Effectiveness of MDA and IRS in Zambia

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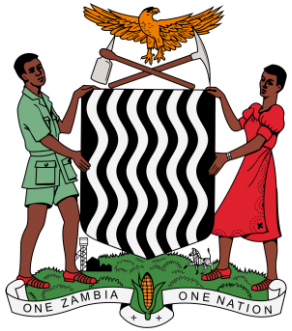
From evidence to action



MACEPA PATH
Malaria Control and Elimination Partnership in Africa

CAMRE
Center for Applied Malaria Research and Evaluation

Rationale and primary study objective

- Zambia has made considerable progress in achieving universal access to vector control and prompt diagnosis and treatment of malaria, and is now aiming for malaria elimination (nationally but focused sub-nationally currently)

- When combined with universal coverage of vector control (LLINs and IRS), good access to case management, and strong surveillance, mass treatment strategies represent a potential strategy to shorten Zambia's timeline toward elimination

- **Primary objective of this study was to assess the impact of 4 rounds of mass drug administration (MDA) and focal MDA (fMDA) with dihydroartemisinin+piperaquine (DHAp) in Southern Province Zambia**
  - ***For this analysis, will also assess effectives of IRS on malaria outcomes during and after trial***

Overview of trial methods

Intervention groups

- **Mass drug administration (MDA)**
  - Everyone in target area tested with rapid diagnostic test (RDT) (SD Bioline)
  - Everyone provided DHAp regardless of RDT result

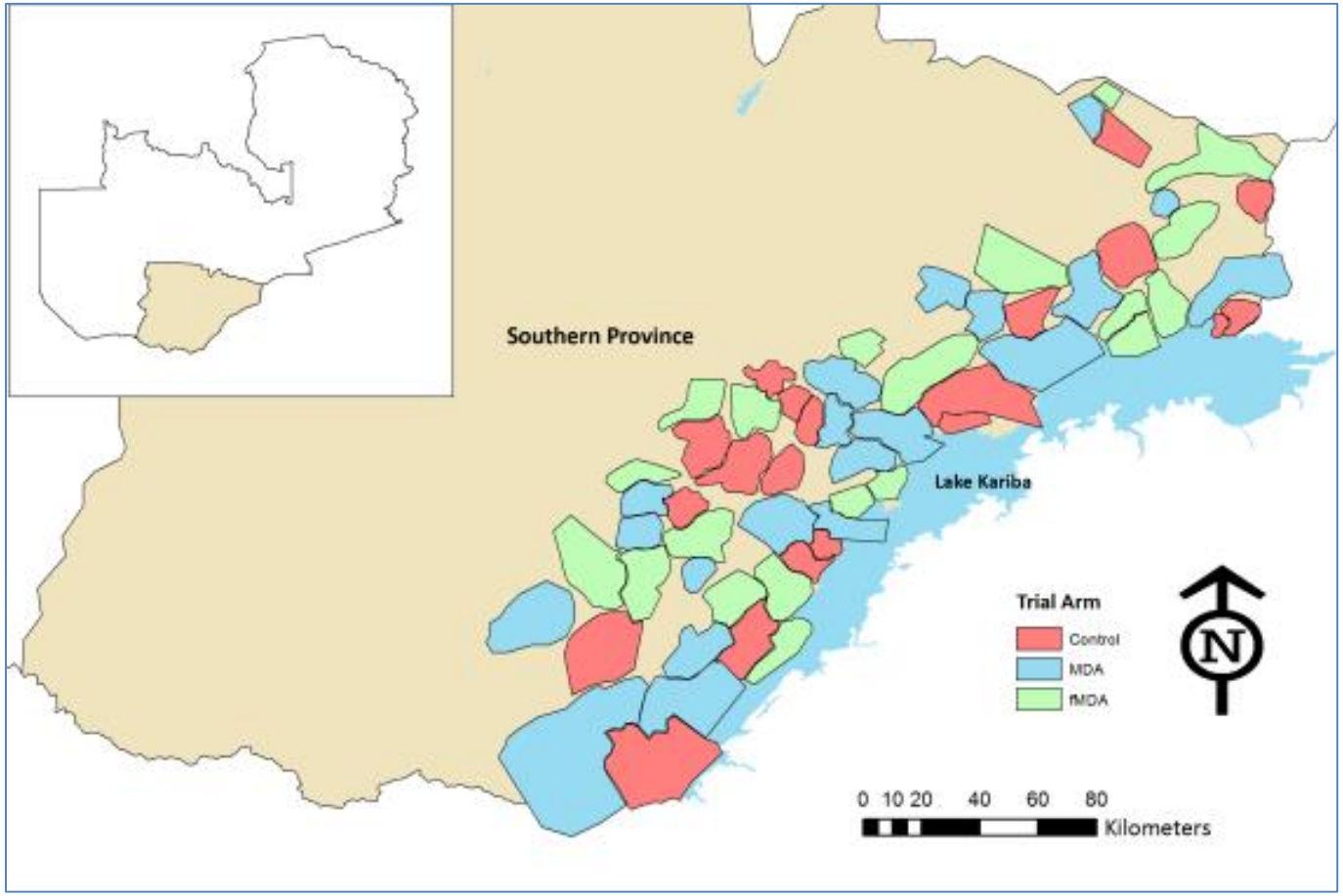
- **Focal MDA (fMDA)** ***This presentation just focuses on MDA***
  - Everyone in target area tested with RDT (SD Bioline)
  - DHAp provided to all RDT-positive individuals, plus all other household members regardless of RDT result

- **Control (standard of care of high-intensity intervention package implemented throughout study area)**

Overview of trial methods

- Community randomized controlled trial to assess impact of MDA/fMDA-DHAp vs. standard of care (control)

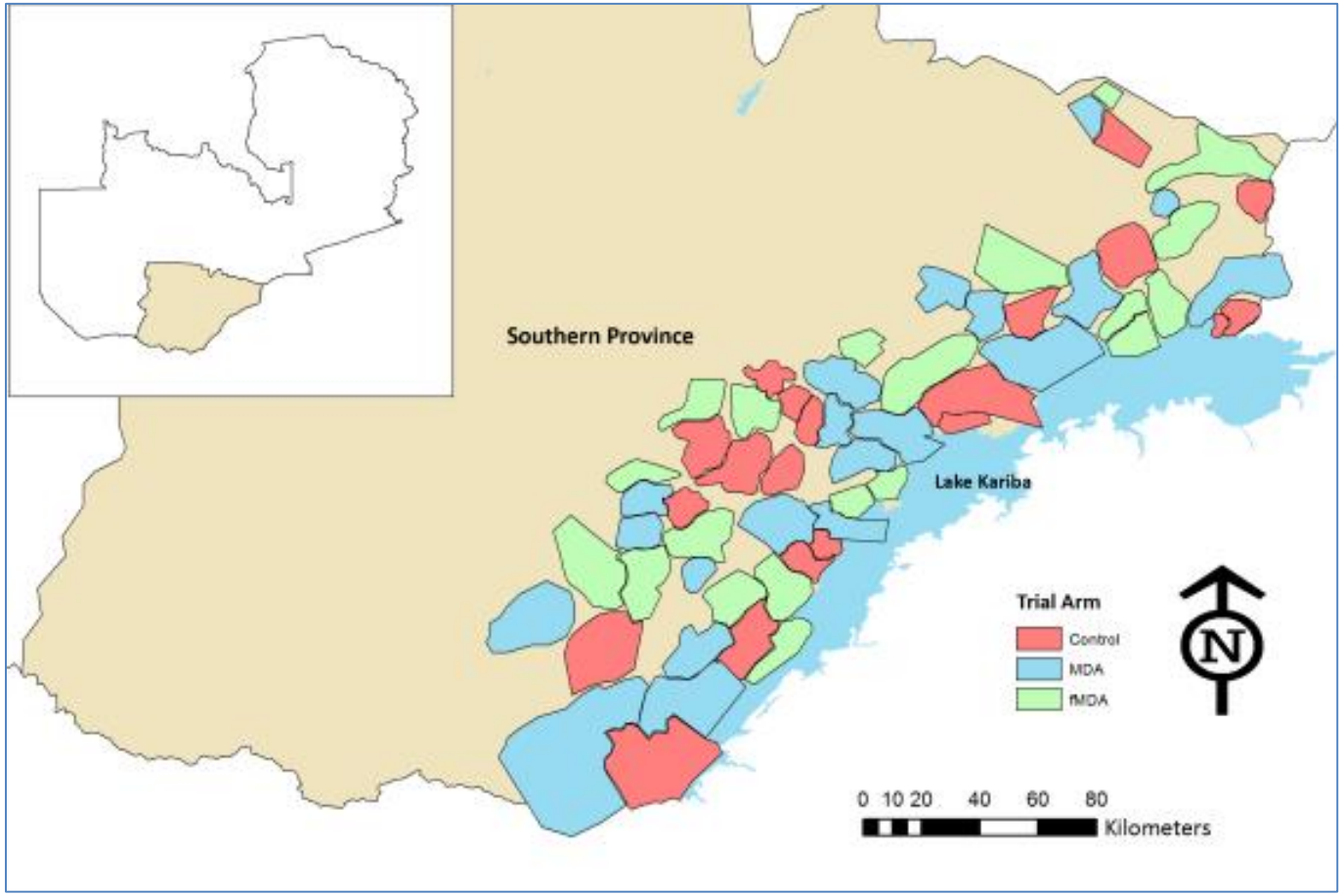
- 60 health facility catchment areas (HFCAs) randomized, stratified by higher (>10% *Pf*PR) and lower (≤10% *Pf*PR) malaria transmission
  - Pop of 330,000 in 56,000 households



See protocol for details – Eisele et al., 2015. *Trials 16:347*.

Overview of trial methods

- Standard of care – ***high-intensity intervention package*** – implemented throughout entire study area
  - ***Targeted IRS-Actellic***
  - High coverage LLINs
  - Improved surveillance (DHIS2)
  - Expansion of CCM with CHWs



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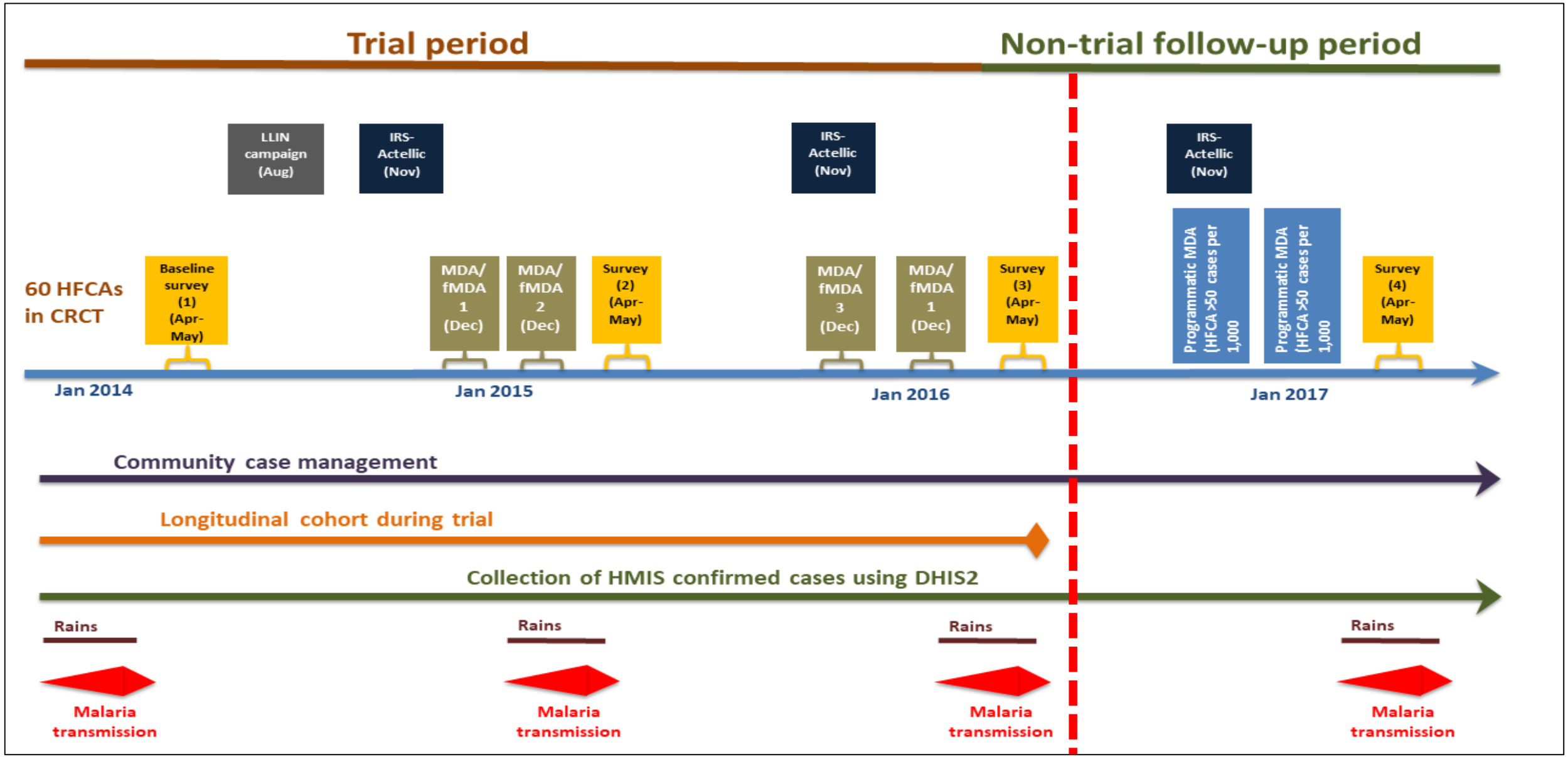
Study timeline



Outcome measures and analyses

Primary outcomes presented here / analysis

1. Malaria parasite prevalence in children
   - Impact of MDA and association of IRS on parasite prevalence assessed with random effects logistic regression
     - *Unable to assess MDA*IRS interaction in this model due to limited number of infections (0 in low transmission strata exposed to MDA and IRS*

2. Confirmed malaria case incidence
   - Effectiveness of MDA and IRS assessed with an interrupted-time series analysis with interaction included between MDA*IRS

Data source

3 cross-sectional surveys in each arm used in this analysis (RDTs and slides)

- April-May 2015, 2016 and 2017
- n = 6,647 children total

Monthly HMIS data from health facilities and HFCA populations

Intervention coverage 2012-2017

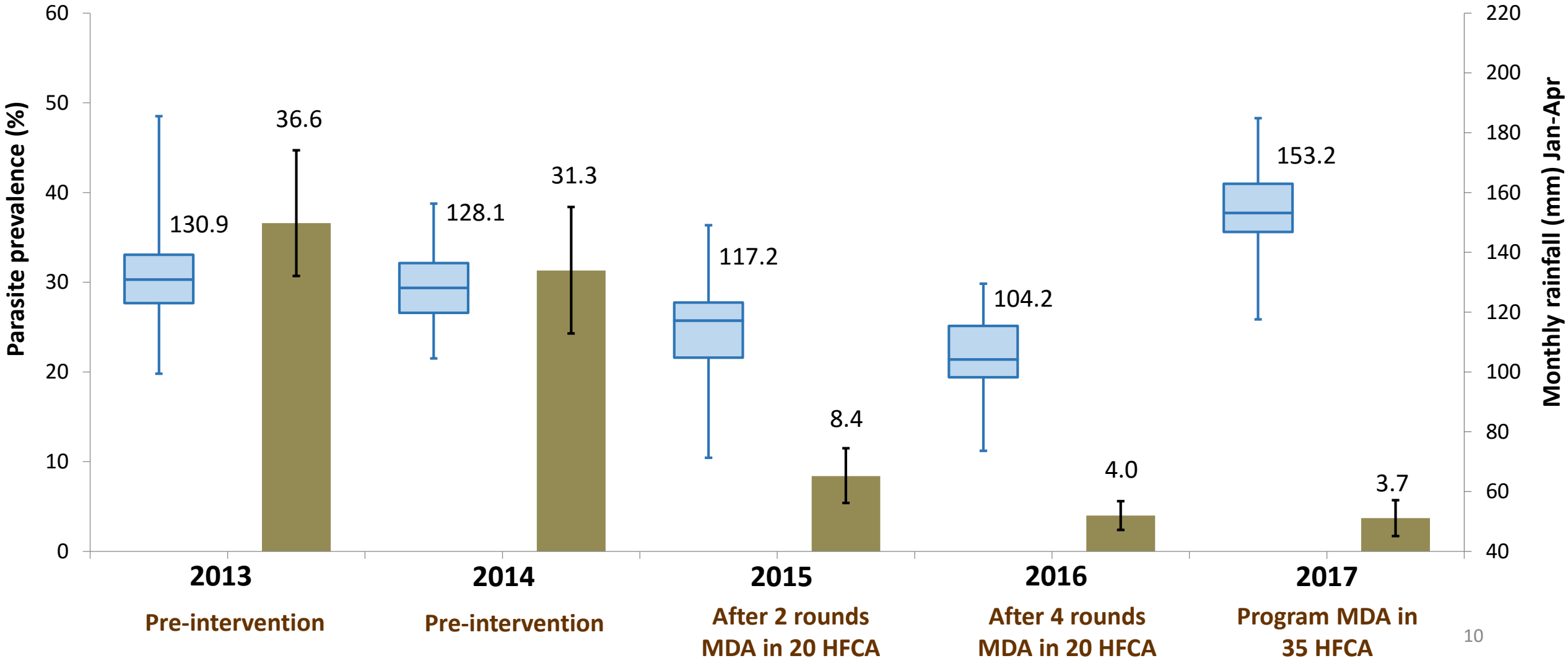
Intervention	Pre-trial surveys 2012-13*	2014	2015	2016	2017
Vector control indicator (% household with child <6 years)	n = 2,516	n = 3,008	n = 2,105	n = 2,485	n = 2,174
Household ≥ 1 ITN	74.8 (70.2 – 79.424)	77.9 (74.1 – 81.7)	84.7 (79.5 – 89.8)	80.8 (77.4 – 84.2)	56.6 (52.2 – 61.1)
Slept under LLIN last night		46.8 (42.5 – 51.2)	64.9 (59.8 – 70.0)	60.7 (56.8 – 64.6)	40.4 (36.2 – 44.7)
IRS-Actellic past 12 months	27.60 (15.98 – 39.22)	12.9 (8.2 – 17.5)	36.9 (28.4 – 45.4)	51.8 (45.0 – 58.5)	47.1 (39.3 – 54.8)
Any LLIN or IRS	80.52 (75.74 – 85.31)	80.1 (76.4 – 83.7)	90.4 (86.6 – 93.9)	89.9 (87.4 – 92.6)	75.1 (70.3 – 80.0)

Intervention coverage 2012-2017

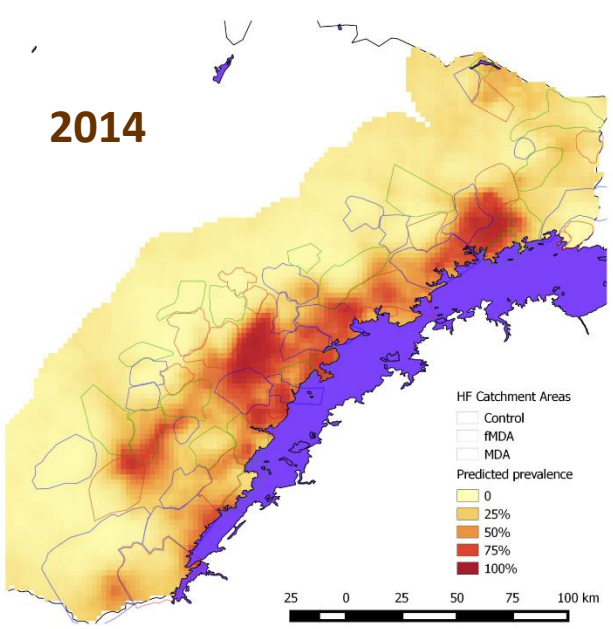
Intervention	Pre-trial surveys 2012-13*	2014	2015	2016	2017
Case management indicator (% children)	n = 2,365	n = 3,008	n = 2,105	n = 2,485	n = 2,174
Of children with fever, % taken for treatment at a public or private provider*	49.62 (45.03 – 54.20)	65.7 (60.7 – 70.7)	63.0 (55.8 – 70.2)	64.3 (56.6 – 72.0)	70.0 (60.7 – 79.3)
Of those taken for treatment, % went to CHW	7.54 (4.73 – 10.35)	11.9 (6.3 – 17.5)	15.7 (7.6 – 23.8)	15.8 (10.7 – 20.0)	14.3 (6.2 – 22.4)
End of year number of CHWs providing malaria case management in study area	187	423	426	426	445
Mean distance (km) from child's house to malaria treatment provider	4.22	4.06	1.83	1.90	2.11
% households within 1.5 km from a malaria treatment provider	15.9 (9.2 – 22.6)	27.1 (19.5 – 34.7)	60.3 (49.0 – 71.6)	57.4 (47.5 – 67.3)	56.2 (47.9 – 64.6)

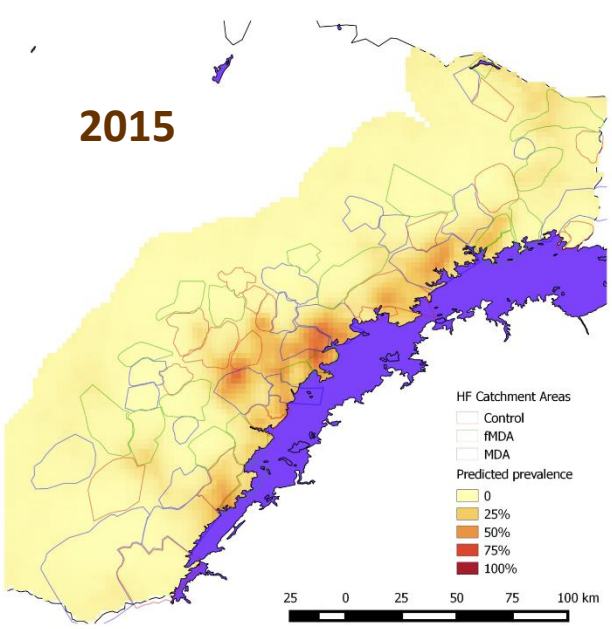
Trend in child parasite prevalence and rainfall 2013-2017

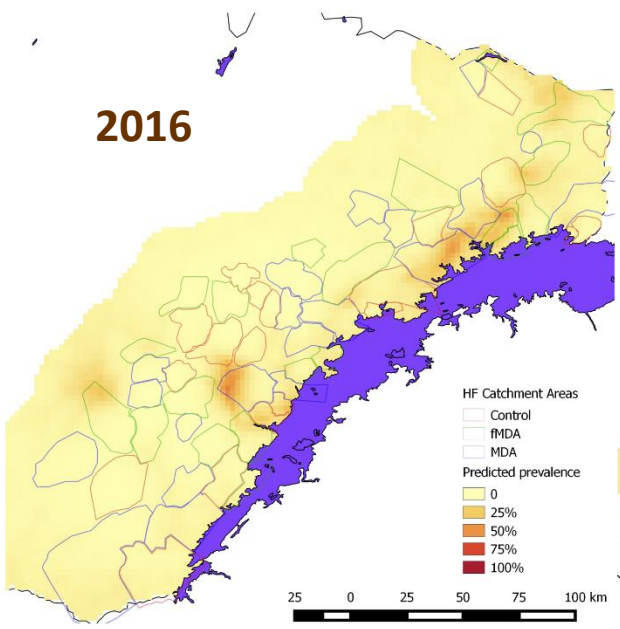
From household surveys conducted in study area during high transmission season (April-May)

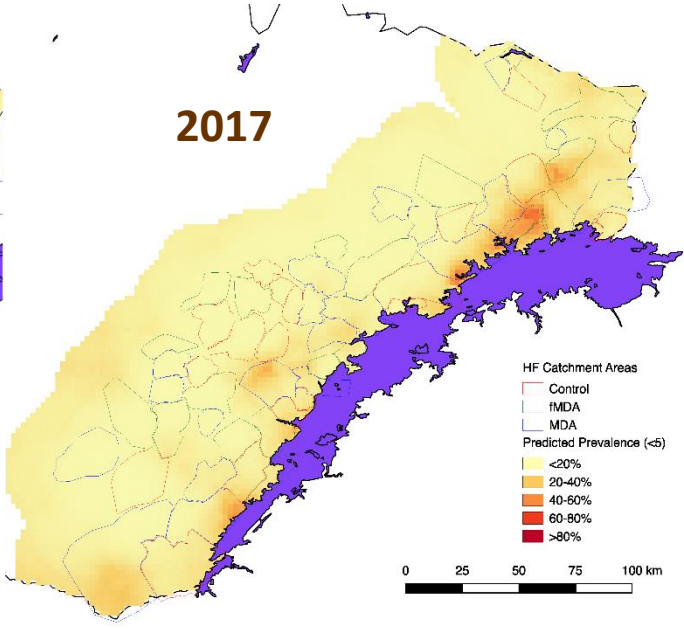


Distribution of parasite prevalence 2014-2017



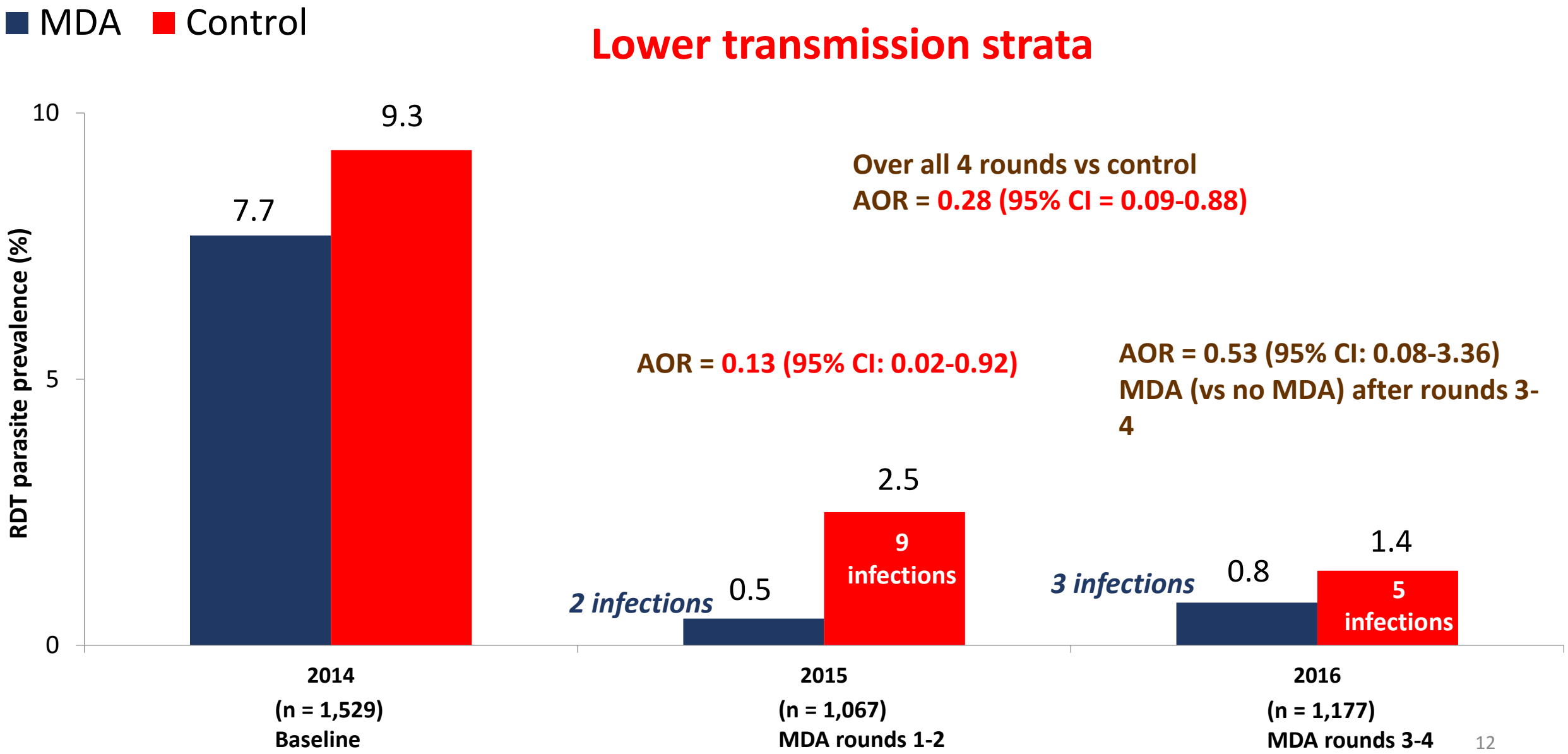






31.3% prevalence **8.4% prevalence** **4.0% prevalence** **3.7% prevalence**

4 rounds of MDA: Child parasite prevalence



Factor associated with child parasite infections 2015-2017

During and after trial (2015-2017 surveys)	Lower transmission		Higher transmission		Lower and higher pooled	
Factor	AOR	95% CI	AOR	95% CI	AOR	95% CI
	n=3,265 children in 30 HFCAs		n=3,382 children in 30 HFCAs		n=6,647 children in 60 HFCAs	
IRS	0.31*	0.13-0.73	0.60*	0.44-0.81	0.56*	0.43-0.74
Distance to the nearest malaria provider	1.21*	1.06-1.41	1.11*	1.02-1.21	1.13*	1.05-1.21
Slept under LLIN	1.46	0.73-2.93	0.80	0.60-1.06	0.89	0.68-1.15
RFE during peak transmission (Jan-Apr)	1.00	0.96-1.03	1.03*	1.02-1.04	1.02*	1.01-1.04
EVI during peak transmission (Jan-Apr)	0.47	0.71-3.04	1.20	0.92-1.56	1.25*	0.98-1.60

*$p<0.05$

All models accounted for year (for pooled analyses across years), trial MDA exposure, programmatic MDA exposure, child age, sex, household wealth quintile, altitude, and transmission strata (for pooled analyses across both high and low), with HFCA included as a random effect

Factor associated with child parasite infections 2016-2017

Post-trial (2016-2017 surveys)	Lower transmission		Higher transmission		Lower and higher pooled	
	AOR	95% CI	AOR	95% CI	AOR	95% CI
Factor	n=2,198 children in 30 HFCAs		n=2,110 children in 30 HFCAs		n=4,578 children in 60 HFCAs	
IRS	0.17*	0.05-0.61	0.78	0.52-1.16	0.70	0.49-1.02
Distance to the nearest malaria provider	1.24*	1.05-1.45	1.12	0.99-1.27	1.15*	1.04-1.26
Slept under LLIN	1.21	0.51-8.88	0.84	0.57-1.24	0.89	0.62-1.62
RFE during peak transmission (Jan-Apr)	1.02	0.97-1.07	1.00	0.98-1.02	1.00	0.99-1.02
EVI during peak transmission (Jan-Apr)	2.04	0.71-5.84	1.07	0.74-1.56	1.22	0.87-1.71

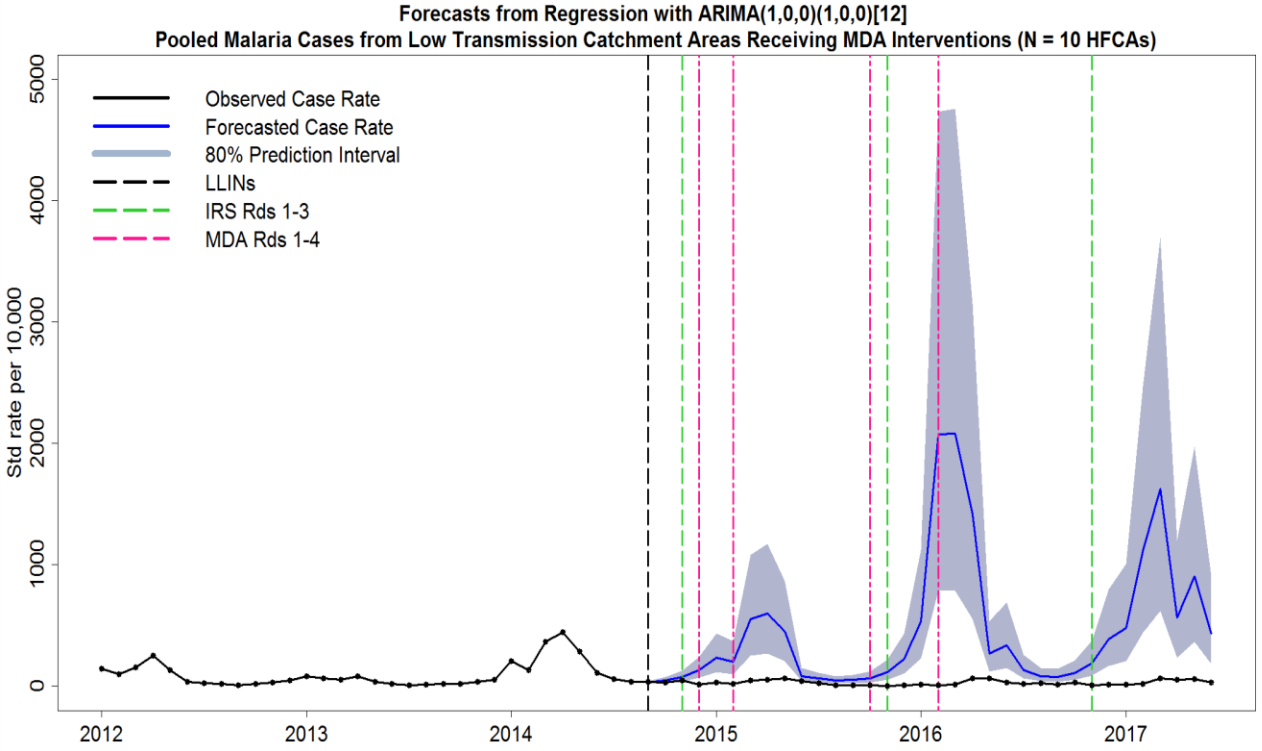
*$p<0.05$

All models accounted for year (for pooled analyses across years), trial MDA exposure, programmatic MDA exposure, child age, sex, household wealth quintile, altitude, and transmission strata (for pooled analyses across both high and low), with HFCA included as a random effect

ITS model results for MDA

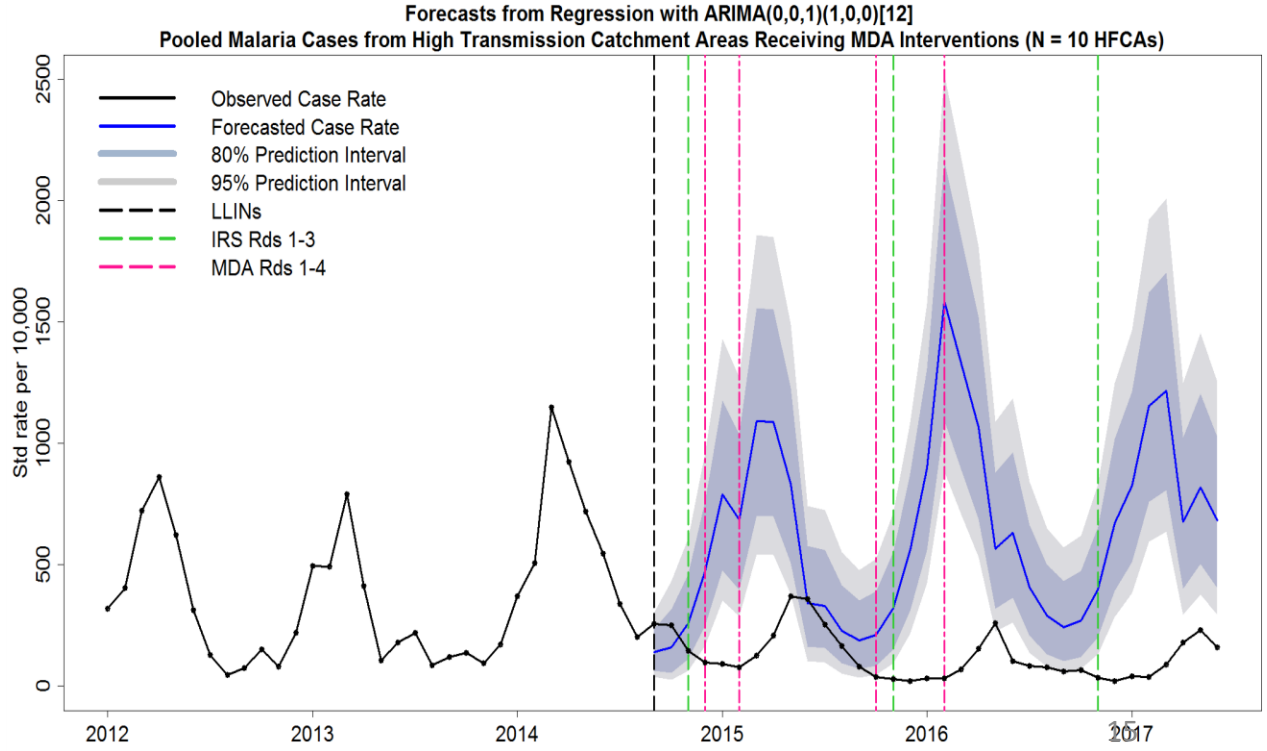
Lower transmission areas receiving 4 rounds of MDA

Intervention	IRR	95% CI
MDA (level change)	0.49	0.33 – 0.75
IRS (level change)	0.52	0.35 – 0.77
Monthly LLIN coverage	1.00	0.98 – 1.02



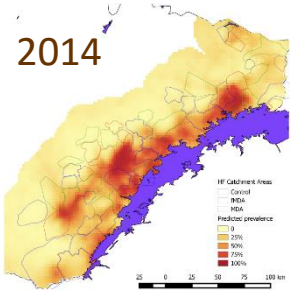
Higher transmission areas receiving 4 rounds of MDA

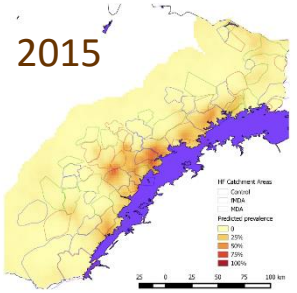
Intervention	IRR	95% CI
MDA (level change)	0.57	0.40 – 0.83
IRS (level change)	0.48	0.33 – 0.70
Monthly LLIN coverage	0.99	0.98 – 0.99

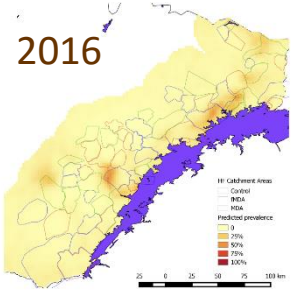


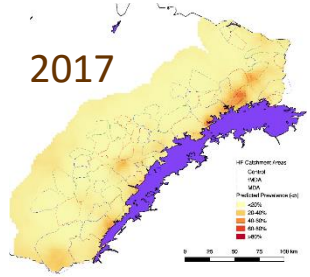
Conclusions

- **High-intensity intervention package achieved throughout study area (standard of care)**
  - Very high IRS and fresh LLIN coverage achieved during trial
    - ***~50% IRS (Actellic) coverage in 2016 and 2017***
    - Entomological data shows vector population shifted from primarily *An funestus* to *An arabiensis in some areas*
  - Vastly improved access to diagnosis and treatment via community-case management, with bulk of scale-up occurring in late 2014
    - Distance to nearest malaria provider was cut in half from over 4 km to 2 km with the addition of 236 CHWs in the study area by the end of 2014
  - Improved surveillance using DIHS2, including at community level



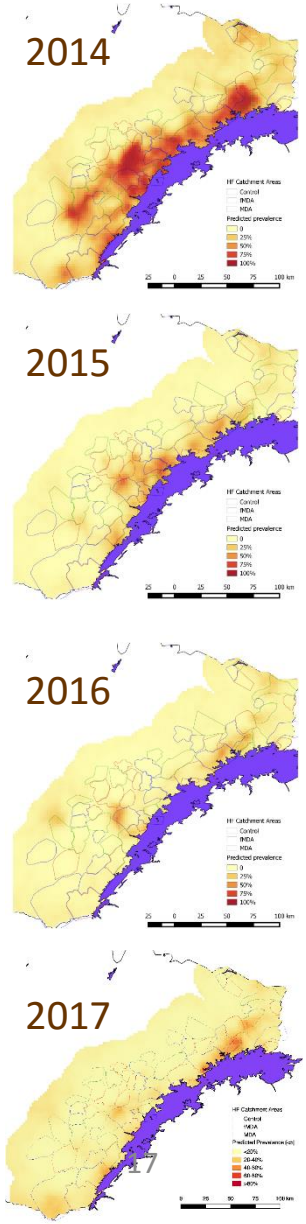






Conclusions

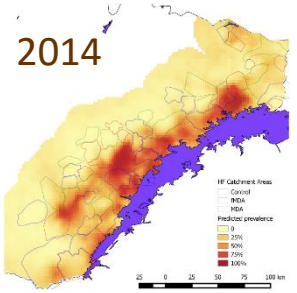
- **Substantial drop in malaria during the MDA trial, irrespective of MDA exposure**
  - Parasite prevalence decreased by 87% during trial (from 31% to 4%)
    - Decreased by 84% in areas of lower transmission (from 9% to 2%)
    - Decreased by 89% in areas of higher transmission (from 53% to 6%)
  - Confirmed case incidence decreased by 70% from 2013 (42.2 per 1,000) to 2016 (12.9 per 1,000) and remained low in most areas in 2017
  - Malaria prevalence remained very low (3.8%) 15-months post MDA - well below baseline levels - even in HFCA that never received any mass treatment
    - 2017 had more rain between Jan-Apr as compared to these same months in previous 4 years

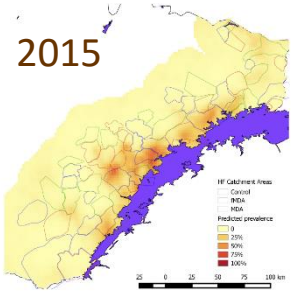


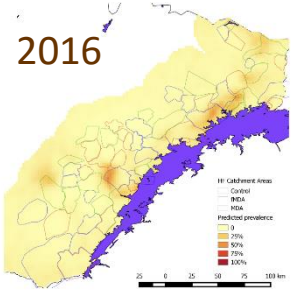
Conclusions

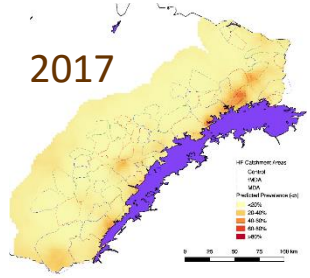
- Biggest impact of MDA occurred after the first 2 rounds and in areas of lower transmission, when measured during peak transmission season

- In lower transmission setting (compared to control):
  - 87% (8-98%) relative reduction in odds of parasite infection in children
    - Significant reduction across all 4 rounds as well
  - 41% (22-54%) larger decline in confirmed case incidence



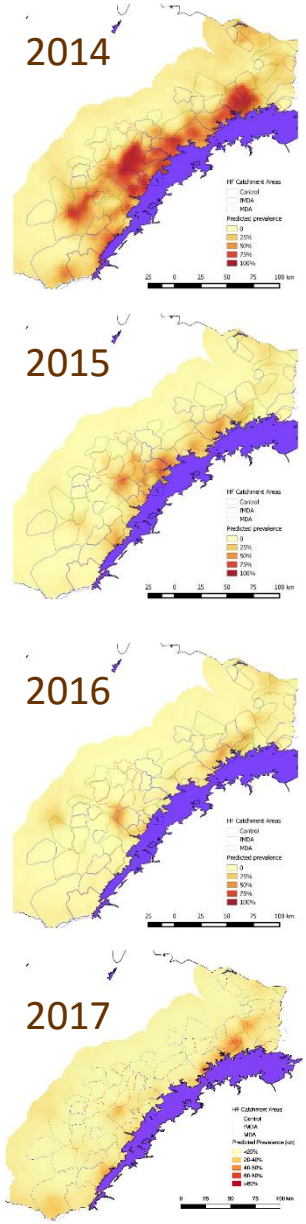






Conclusions

- IRS-Actellic were consistently associated with declines in malaria outcomes during and after the trial and likely major reason why prevalence remained low 15-months post MDA
  - As was improved access to malaria diagnosis and treatment through CCM
- Targeted IRS coverage remained at ~50% coverage in 2017
  - While significantly protective across transmission strata, IRS appears most impactful in lower transmission areas in this setting
- ***Results suggest MDA should be considered in similar settings in combination with IRS (or good vector control), and only once very good access to diagnosis and treatment for malaria has been established***



Thank you!

Community in the study area of Southern Province

PATH-MACEPA

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