Immunological & Parasitological Impact of Co-deployment of IRS & Bed Nets for malaria mosquito vector control in Uganda

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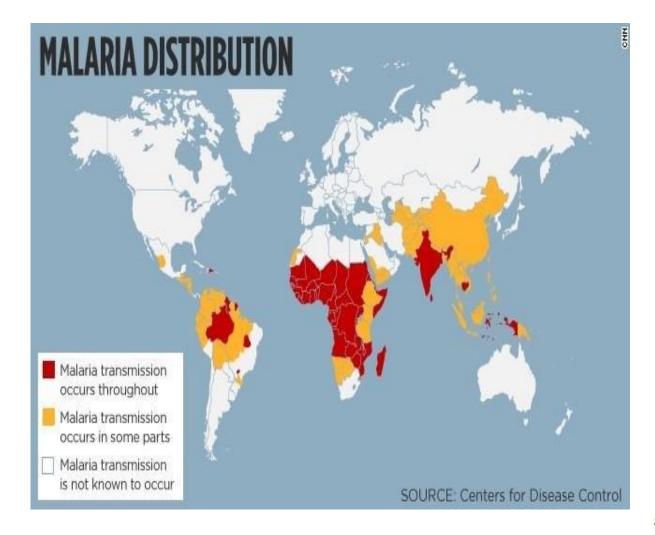
Supervision & Doctoral committee

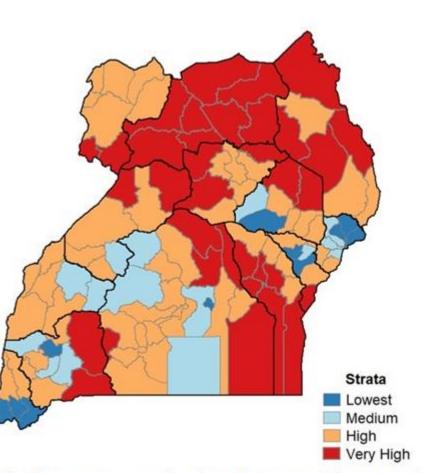
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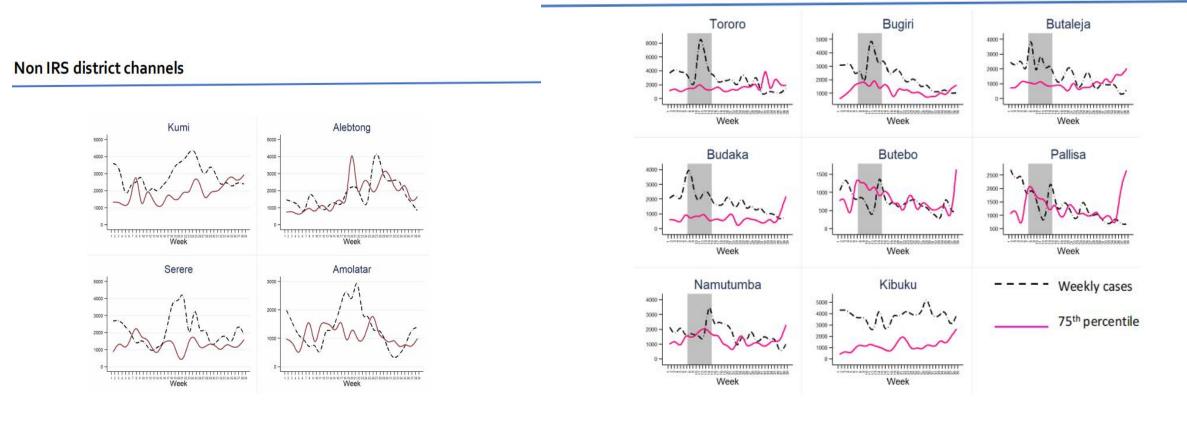




Stratification map of Uganda showing regions with the most malaria burden. Credit: The Uganda Malaria Reduction Strategic Plan (2021-2025)

# Background

#### All 7 districts (with grey bars-IRS weeks) have cases at or below the epidemic threshold



### IRS reduces malaria incidence, but for a short period

# Multiple interventions vs test positivity

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A

Bil

A

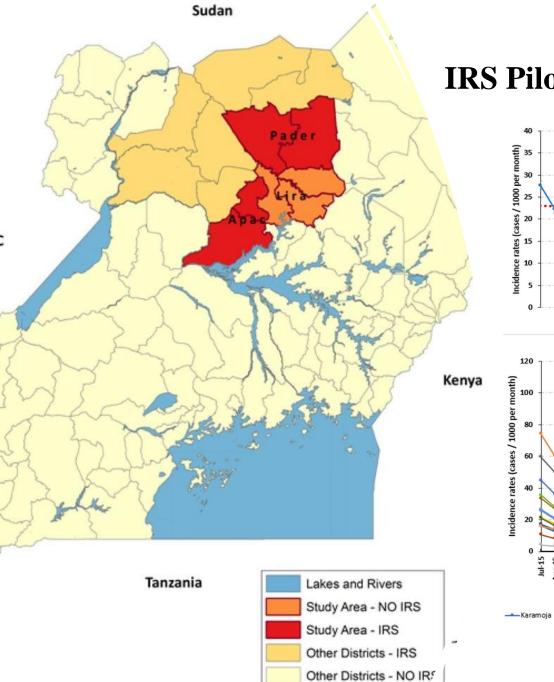
#### Subcounties with the highest burden yet having key interventions

- Agikdak-86%
- Aputi-79%
- Arwotcek-76%
- Etam-74%
- Amolatar T/C-64%
- Acii-54%
- Namasale T/c-44%
- Awelo-43%
- Aputi-37%
- Muntu-36%
- Namasale-29%

#### key interventions & no. of subcounties benefiting out of 16

- IRS-8 sub counties
- HAAM -6sub counties
- ICCM-16 sub counties
- ITNS-16 sub counties

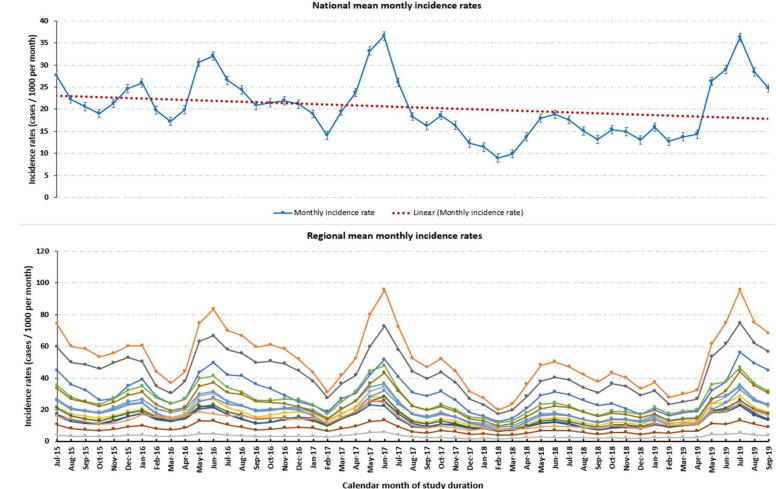
Organisation unit	TPR -Test Positivity Rate				Malaria Incidence Per 1000 population			
name	Wk7	W8	W9	WIO	Wk6	W7	<b>W</b> 8	W9
cii Health Centre II	52%	44%	51%	54%	524	438	512	536
lyecmeda Health Centre III	65%	62%	68%	47%	565	568	589	470
mai Community Hospital	69%	96%	75%	79%	306	424	396	383
molatar Health Centre IV	67%	63%	52%	64%	285	421	330	116
namwany Health Centre III	49%	35%	42%	43%	471	351	367	397
puti Health Centre III	62%	48%	51%	37%	565	473	494	358
rwotcek Health Centre II	82%	68%	67%	76%	812	676	663	748
wonangiro Health Centre III	60%	55%	85%	86%	523	554	770	742
iko Health Centre III	68%	54%	58%	44%	587	470	580	437
tam Health Centre III	50%	48%	68%	74%	317	290	507	605
lakatiti Health Centre III	52%	49%	36%	36%	516	491	363	364
Jamasale Health Centre III	48%	48%	41%	29%	338	338	250	177
molatar District	61%	54%	56%	54%	497	472	487	445



55

110

#### **IRS Piloted districts & trends in malaria incidence**



🛶 Karamoja 🛶 Acholi 🛶 Bunyoro 💁 Tooro 🛶 North Buganda 👞 East Central - Busoga 🛥 South Buganda 🛥 Kigezi 🛥 West Nile 📥 Teso 🛥 Ankole 🛥 Bukedi 🛶 Lango 🛶 Bugisu 🛶 Kampala

# Study hypothesis

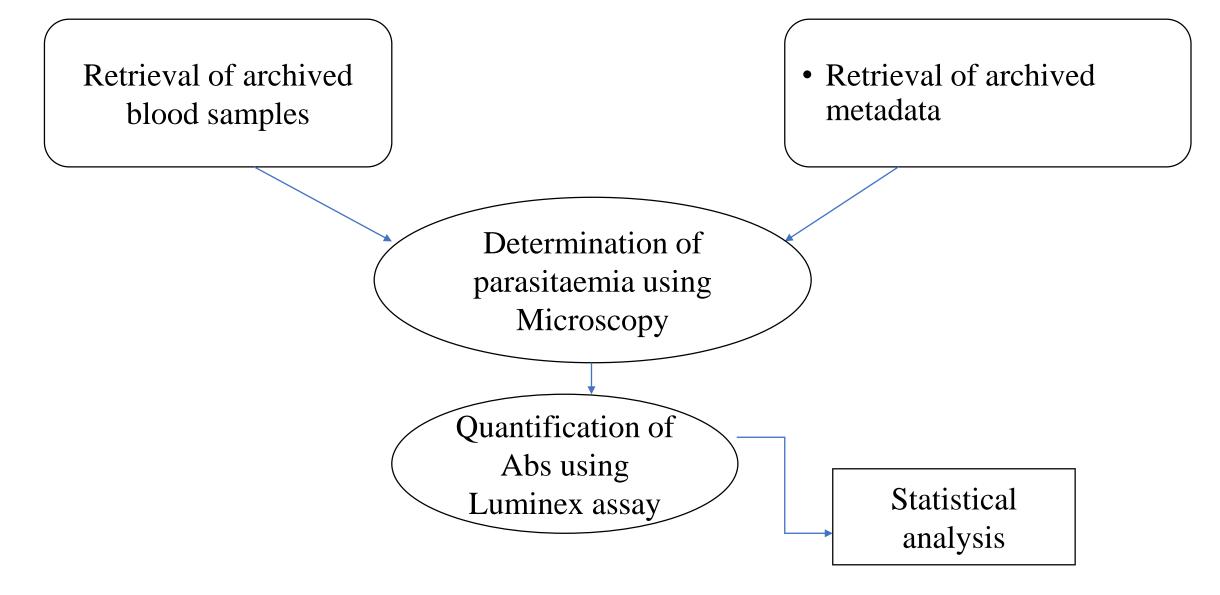
• In highly endemic areas, interventions that reduce parasite transmission may prevent the development of immunity due to reduced exposure, ultimately resulting in an increased overall 'rebound' burden of severe malaria .

- In the absence of effective vaccines to replicate the premunition state, intensified control measures may yet result in changing patterns of malaria morbidity and mortality.
- Interventions such as intermittent preventive therapy, indoor residual spraying if inconsistently applied have been shown to put pressure on parasite and vector genome to induce SNP.
- When inconsistently applied, they have also been associated with activation of var genes of the PfEMP1 family associated with chronic & severe forms of *P.falciparum* infections and immune evasion.
- This reservoir is in turn enabled by extreme antigenic diversity of the parasite and turnover of new variants which are usually resistant to common anti-malarial drugs such as ACTs.
- They are usually also un-responsive to vaccines such as RTS,S & R21MM since their haplotypes are not incorporated in the recombinant vaccine.

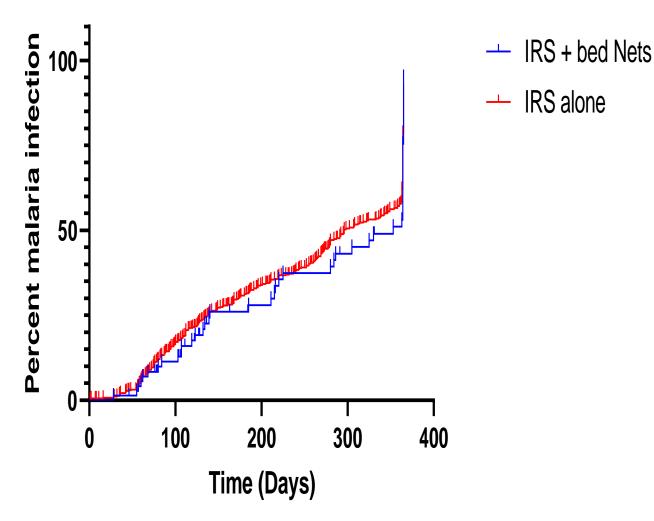
# Study objectives

- 1. Ascertain the parasitological and immunological benefits of singular (IRS alone) versus multiple interventions (IRS & bed nets) for malaria vector control in areas of Eastern Uganda with high malaria.
- 2. Determine the effects of co-deployment of IRS + LLINS on serum expression of total IgG against signature *P.falciparum* antigens in blood samples of children from Malaria endemic areas of Eastern Uganda
- 3. Compare levels of total IgG against malaria specific antigens in blood samples of children with severe versus mild malaria in areas with co-deployment as a measure of immune protection.
- 4. Identify P.falciparum specific antigens that can best predict for malaria infections among children from disease endemic areas of Eastern Uganda

### **Summary of Laboratory methods**

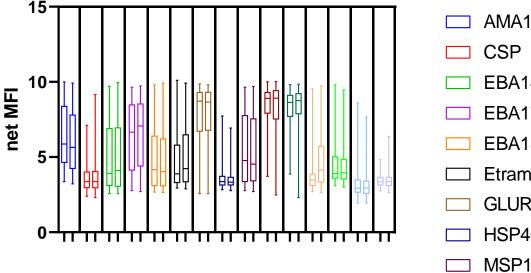


### Results



- There was no significant difference (p=0.4466) in the survival rate between the two population though children from household with dual interventions had less malaria infections (median survival for IRS only households=296 days while that of IRS +bed nets=353 days).
- In the first 60 days , there was almost no malaria incidence in both arms of the study population; a proof of the effectiveness of either malaria mosquito vector control measures

### Results

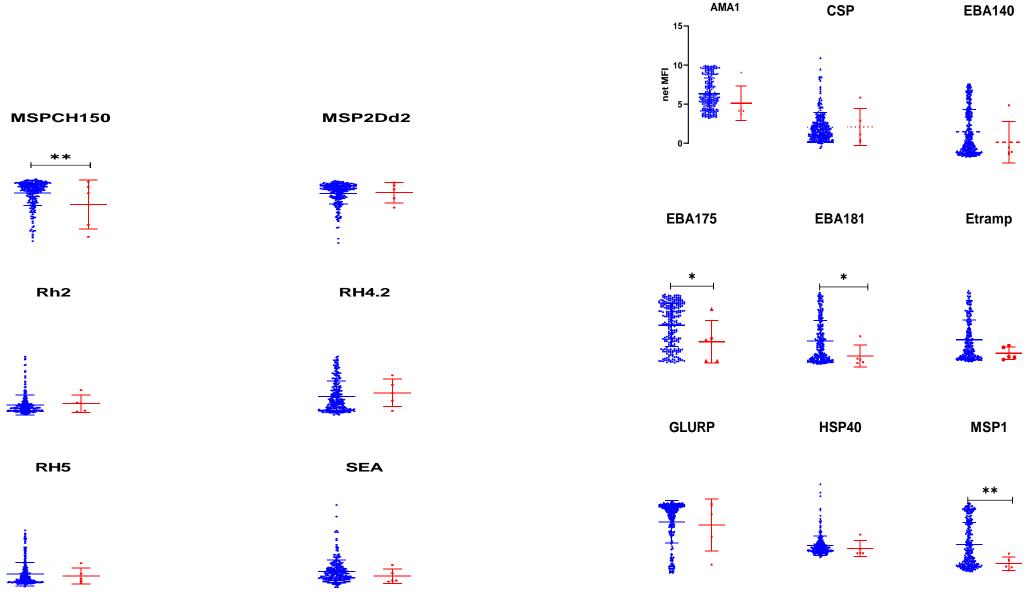


Pf Antigen

CSP EBA140 EBA175 EBA181 Etramp5 GLURP HSP40 MSP1 MSP2CH150 MSP2Dd2 Rh4 Rh5 SEA TT

- There was no significant difference in serum total IgG level against signature antigens across the two groups.
- For certain antigens, the total IgG level was higher for the case population (AMA1, CSP, EBA181, GLURP, and MSP1-19) while others (EBA140, Etramp5Ag1, MSP2Dd2 and MSP2 CH150) for control.
- There were almost equal IgG titers against tetanus toxoid for the two sets of population.
- Highest titers were noted for IgG against Merozoite Surface Proteins (MSP2CH150 & MSP2Dd2), EBA175 and GLURP
- Least titers were noted for total IgG response against CSP, HSP40, RH4.2 & Pf SEA.

### Children with severe malaria had reduced antibodies



### Cost of co-deployment

Intervention	Unit				Sensitivity analysis		
		Distribution method	Economic cost per unit	Marginal economic cost per unit	Lower value	Upper value	
Long lasting insecticide-treated bednets (LLIN)	Net delivered	Mass campaign through community organizations [55]	\$8.52	\$8.37	\$4.26	\$17.04	
Indoor residual spraying (IRS)	Person protected	Annual mass campaign [55]	\$0.73	\$0.34	\$0.34	\$1.46	
School-based intermittent screen and treat (IST)	Child screened	School-based distribution [56]	\$6.32	\$2.89	\$3.16	\$12.63	

All costs are in 2012 USD. doi:10.1371/journal.pone.0107700.t003

## **Conclusion & recommendation**

- Co-deployment may not be necessary for areas of High Malaria transmission such as many parts of Uganda. Deployment of singular interventions may be more effective in such settings
- Co-deployment may be more effective in areas/countries nearing elimination
- Interval of Application of IRS and Net distribution must be scientifically pre-determined rather than reactionary as it is currently
- Introduction of R21MM to the already available control interventions may not come with real additional Immunological & parasitological benefits yet it attracts huge cost.
- For highly malaria endemic areas such as northern Uganda, development of Naturally acquired immunity may be a safe and cost-effective way of fighting malaria

