Entomological observations surrounding a mass drug administration trial against lymphatic filariasis in Papua New Guinea

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JOINT INTERNATIONAL TROPICAL MEDICINE MEETING

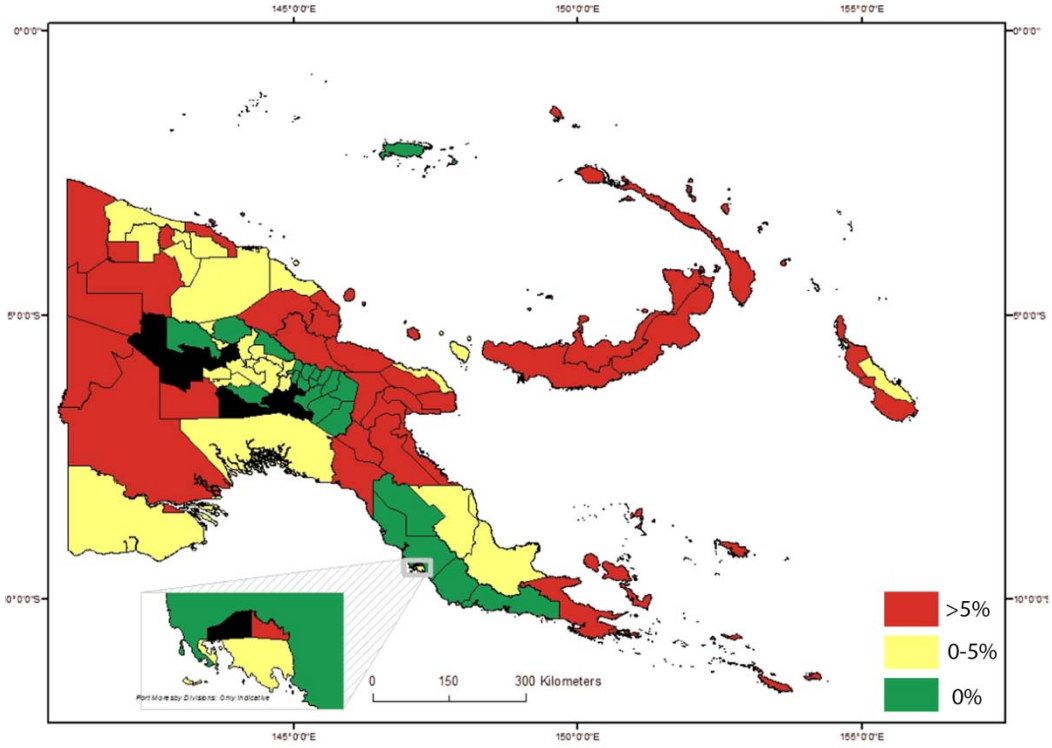
Background

- *Lymphatic Filariasis* (**LF**) is a mosquito transmitted disease caused by filarial worms
- Approximately 120 million people are living with LF, and over 40 million are seriously incapacitated and disfigured by the disease (WHO numbers from 2006)
- Symptoms include the *elephantiasis* syndrome which is marked by severe swelling in the arms, legs or genitals
- LF elimination is moving forward with mass drug administration of albendazole + diethylcarbamazine (DA) as one of the main strategies
- addition of ivermectin to this regimen is being considered (in areas with onchocerciasis and high transmission) - **IDA**

Bockarie, 2002

LF endemicity in PNG

- *Wuchereria bancrofti* (**W*b***) is the only known causative agent of LF in PNG
- Spread only by Anopheles mosquitoes
- very limited MDA has been done
- still a major health problem many areas in PNG
- very high levels of local heterogeneity
- Seropositivity levels of up tp 92% in endemic areas



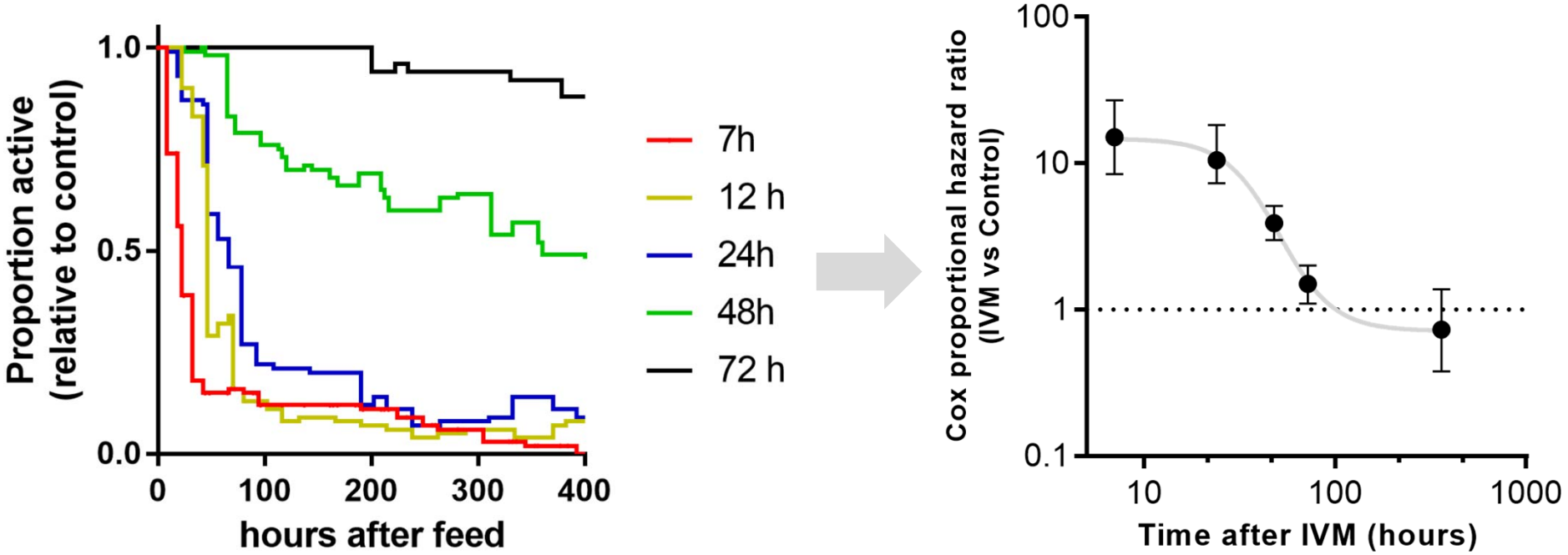
Modified from *Graves et al. Parasites & Vectors 2013 6:7*

Aims

- The **aim of this study** was to evaluate vector parameters including prevalence of *Wuchereria bancrofti* and *Plasmodium* in the mosquito population surrounding a clinical trial evaluating safety of a triple drug regimen albendazole + DEC+ ivermectin (IDA)
- cluster randomized trial comparing IDA (IVM 200mg/kg; DEC 6mg/kg; ALB 400mg) and DA (DEC 6mg/kg; ALB 400mg); clusters were villages
- The trial was conducted in 24 villages in Bogia district, along the North coast of Madang province, PNG. Mosquitoes were collected in 4 of these villages

***Anopheles farauti* survival after ivermectin ingestion**

Experiment: colony mosquitoes were fed on a ivermectin (IDA) treated volunteer at 7, 24, 48, 72 and 360 h post treatment and then monitored for survival



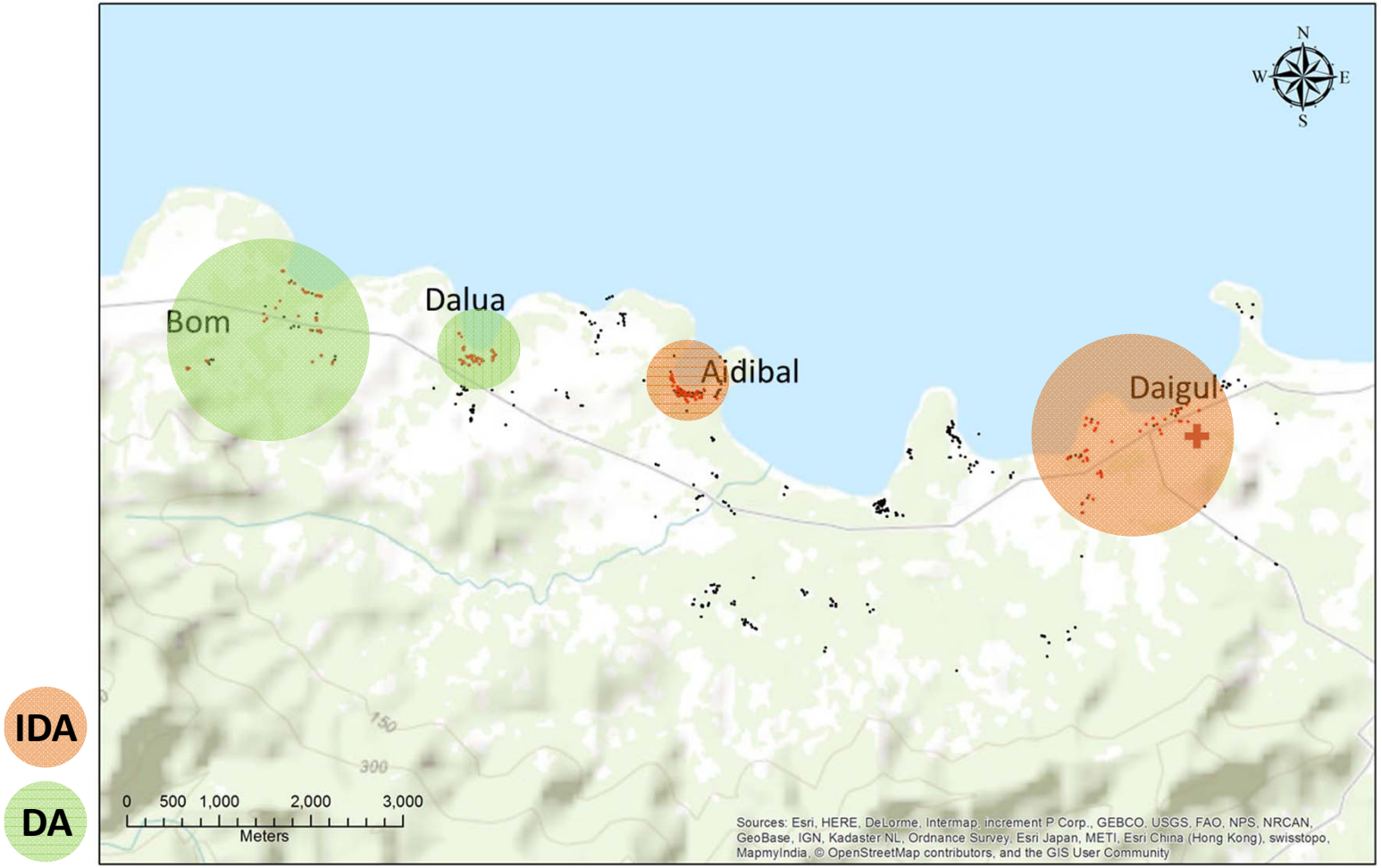
Study site – PNG North Coast

- diverse biting intensity ranging from '**low**' to '**very high**' on short spatial scales, despite near universal LLIN coverage
- LLINs are the only vector control tool used in this area
- malaria transmission seems to be on the rise in several areas
- Human-vector contact occurs mostly in the peri-domestic space

>100 per person/night

3-5 per person/night

Study Site



Study site: The study was conducted in 4 villages in Bogia district on the North Coast of PNG. The villages of Aidibal and Daigul were exposed to double drug (DA) regimen (albendazole + diethylcarbamazine), while Dalua and Bom were exposed to triple drug (IDA) regimen (albendazole + diethylcarbamazine + ivermectin).

Baseline

Baseline characteristics of the clinical trial study population

	AB+DEC	AB+DEC+IVM
Participants n (%)	2193 (47.9)	2386 (52.1)
Female n (%)	1045 (47.7)	1111 (46.6)
Age in years (Median)	16	12
FTS (+)	**494 (22.5)**	**522 (21.9)**
MFS (+)	**94 (3)**	**87 (2)**
Day 1 follow up n(%)	1942 (89)	2210 (93)
Day 2 follow up n(%)	1581 (72)	2150 (90)

Methods – mosquito collections

- mosquitoes were collected for 3-4 nights (6 hours or 12 hours per night), end of 2016-2017
- Villages were surveyed twice; once before the MDA and and once 4-6 weeks after the MDA
- 16-18 volunteer mosquito collectors performed standard outdoor human landing catches (HLC)
- Where possible, the same HLC collectors were engaged in the pre-MDA and post-MDA collections.
- Mosquitoes were stored separately according to collection time, species and feeding status

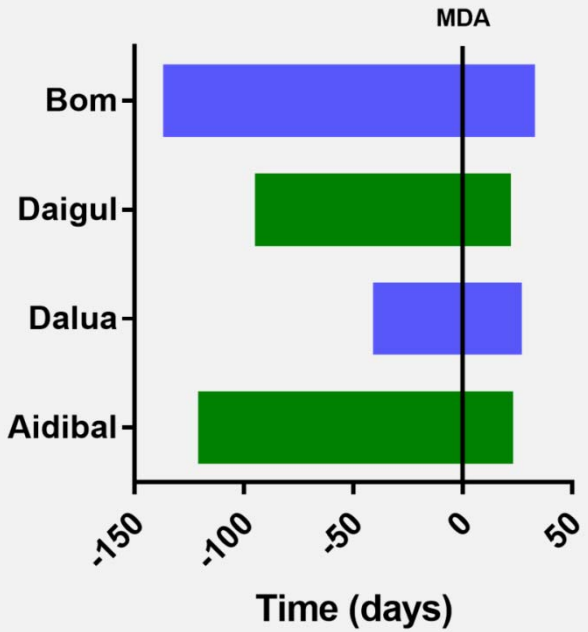


Figure 2: Time between pre and post MDA collections. Left edge of the bar represents pre-MDA collection/ right edge represents post MDA collection

Methods

- PCR analysis for *Wuchereria bancrofi* (*Wb*) infection
- CS Elisa for Plasmodium infection
- matching of collection locations with available household GPS/census data
- prevalence of *Wb* in individual mosquitoes from variable-pool-size pooled samples using Bayesian MCMC estimation
- spatial modelling using spatial inference methods (kriging)

Results – collection effort

- Mosquitoes were collected in a total of 147 separate locations and by 83 individual HLC collectors
- This resulted in a total of 391 HLC 'collections' (as defined as 1-location-1-person-1-time) and a total of 2562 person-hours collection time
- A total of 27,141 anopheles mosquitoes where collected in the 8 surveys (14,622 before the MDA and 12,519 after the MDA)
- Mosquitoes were stored in a total of 8829 pools with an average pool size of 3.2 (range 1-14)

Results – Biting intensity

- Over 95% of all collected mosquitoes were *Anopheles farauti 1*

	Aidibal (IDA)		Daigul (IDA)		Bom (DA)		Dalua (DA)	
	Pre-MDA	*Post-MDA*	*Pre-MDA*	*Post-MDA*	*Pre-MDA*	*Post-MDA*	*Pre-MDA*	*Post-MDA*
Minimum	1	2	40	2	18	22	46	6
25% Percentile	8.25	20	144	138	50.5	77.5	109	39
Median	**27.5**	**30**	**210**	**166**	**104**	**154**	**172**	**64**
75% Percentile	53.5	46	258	249	149.5	244	303	100
Maximum	154	140	414	576	358	1132	480	328
n (collections)	36	65	47	49	48	48	49	49

Biting intensity in each village before and after the MDA. Biting intensity is given in bites per person per night.

- No difference between IDA/DA before and after the MDA
- Large degree of heterogeneity in biting intensity between villages in general

Results – *Wb* infection prevalence (unfed mosquitoes*)

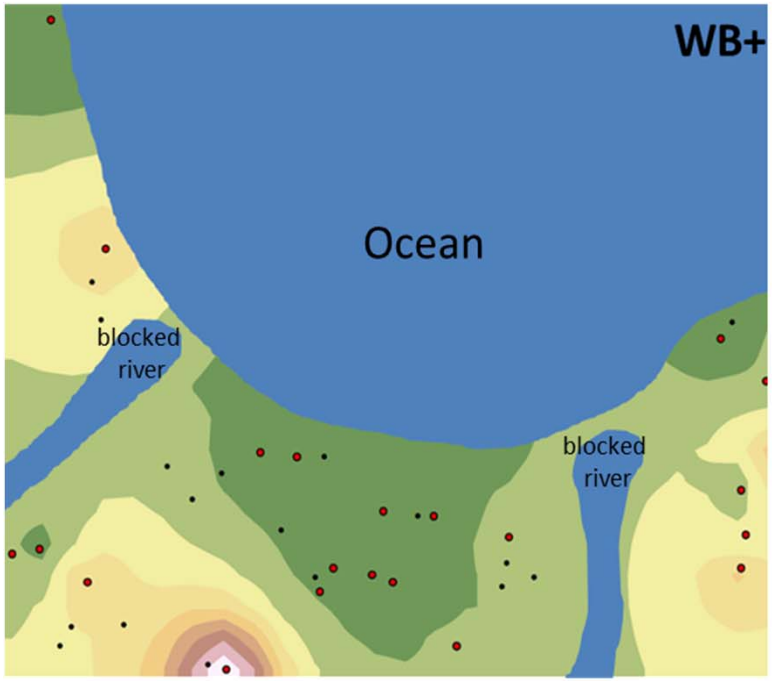
Estimated infection prevalence in the mosquito population in the four villages.

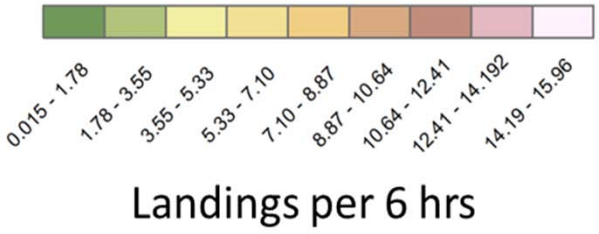
Village	Pre_MDA	Post_MDA
Aidibal (IDA)	0.5% (0.1-1.2%)	0.3% (0-1%)**
Bom (DA)	1.0% (0.5-1.8%)	0.1% (0.0-0.3%)***
Daigul (IDA)	0.3% (0.1-0.7%)	0.1% (0-0.3%)**
Dalua (DA)	4.7% (3.8-5.7%)	0.6% (0.1-1.3%)***

- Significant decrease in Wb positivity in the mosquito popualtion after the MDA
- No apparent difference between IDA and DA villages in terms of level of decrease (1 year follow-up will provide more information)

Results – Exposure mapping (Wb infected mosquitoes)

Example: Dalua village





Results – *Malaria*

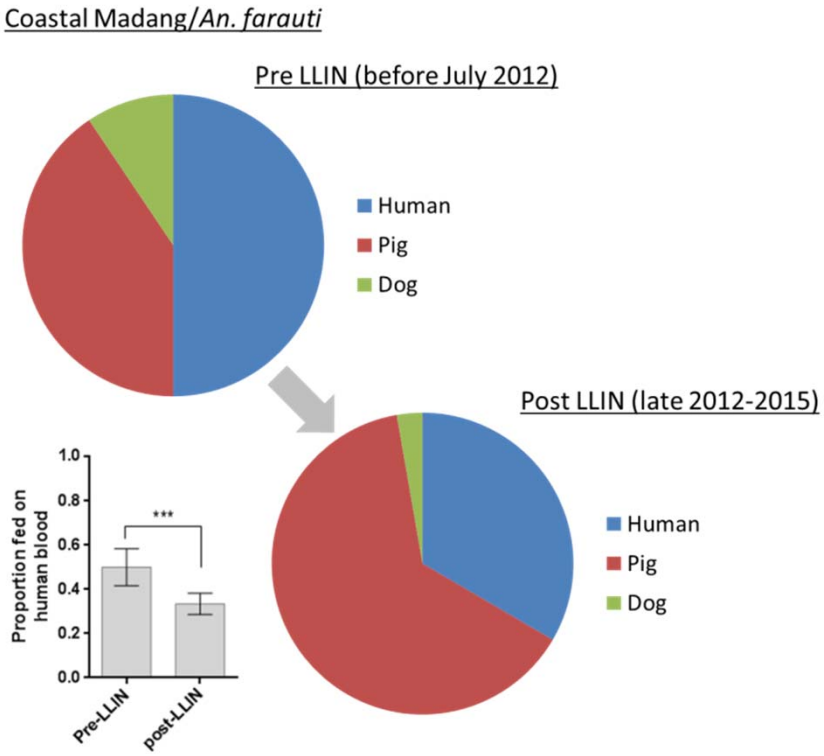
- preliminary results indicate (344 pools, 2960 mosquitoes from 1 village, Daigul) that approximately 1.4% (0.9-2.0%) of mosquitoes are infected with malaria
- In combination with the high biting rates, this indicates very high malaria transmission, with EIRs between exceeding 1000 per person year

Discussion

- Anopheline biting intensity on the PNG North Coast study villages is **very high** with high levels of vector-borne disease transmission -> **no residual transmission but full-blown hyperendemicity for malaria**
- *Wb* infections rates in the vector population were higher prior to the MDA as compared to afterwards
- *Wb* presence in the mosquito population was not abolished by the MDA, i.e., positive mosquitoes were still detected after the MDA
- Ivermectin effect on Anopheles mosquito abundance was not noticed
- One-year follow-up will provide more detailed insights into the effect of this single round MDA with the triple drug regimen

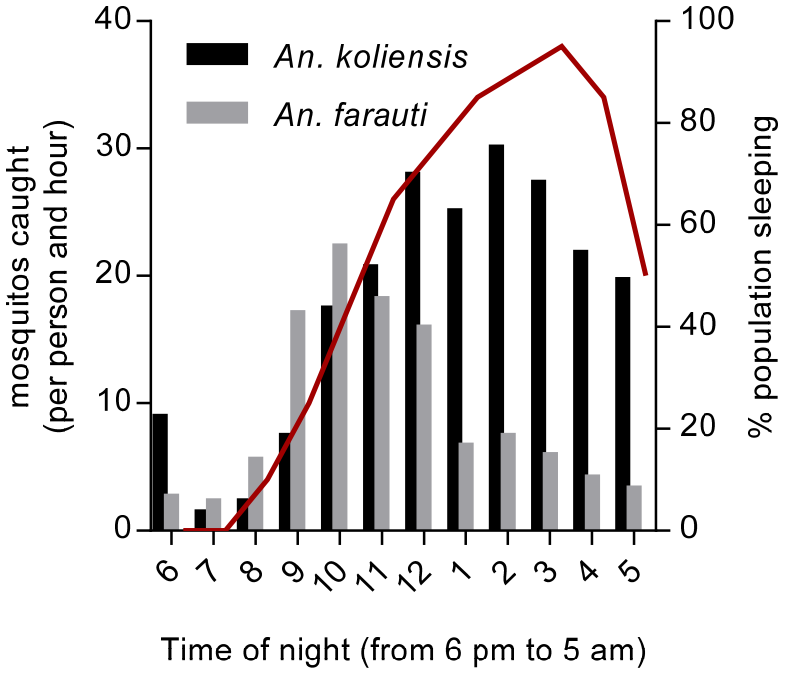
Discussion

Human vs alternative host biting pre- post LLIN



- Over two-thirds of hosts are pigs

Early peak biting time



- Early biting – no LLIN protection

Acknowledgements

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