Maximising malaria prevention. Effectiveness of seasonal malaria chemoprevention in Mozambican children: A cluster-randomised controlled trial

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Seasonal malaria chemoprevention in Mozambique significantly reduces childhood malaria, with effectiveness increasing through strict treatment adherence

Introduction

We assessed the effectiveness of seasonal malaria chemoprevention (SMC) with sulfadoxine-pyrimethamine plus amodiaquine (SPAQ) in children 3–59 months during the high transmission season in two districts of Nampula province, Mozambique. By comparing analyses on intention-to-treat (ITT), including children receiving at least one SMC dose, and per-protocol (PP), excluding children who did not receive a full course of SMC, the study aimed to provide a comprehensive understanding of the impact of SMC under different adherence scenarios.

Methods

- We conducted an open-label cluster randomised controlled (cRCT) trial in Nampula province between January and April 2022.
- Randomisation was at the community level, including 114 clusters in the control arm and 76 in the intervention arm.
- We fitted random-effects Cox proportional hazards regression models for recurrent events, using ITT and PP analyses.
- Models were adjusted for demographic variables and household malaria prevention methods.
- In our sensitivity analyses, we considered two different assumptions for the susceptibility of children to malaria post-infection: either the day after or 21 days after a previous case.

Results

- In total, 3,115 children were recruited and randomised at baseline.
- ITT analysis showed significant reductions in rapid diagnostic test (RDT)-confirmed malaria cases. Adjusted hazard ratios of RDT-confirmed malaria ranged from 0.27 (95 percent confidence interval [95% CI]: 0.21–0.33, p=<0.001) assuming susceptibility to reinfection immediately after the previous case, to 0.19 (95% CI: 0.14–0.25, p=<0.001) assuming immunity to reinfection within 21 days of the previous case.
- The PP analysis showed a stronger effect, with adjusted hazard ratios for RDT-confirmed malaria reducing to 0.11 (95% CI: 0.07–0.14, p=<0.001) within 21 days of the previous case.

Conclusion

SMC is an effective way to prevent malaria in children under five in Mozambique. Our study found the impact of SMC was higher under strict adherence to the treatment protocol. Results from this study hold substantial significance for public health, particularly in regions with a similar seasonal malaria burden to northern Mozambique, highlighting the importance of implementing methods to encourage treatment adherence.

Figure 1. Study sites in Nampula province, northern Mozambique

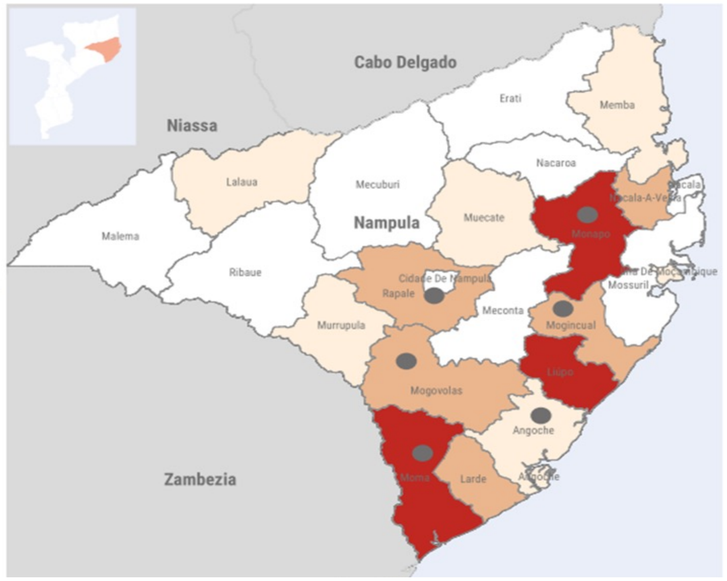

Figure 2. Field implementation

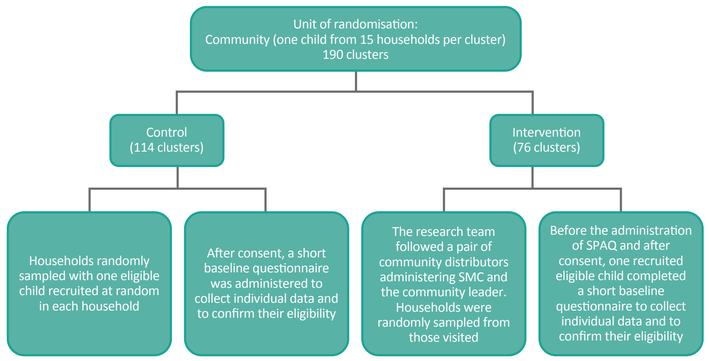

Figure 3. Statistical analysis according to the PP assumption

Model			Excluding children in intervention arm who did not receive full course of SMC in each cycle and children in control arm who received day 1 SPAQ in any cycle			
Outcome	Model description	Covariate adjustment	Analytic sample (n)	Hazard ratio	95% CI	P value
Fever	Model 1: Time to first incidence of caregiver-reported fever	A: unadjusted	1,336	0.28	0.24–0.32	<0.001
		B: child age and sex	1,336	0.28	0.24–0.32	<0.001
		C: B + net use and IRS	939	0.26	0.21–0.30	<0.001
RDT-confirmed malaria	Model 2: Time to first incidence of RDT-confirmed malaria cases (caregiver report and logbook record)	A: unadjusted	1,338	0.22	0.19–0.27	<0.001
		B: child age and sex	1,338	0.22	0.19–0.27	<0.001
		C: B + net use and IRS	941	0.2	0.16–0.25	<0.001
	Model 3: Random-effects model for time to recurrent incidence of RDT-confirmed malaria cases (caregiver report and logbook record) assuming susceptibility to reinfection immediately after previous case	A: unadjusted	1,338	0.19	0.16–0.22	<0.001
		B: child age and sex	1,338	0.19	0.15–0.22	<0.001
		C: B + net use and IRS	941	0.17	0.13–0.21	<0.001
	Model 4: Random-effects model for time to recurrent incidence of RDT-confirmed malaria cases (caregiver report and logbook record) assuming immunity to reinfection within 21 days of the previous case	A: unadjusted	1,338	0.12	0.09–0.15	<0.001
		B: child age and sex	1,338	0.12	0.09–0.15	<0.001
		C: B + net use and IRS	941	0.11	0.07–0.14	<0.001

Figure 4. Statistical analysis according to the ITT assumption

Model			Including children in the intervention arm who did not receive a full course of SP+AQ in each cycle and children in the control arm who received day 1 SPAQ in any cycle			
Outcome	Model description	Covariate adjustment	Analytic sample (n)	Hazard ratio	95% CI	P value
Fever	Time to first incidence of caregiver-reported fever	A: Unadjusted	1654	0.43	0.38–0.49	<0.001
		B: child age and sex	1654	0.43	0.38–0.49	<0.001
		C: B + net use and IRS	1145	0.38	0.32–0.44	<0.001
RDT-confirmed malaria case	Time to first incidence of RDT-confirmed malaria cases (caregiver report and logbook record)	A: Unadjusted	1665	0.38	0.33–0.45	<0.001
		B: child age and sex	1665	0.38	0.32–0.44	<0.001
		C: B + net use and IRS	1153	0.33	0.27–0.39	<0.001
	Random-effects model for time to recurrent incidence of RDT-confirmed malaria cases (caregiver report and logbook record) assuming susceptibility to reinfection immediately after previous case	A: Unadjusted	1665	0.31	0.26–0.37	<0.001
		B: child age and sex	1665	0.31	0.26–0.37	<0.001
		C: B + net use and IRS	1153	0.27	0.21–0.33	<0.001
	Random-effects model for time to recurrent incidence of RDT-confirmed malaria cases (caregiver report and logbook record) assuming susceptibility to reinfection within 21 days of previous case	A: Unadjusted	1665	0.22	0.18–0.28	<0.001
		B: child age and sex	1665	0.22	0.18–0.28	<0.001
		C: B + net use and IRS	1153	0.19	0.14–0.25	<0.001

Acknowledgements

Communities of Lalaua and Muacate, National Malaria Control Programme, Centro de Investigação em Saúde de Manhiça