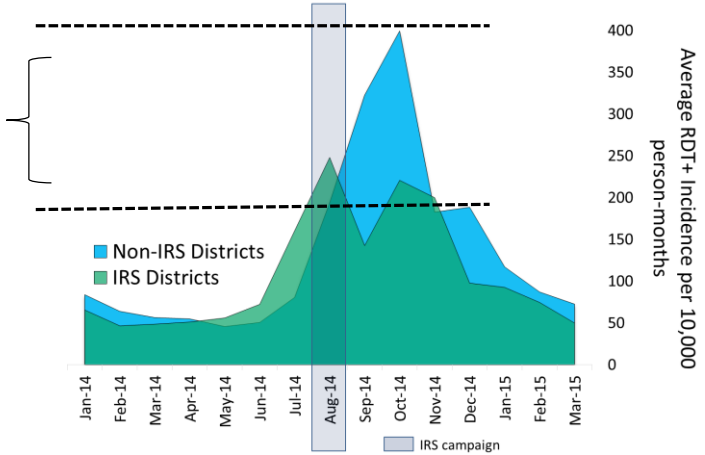


Entomological impact of 3GIRS in Mozambique

After PMI AIRS spraying in 2016, **50% fewer** *An. funestus* were collected from IRS villages than in non-IRS villages

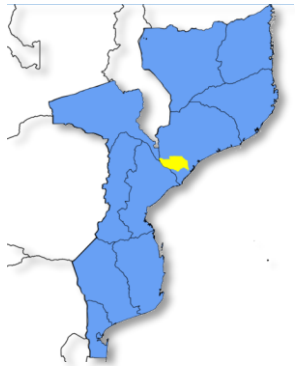
Epidemiological impact of 3GIRS in Mali

After PMI AIRS spraying in 2014, incidence of malaria **dropped 36%** in IRS districts compared to non-IRS districts (76,260 cases averted)[1]



Epidemiological impact of 3GIRS in Zambia

IRS using Actellic-CS, the first approved and widely used 3GIRS chemical, appears to substantially reduce malaria burden under standard operational conditions in Zambia. Its effectiveness was associated with twice the effect of non-Actellic IRS in this setting.



Further evidence of the overall cost-effectiveness of 3GIRS in a high- transmission setting[2]

Full first year results of the NgenIRS-led cluster randomized trial in Mozambique will provide are expected to be shared in October 2018 at ASTMH

[1]Wagman et al. 2018. *Malaria Journal* 17:19

[2]Chaccour et al. 2018. *BMJ Glob Health* 3:e000610.

Building an evidence base

Mali: Observational analysis of impact of IRS (including 3GIRS) from 2011-2014 in Segou:

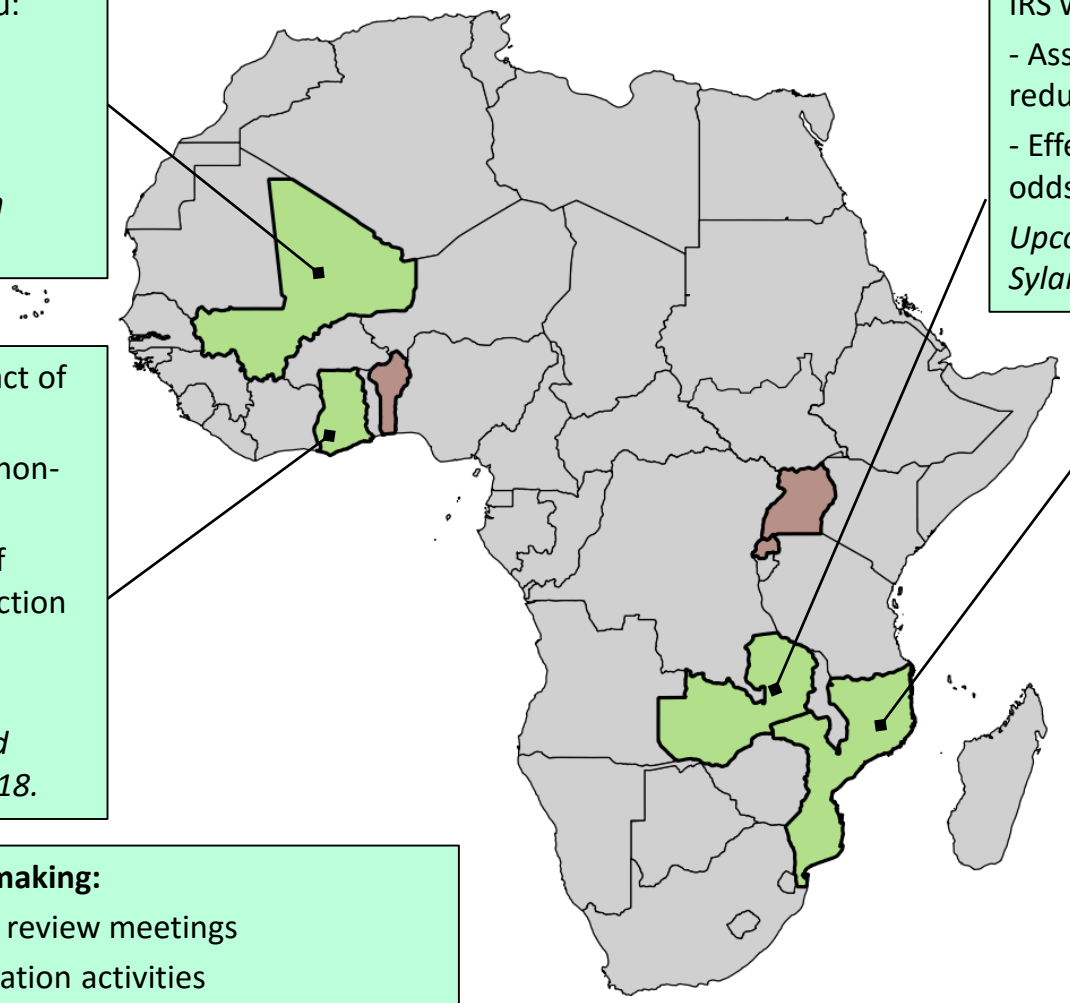
- ~500K people protected over the 3 years
- ~300K cases of malaria averted

Upcoming analysis of introduction of IRS in Mopti and of Sumishield

Ghana: Observational analysis of the impact of 3GIRS in Northern Ghana:

- Fewer malaria cases in IRS districts than non-IRS districts from Jan 2014 to Jan 2017
- In 2015, ~24% decrease in the number of suspected malaria cases following introduction of IRS in Kumbungu District

Upcoming analysis of previously unsprayed areas and introduction of Sumishield in 2018.



Zambia: Retrospective evaluation of the effectiveness of IRS with Actellic on malaria transmission

- Association between increased coverage of IRS and reduced malaria prevalence and confirmed case incidence
- Effectiveness of IRS with Actellic: ~26% reduction in the odds of malaria infection

Upcoming analysis of Sumishield by NMEC and possible Sylando trial.

Mozambique

Global Standards:

- Costing Framework
- Standardized IRS M&E

Decision-making:

- Evidence review meetings
- Dissemination activities
- Synthesis of decision-making processes

Building an evidence base

Ghana

- In 2015 there was a ~24% decrease in the suspected malaria cases in IRS areas

Mali

- Over 300K cases were averted in 3 years of IRS in the Ségou region
- The removal of IRS in Bla was associated with a 70% increase in malaria cases

Mozambique

- As part of a RCT there was a ~50% reduction in *An. funestus* densities over six months post intervention

Zambia

- The odds of malaria infection were reduced by ~26% in areas with IRS
- Improvement of enumeration led to increased impact through better coverage
- Combining IRS and drug-based interventions (MDA – Zambia, SMC – Mali) leads to a greater impact than either strategy alone

Further evidence for decision making

What do I spray and where?

- What evidence is needed to show the effect of rotation both entomologically and epidemiologically?

How is my program doing?

- What are the benefits of standardized analysis of routine data?

Is IRS worth the investment?

- What are the additional benefits that outweigh the cost of 3GIRS – how do we measure cost-effectiveness?

How does IRS fit into my toolbox?

- What is the increased effect of IRS over other tools as they become available?

At what point can I switch strategies?

- Is there a threshold at which IRS can be removed and what is the effect before this threshold?

Focus on Mozambique

BMJ Glob Health 2018;**3**:e000610. doi:10.1136/bmjgh-2017-000610 Protocol

BMJ Global Health

Combination of indoor residual spraying with long-lasting insecticide-treated nets for malaria control in Zambezia, Mozambique: a cluster randomised trial and cost-effectiveness study protocol

Carlos J Chaccour,[1,2] Sergi Alonso,[1,2] Rose Zulliger,[3] Joe Wagman,[4] Abuchahama Saifodine,[5] Baltazar Candrinho,[6] Eusébio Macete,[2] Joe Brew,[1] Christen Fornadel,[7] Hidayat Kassim,[8] Lourdes Loch,[9] Charfudin Sacoor,[2] Kenyssony Varela,[9] Cara L Carty,[4] Molly Robertson,[2,4] Francisco Saute[2]

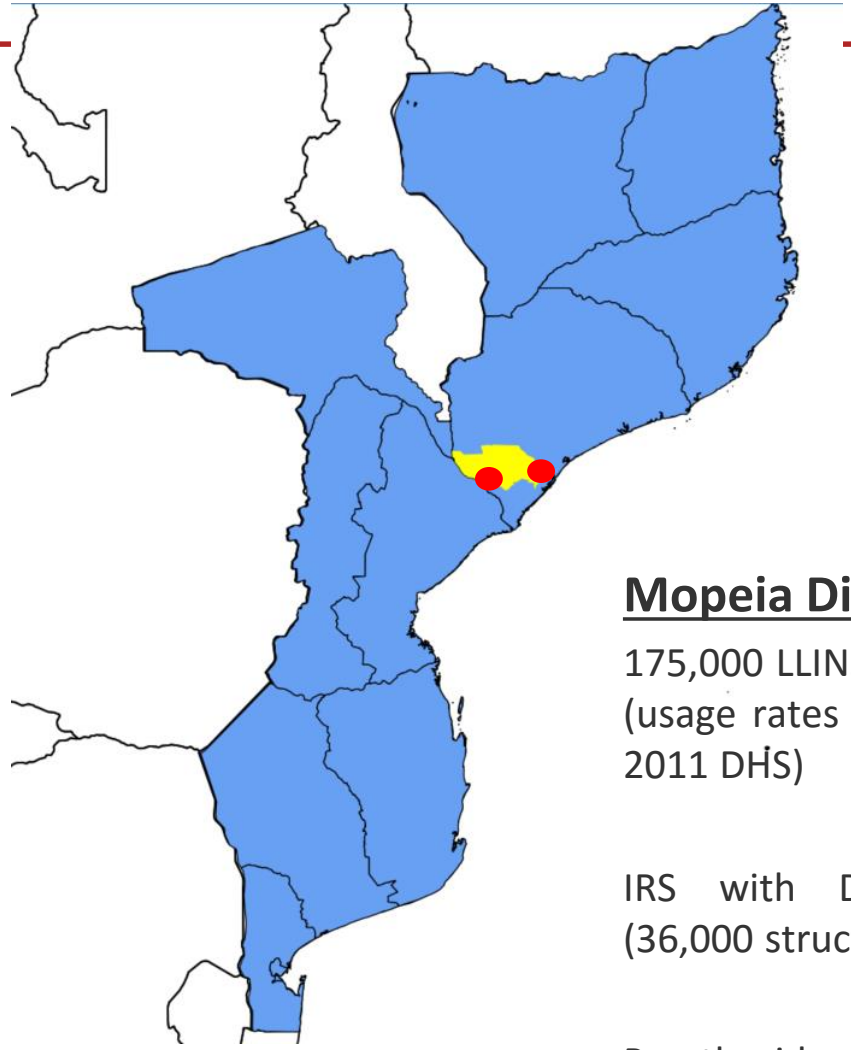
Dr. Francisco Saute (MD, MSc, PhD)

Deputy Director for Science

Manhica Health Research Center/ Mozambique

CRT in Mozambique

A cluster randomized trial (CRT) to determine the **public health impact** & **cost effectiveness** of IRS with Pirimiphos-Methyl (Actellic®300 CS, Syngenta AG, Basel Switzerland) in communities with high levels of LLIN access



Mopeia District

7,614 km^2

160,000 total population (2014 Estimate)

17,500 children <5 years (2016 Study Census)

<5 malaria prevalence = 54% (2011 DHS)

1 District Hospital and 11 local Health Facilities

An. gambiae s.l. & *An. funestus* s.l.

Mopeia District

175,000 LLINs distributed in 2014/15 (usage rates estimated ~40% in <5's 2011 DHS)

IRS with Deltamethrin in 2014 (36,000 structures sprayed)

- Pyrethroid resistance detected in neighboring Mocuba & Morrumbala districts in 2015

Mozambique - Overview of cost trial

2 years of follow up

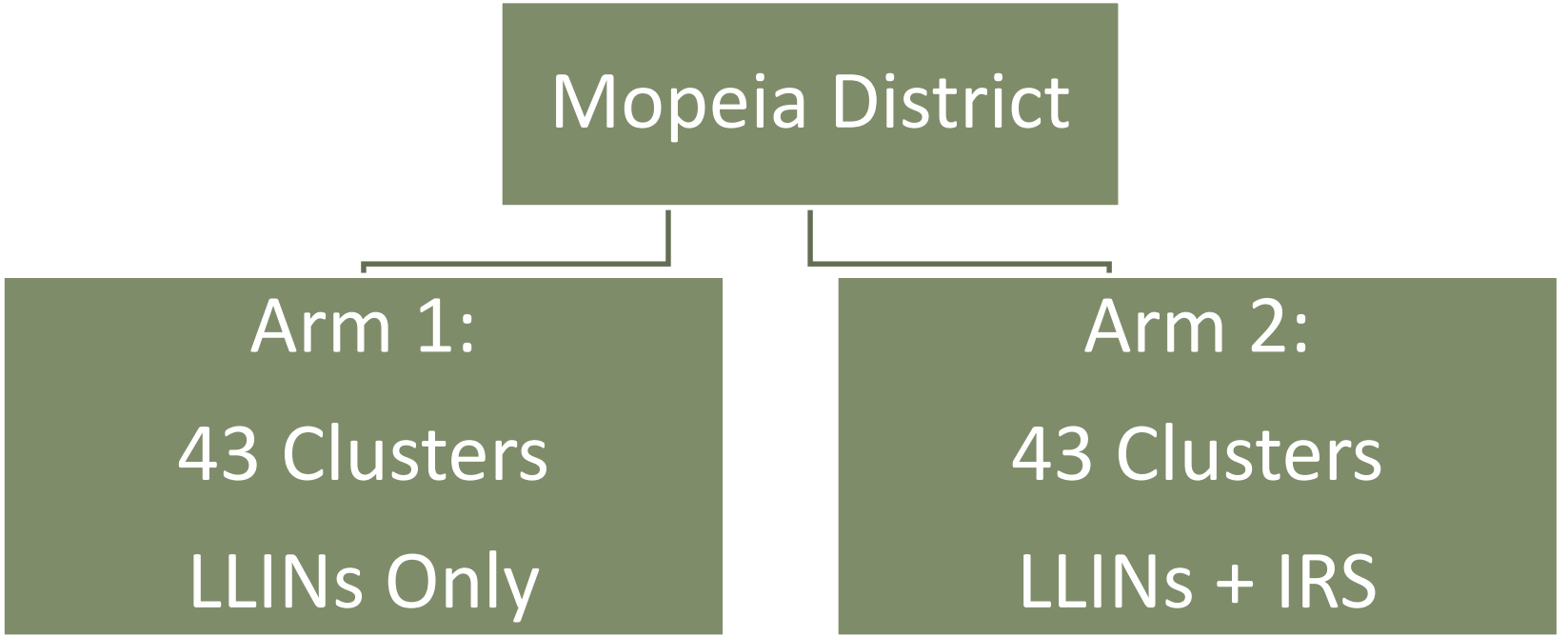
2016 –

IRS with Actellic

2017 –

IRS with Actellic +

Mass Distribution of new LLINs scheduled for entire district (MoH/PMI)



Active Cohort

18 children per cluster (774 per arm)

Monthly follow up

- True ≤5 incidence
- Health behavior & HH spending data

Cross Sectional Surveys

April 2017 & April 2018

(385 per arm)

- Community prevalence
- Health behavior & HH spending data

Enhanced Passive Surveillance

Continual

- Secondary incidence measure – symptomatic cases presenting to a HF
- Health Systems costs

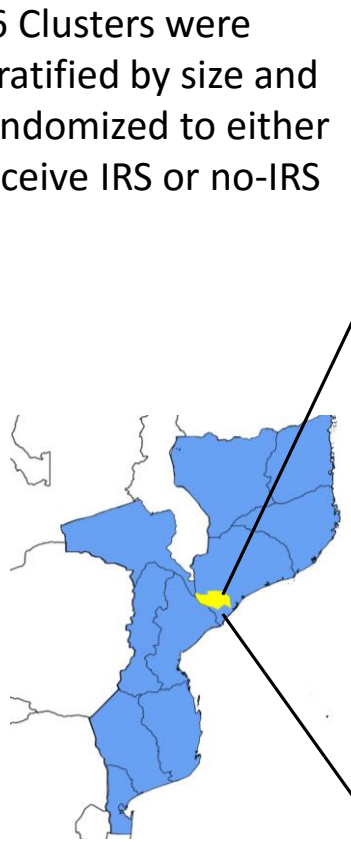
Enhanced Entomological Surveillance

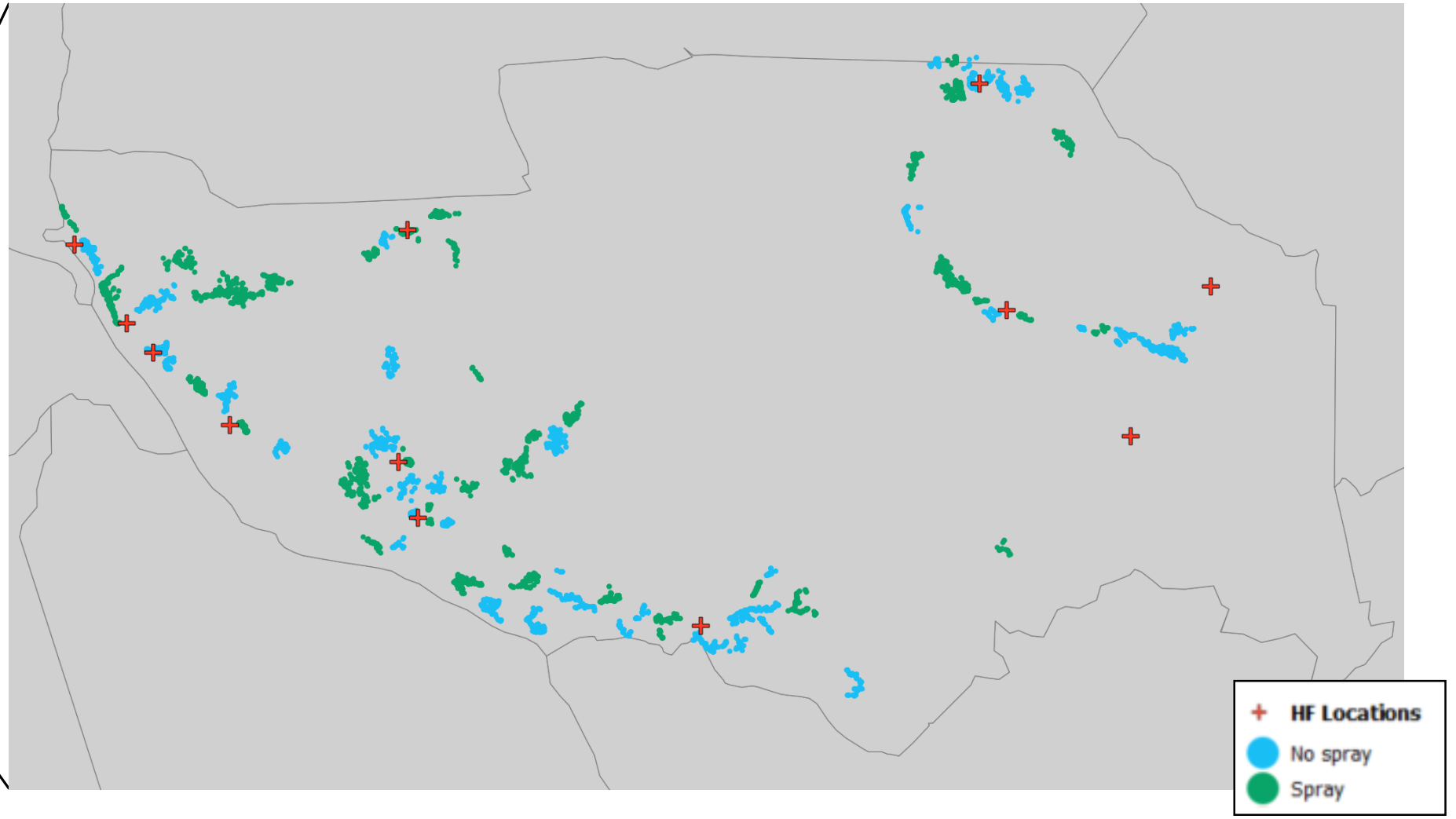
Continual

- Vector densities and biting rates
- Entomological Inoculation rates

Mozambique - Overview of cost trial

86 Clusters were stratified by size and randomized to either receive IRS or no-IRS





Mozambique RCT analysis plan

Crude analysis

Incidence:

- Passive
  - TPR, Incidence/village (RR)
  - % positive
- Active cohort + family health economics
  - Incidence, RR (IRS vs no IRS)
  - Net use/behavior

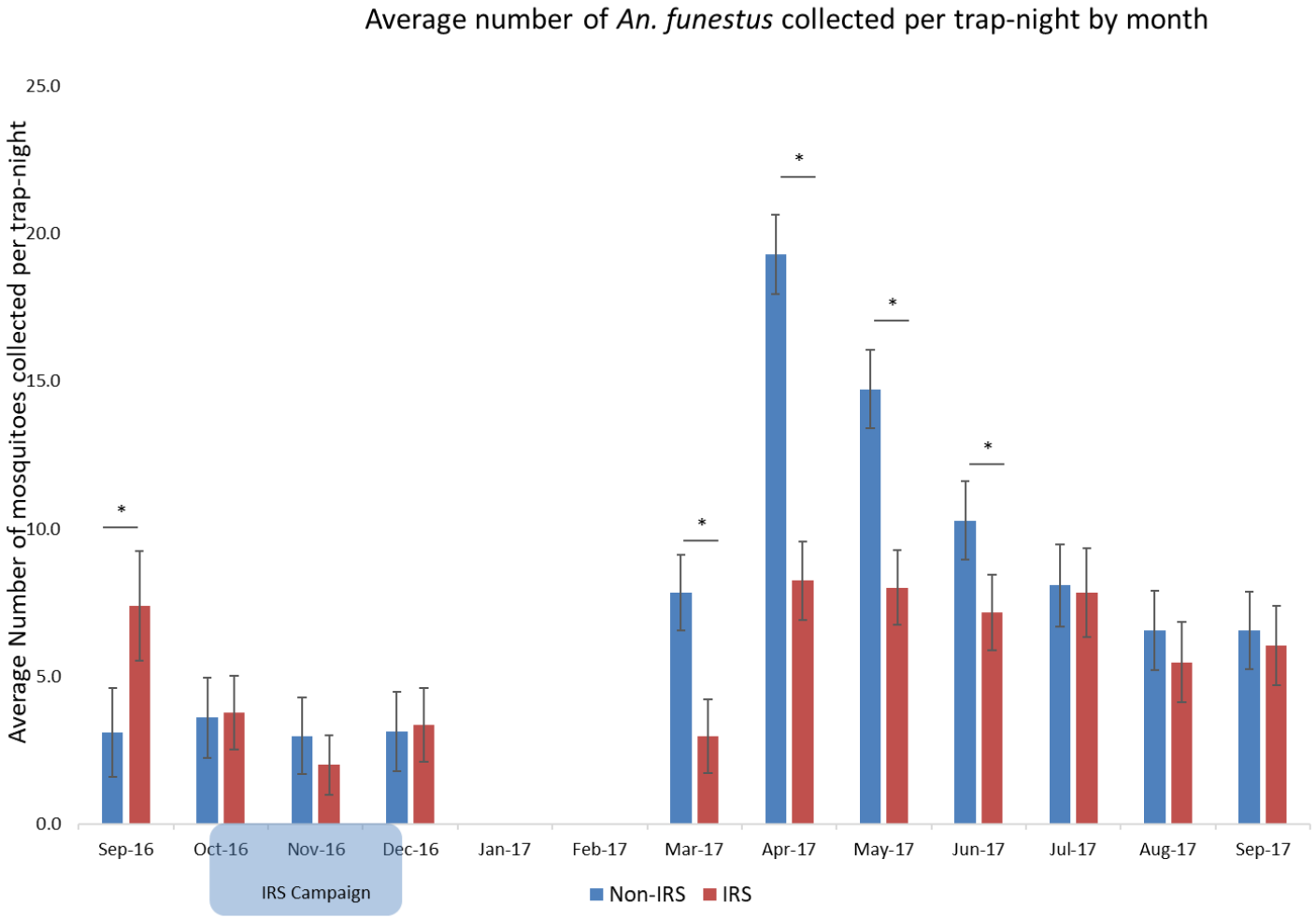
Year 1 prevalence

- Odds ratio
- Net use/behavior

Analysis Considerations

- Cluster design + cluster stratification
- Confounding variables (SES, house type)
- Repeated measures for active cohort

Mozambique RCT – Preliminary entomological results

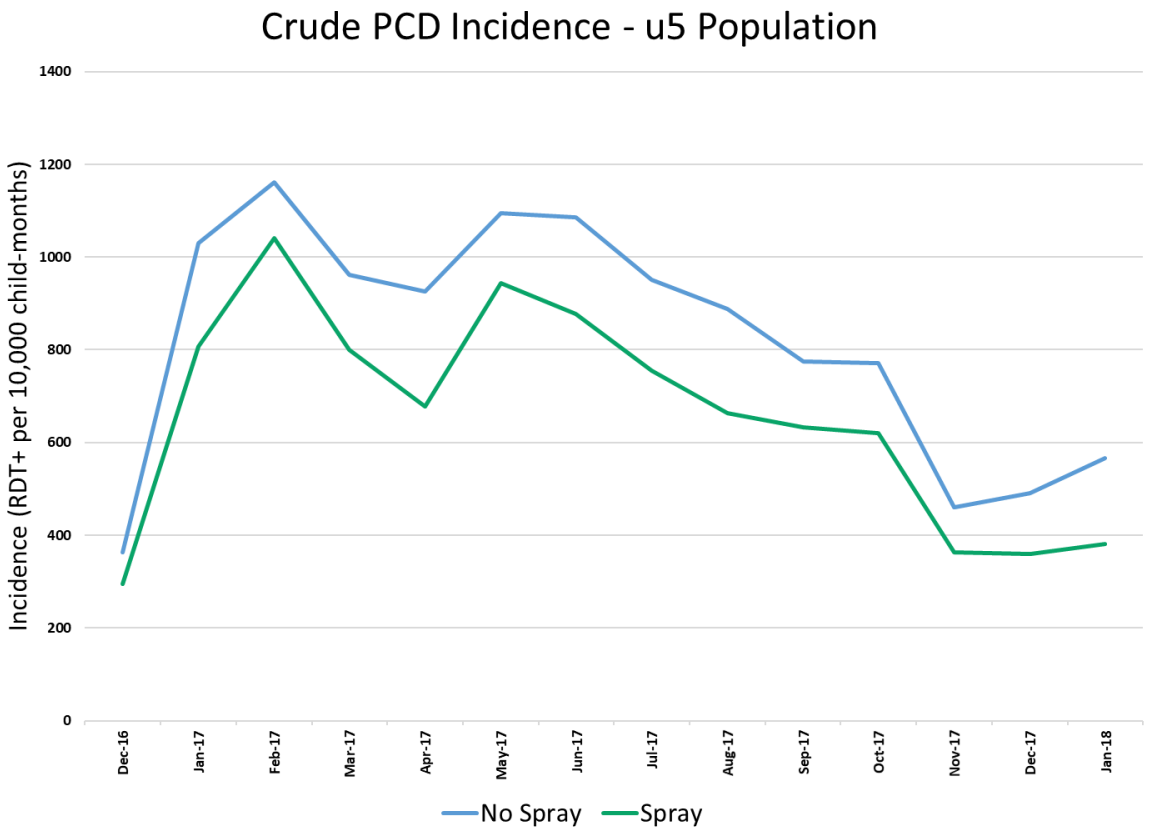


Monthly differences in the mean number of *An. funestus* collected in CDCLTs per trap night between non-IRS and IRS sites.

Means presented are the geometric mean number of mosquitoes collected per trap-night.

A two-way t-test compares densities from non-IRS and IRS clusters (* = $p<0.05$)

Mozambique RCT – Preliminary epidemiological results



According to the 2015 MIS, in Zambezia 56.9% of all febrile children under 5 sought care at a formal health facility [1]

12-month (Dec – Nov) Cumulative Incidence Rate Ratio

	Exposed	Unexposed	Total	
Cases	9277	12281	21558	
Person-time	131328	140760	272088	
Incidence rate	.0706399	.0872478	.0792317	
	Point estimate		[95% Conf. Interval]	
Inc. rate diff.	-.0166079		-.0187167	-.014499
Inc. rate ratio	.8096471		.7880254	.8318409 (exact)
Prev. frac. ex.	.1903529		.1681591	.2119746 (exact)
Prev. frac. pop	.0918771			
(midp) Pr(k<=9277) =				0.0000 (exact)
(midp) 2*Pr(k<=9277) =				0.0000 (exact)

RR of 0.81 (CI_{95} 0.79 – 0.83)

Approximately 2181 u5 health facility cases averted in 12 months
Adjusted for a health care utilization rate of 56% = approximately 3895
Total u5 cases averted in 6 months

[1] Ministério da Saúde (MISAU), Instituto Nacional de Estatística (INE), ICF Internacional, 2015. *Inquérito de Indicadores de Imunização, Malária e HIV/SIDA em Moçambique 2015*. Maputo, Moçambique.
Rockville, Maryland, EUA: INS, INE e ICF International.

Preliminary Results – Cross Sectional Survey

	Study Arm		
	No Spray	Spray	Total
Demographics			
Total participants	449 (54.9%)	369 (45.1%)	818
Under 5	208 (46.3%)	213 (57.7%)	421 (51.5%)
Household has at least one net	255 (56.8%)	184 (49.9%)	439 (53.7%)
Malaria case in household, last 30 days	206 (45.9%)	170 (46.1%)	376 (46.0%)
Sought care for malaria, last 30 days	176 (39.2%)	154 (41.7%)	330 (40.3%)
Outcome			
RDT+	191 (42.5%)	164 (44.4%)	355 (43.4%)

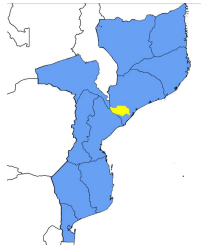
(OR=1.07, CI_{95} 0.80 – 1.4)

Summary & Future Directions

Preliminary Observations:

**These general observations are made at the highest summary levels – by spray status. Final analysis will utilize models that account for the effects of clustering, stratification, and random effects **

- Enhanced passive case detection shows a significant reduction in u5 RDT confirmed malaria incidence from IRS clusters **(2017 RR=0.81)**



- Very High burden district (prevalence rates > 50%)
- Low utilization of formal healthcare systems
- Good LLIN access
- Vectors still susceptible to pyrethroids

Future Directions:

- Formal analysis plan will be carried out on complete datasets (PCD, Cross, ACD) beginning 4Q 2018
- Modeling activities

Questions