



A non-randomised controlled trial to assess the protective effect of seasonal malaria chemoprevention in the context of high parasite resistance in Uganda

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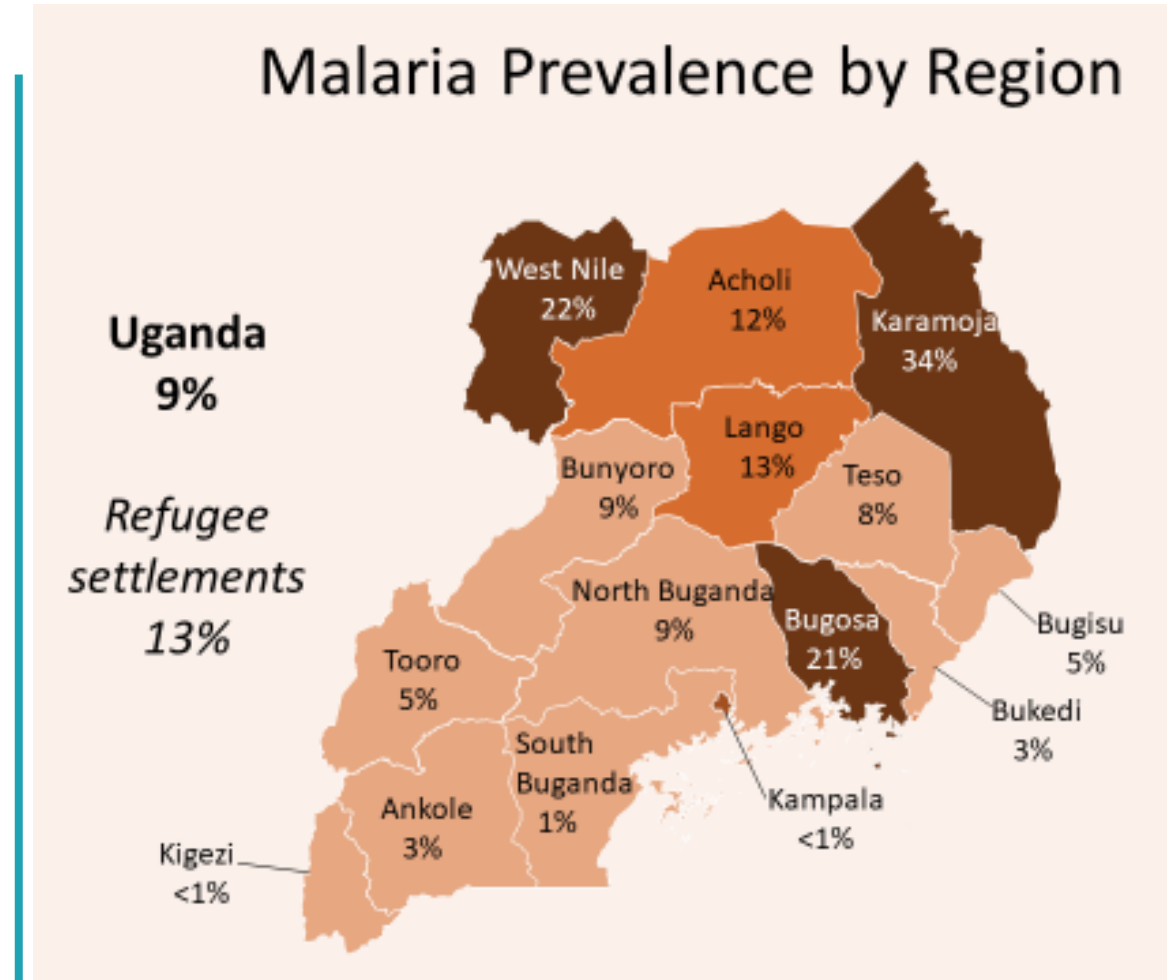
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Background

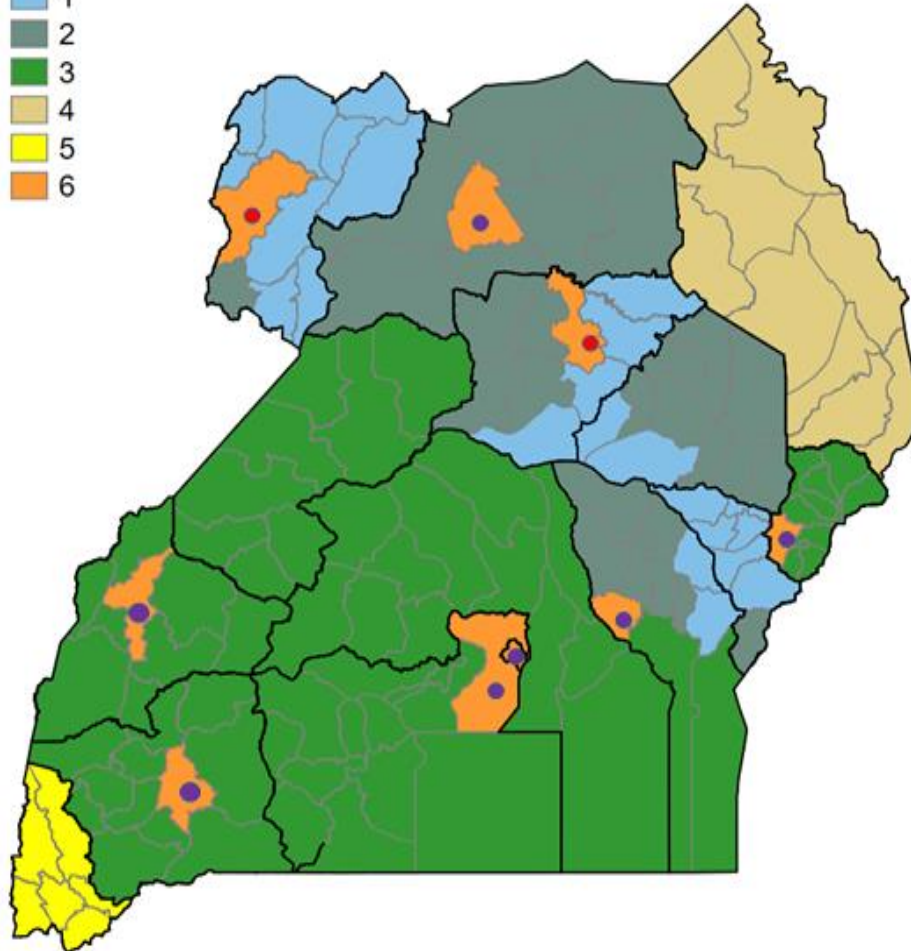
- Malaria is major public health problem in Uganda, affecting almost 100 percent of the population.
- The Karamoja subregion consistently reports the highest prevalence rates; malaria transmission is seasonal.
- The World Health Organization (WHO) has recommended SMC as a malaria control measure since 2012.
- The Uganda Malaria Reduction and Elimination Strategic Plan 2021–2025 proposes seasonal malaria chemoprevention (SMC) to accelerate progress towards malaria elimination.
- Modelling by the Swiss Tropical and Public Health Institute suggests SMC could be a viable malaria prevention strategy in Karamoja.



Percent of children aged 0–59 months who tested positive for malaria by microscopy (UMIS 2019.)

Response to HBHI: Malaria stratification and intervention delivery approaches

Interventions



1	Indoor residual spraying (IRS), continuous long-lasting insecticidal net (LLIN) distribution, community health worker (CHW) outreach services
2	Campaign and continuous LLIN distribution
3	Campaign and continuous LLINs, intermittent preventive treatment (IPT) in infants (now perennial malaria chemoprevention) and IPT schools evaluations in selected districts
4	Campaign and continuous LLINs, CHWs with outreach services, mobile CHWs for nomadic pastoralist communities, SMC evaluation in selected districts
5	Campaign and continuous LLIN distribution, elimination surveillance
6	Urban areas: targeted mass and continuous LLINs followed detailed microstratification, larval source management, private sector integrated community case management and LLIN social marketing

Note: Standard case management and IPTp nationwide

● City

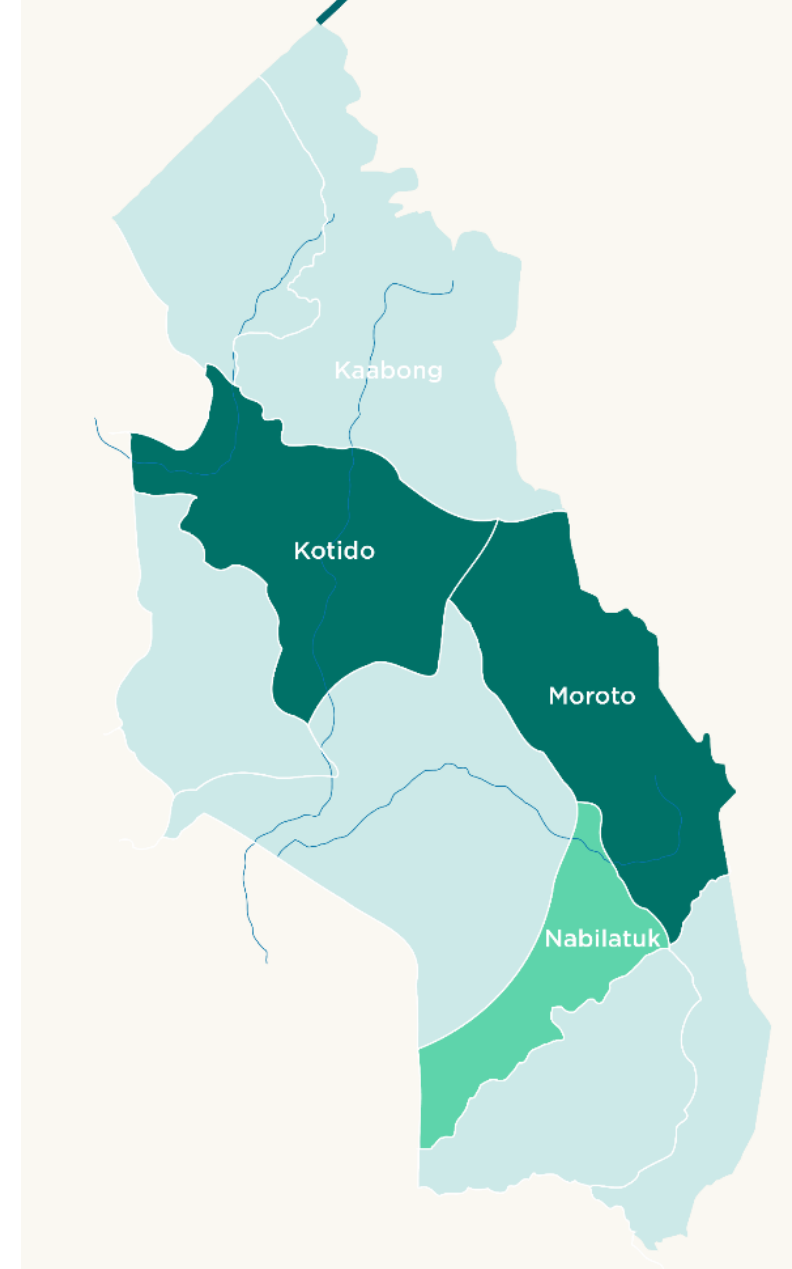
● Districts where rural areas will be covered with IRS

Background

- SMC is the intermittent administration of full treatment courses of antimalarials to children during the malaria season in areas with high transmission.
- It involves administering monthly courses of sulfadoxine-pyrimethamine (SP) and amodiaquine (AQ) during this peak transmission period to those most at risk: children 3–59 months.
- Until recently, SMC has only been adopted and scaled up in Sahelian countries of West and Central Africa, primarily due to concerns over widespread resistance to SP in many parts of East and southern Africa.
- However, the current WHO recommendation has lifted the above restriction.
- It has been suggested that SP may retain its protective effectiveness even in areas where resistance is high.

SMC implementation study, 2021

- The National Malaria Control Division and Malaria Consortium conducted an SMC implementation study in Karamoja, where parasite resistance is assumed to be high and malaria transmission is seasonal.
- The study:
 - conducted in two intervention districts, with a third district (i.e. no SMC) serving as a control.
 - administered SPAQ through five monthly SMC cycles to target population of 90,000 children 3–59 months.
 - implemented May – September to match the prolonged duration of the peak malaria transmission season in Karamoja.
 - adapted the standard door-to-door distribution model and SPAQ administration protocol used in the Sahel to the Ugandan context: village health teams (VHTs), a recognised cadre of community health workers, acted as community distributors.



- Intervention districts
- Comparison district

Study components

Study component	Outcome measure	Participants and sample size
1. End-of-round household survey	Coverage, quality of SMC implementation	1,863 caregivers of children 3–116 months
2. Assessing the feasibility and acceptability of the adapted SMC implementation model	Acceptability among key stakeholders	51 key informant interviews and 26 focus group discussions with caregivers, community leaders, community distributors, health authorities
3. Non-randomised controlled trial (prospective cohort study)	Clinical malaria episodes among SMC-eligible children during the peak transmission season	200 children 3–59 months per district (total 600 children)
4. Resistance markers study	Prevalence of common SP and AQ resistance markers before and after SMC implementation	600 children 3–59 months per arm before and after annual SMC round

nRCT study methods

- A two-arm quasi-experimental prospective study
- Selected communities with comparable malaria attack rates from each district and purposively selected households with at least one eligible child (3–59 months).
- Selected cohort of 200 children per district and followed them using passive surveillance for five months for breakthrough confirmed malaria cases.
- Compared malaria incidence rate per person-month and malaria episodes among children in the two arms.
- Used Kaplan-Meier failure estimates to compare probability of a positive malaria test ('failure' defined as a visit to a health facility or VHT with a confirmed malaria diagnosis).
- Assessed other factors that may influence malaria transmission and infection among children in the two arms using multivariable cox proportional hazards regression model.





Results

Results

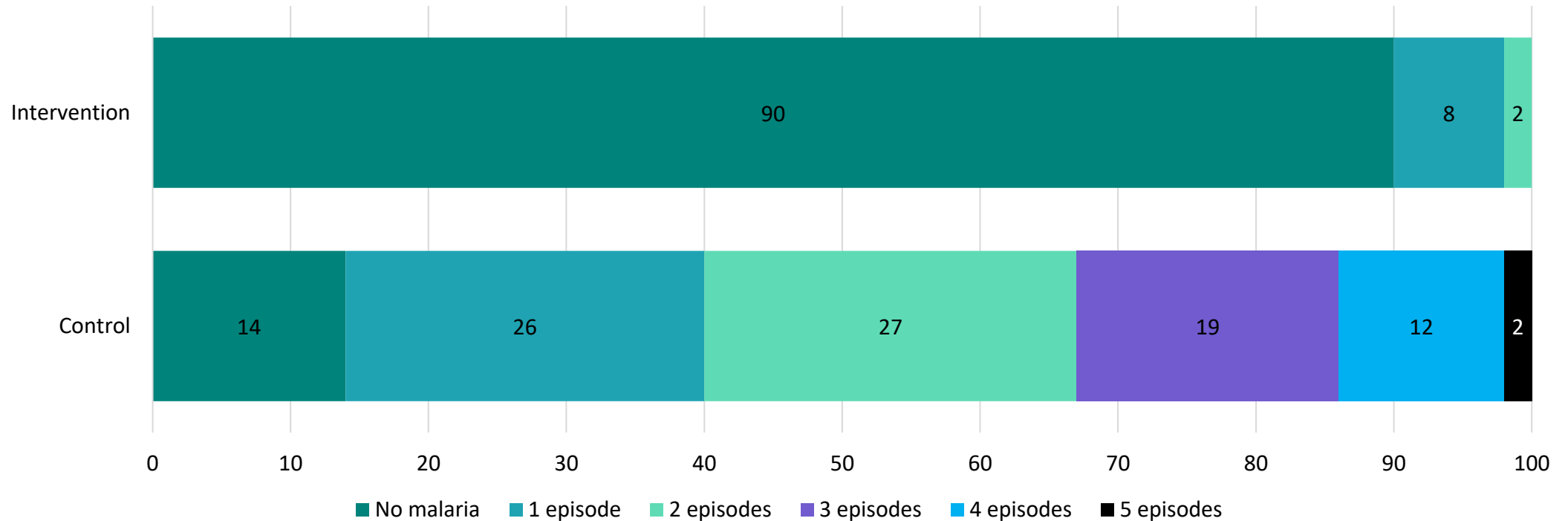
The malaria incidence rate was 3.0 and 38.8 per 100 person-months in the intervention and control groups, respectively.

Children in intervention districts had a 92.2 percent lower risk of developing confirmed malaria in the five-month follow-up versus those in the control district.

Study arm	Person time of observation (months)	Number of episodes	Incidence-rate per 100 person-months	Incidence rate ratio (95% CI)	P-value
Intervention	1982	60	3.0	0.078 (0.063–0.096)	<0.001
Control	997	387	38.8		

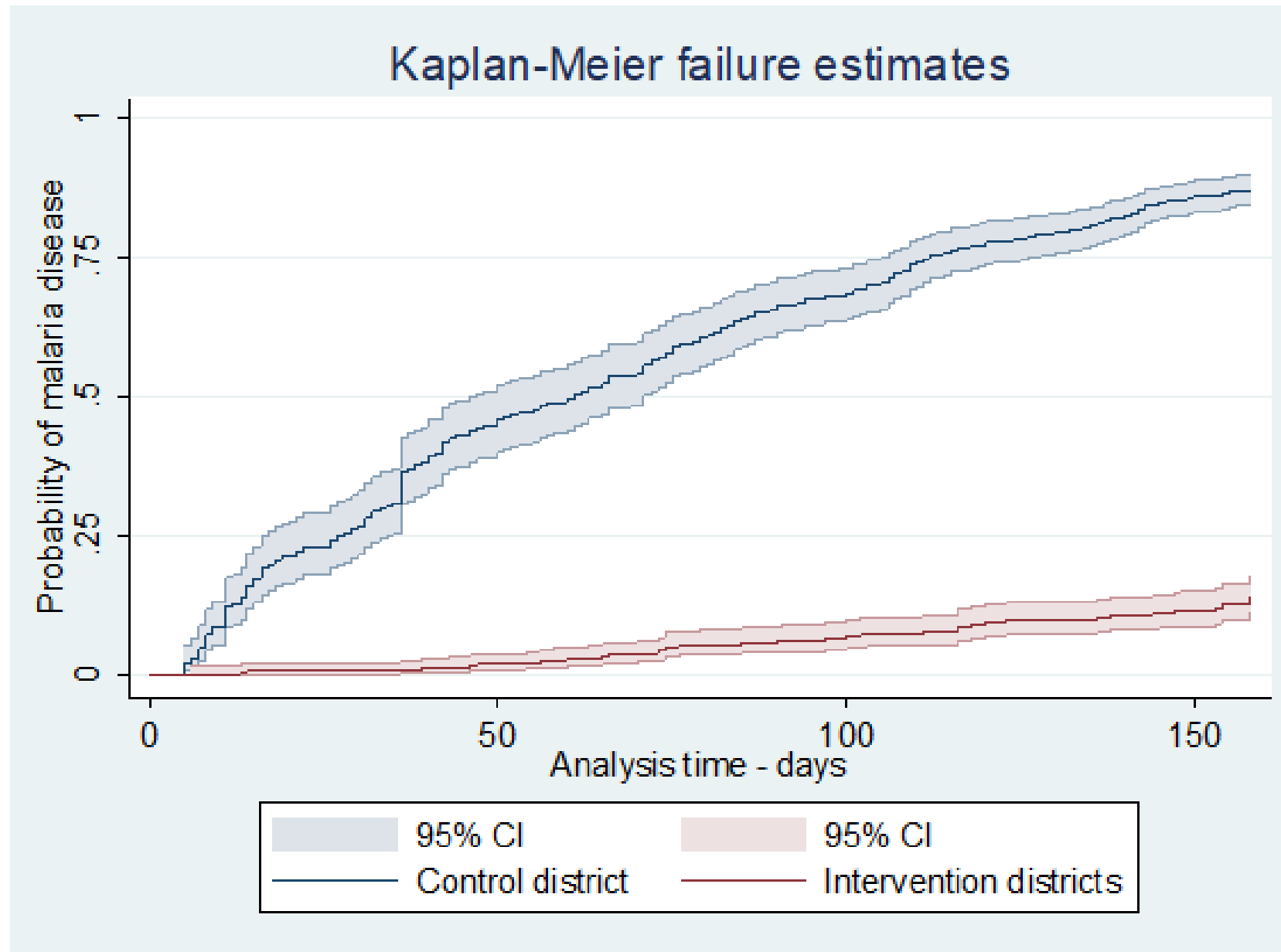
Results

In the intervention areas, 90 percent of children never experienced a malaria episode, versus 15 percent in the control area; 85 percent of children in the control developed at least one episode and 60 percent had at least two over the follow-up period.



Result

Children in control group had higher probability (hazard) of getting confirmed malaria than their counterparts in the intervention group over the follow-up period.



Result

Associations for other predictor variables were non-significant.

Characteristic	Crude hazard ratio (95% CI)	P-value
Intervention versus comparison	0.1 (0.054–0.098)	< .001
Child's gender	1.1 (0.837–1.381)	0.569
Household mosquito net ownership	0.8 (0.607–1.124)	0.224
Child slept under a mosquito net the night before	1.2 (0.628–2.198)	0.614
Indoor residual spraying of the household	1.5 (0.455–5.247)	0.486
Education level of parents	0.9 (0.698–1.133)	0.343
Socio-economic status (wealth index)	0.9 (0.834–1.089)	0.480

Conclusion

Seasonal malaria chemoprevention conferred an excellent protective effectiveness against clinical malaria episodes during the peak malaria transmission season in Karamoja region, Uganda.



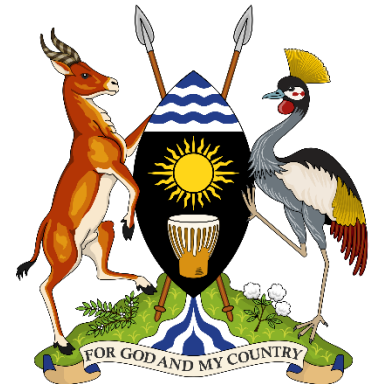
Recommendations: Phase 2 SMC implementation

- Conduct a cluster-randomised controlled trial to determine the effectiveness of SMC using SPAQ and dihydroartemisinin-piperaquine (DP).
- Assess chemoprevention efficacy of SPAQ and DP when used for SMC.
- Conduct routine monitoring of the presence and change of SPAQ and DP resistance markers over time as a result of SMC implementation.
- Evaluate the process of SMC implementation, including coverage, quality of SMC implementation, costing, feasibility and acceptability, and assessment of the role of gender in SMC implementation.
- Scale up to other districts of Karamoja and other regions/older age group to 15 years.

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- Study respondents

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**UGANDA NATIONAL MALARIA
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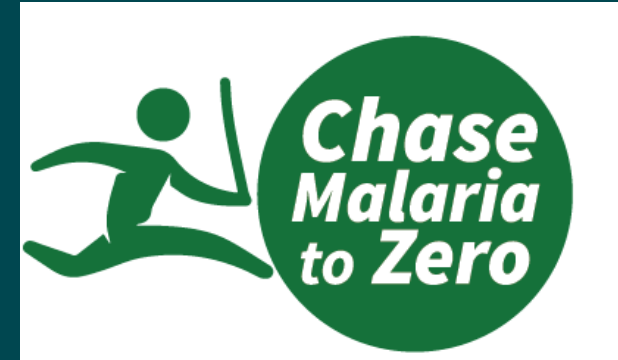
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malaria
consortium

disease control, better health



Thank you

www.malariaconsortium.org/smc