Seasonal malaria chemoprevention: Results from Mozambique implementation study 2020–2021

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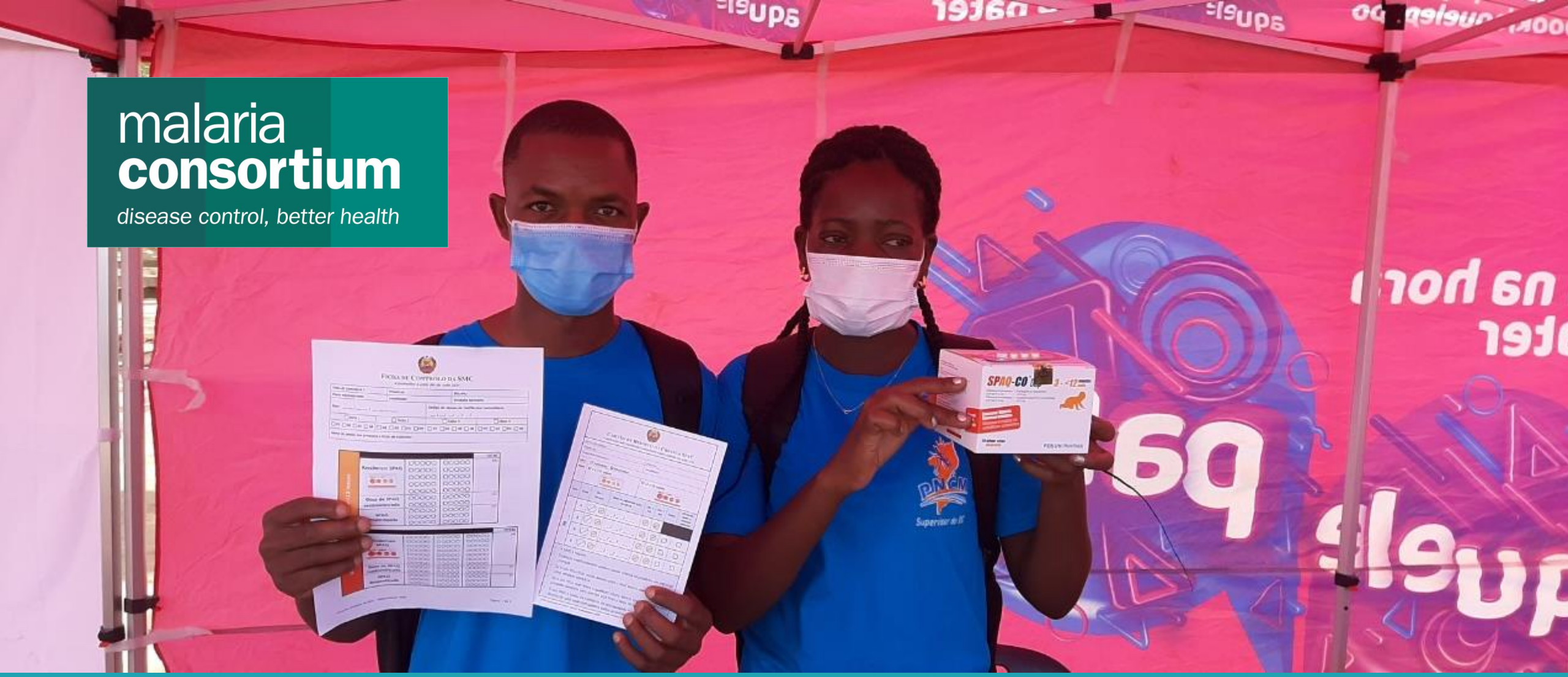


Overview of Mozambique SMC implementation study

Mozambique SMC implementation study 2020–22

- A mid-term review of Mozambique's Malaria Strategic Plan 2017–2022 recommended seasonal malaria chemoprevention (SMC) as a strategy to accelerate impact in the highest-burden locations.

- To explore whether SMC is a viable malaria prevention strategy in Mozambique, the National Malaria Control Programme (NMCP), together with Malaria Consortium, is conducting an implementation study in Nampula province.

- The implementation study will be conducted in two phases: year 1 (2020/21) will focus on determining acceptability and feasibility, with a robust impact evaluation planned in year 2 (2021/22).

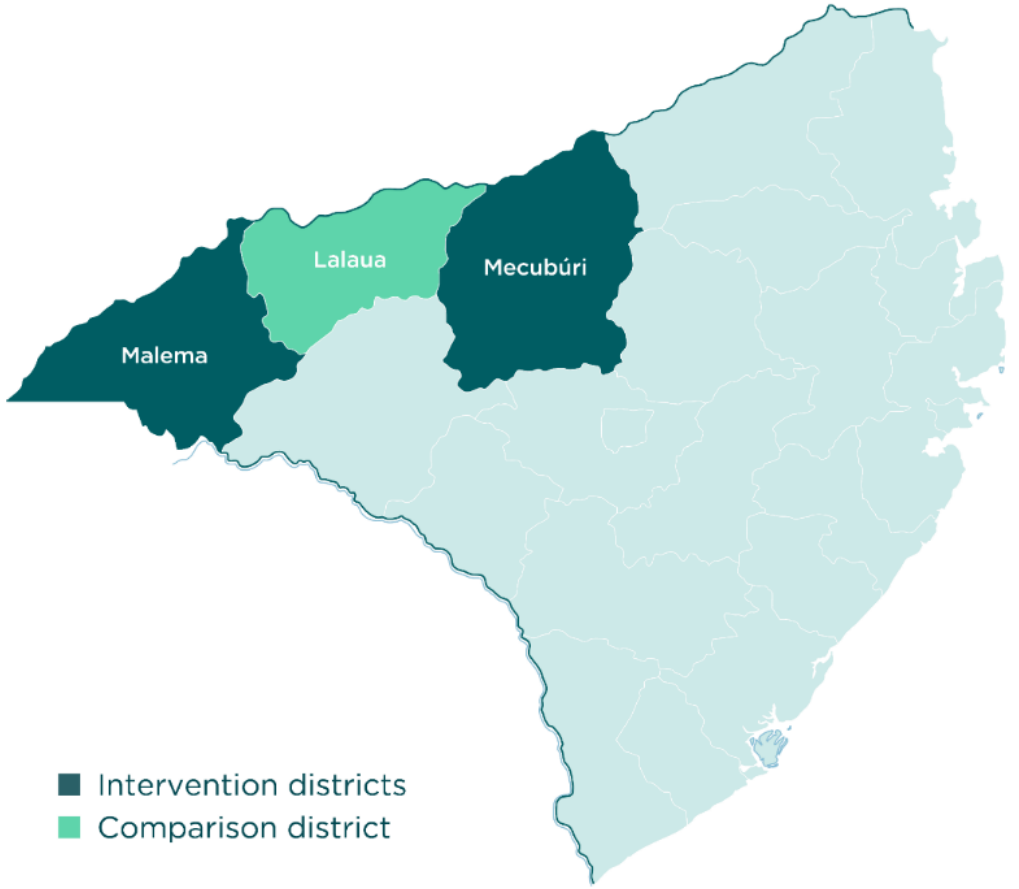
Mozambique SMC implementation study 2020–22

The study uses the standard SMC implementation model commonly used in west and central Africa:

Intervention element	Description
Drug regimen	Three-day course of SP (sulfadoxine-pyrimethamine) and AQ (amodiaquine)
Target age group	3–59 months
Seasonality	Four monthly SMC cycles, November – February
Delivery mechanism	Door-to-door by trained volunteer community distributors
Functional unit	Health facility (HF) catchment areas

Mozambique SMC implementation study: Phase 1

- SMC implemented in two districts; third district serving as control for research components.
- Districts selected based on a suitability ranking exercise in collaboration with NMCP, World Health Organization (WHO) and Clinton Health Access Initiative.
- Target population: 75,000 children 3–59 months
- Four monthly SMC cycles implemented as scheduled: mid-November 2020 to mid-February 2021.
- All intervention components adapted to local context: planning and enumeration, procurement and supply management, community engagement, training, SPAQ administration, supervision, monitoring and evaluation.



Map of study sites in Nampula province, Mozambique

Study aims and objectives

The study aimed to determine the protective effect of SPAQ when used for SMC in this context and to assess the feasibility and acceptability of implementing SMC.

Objectives

- Determine baseline prevalences of SP/AQ resistance and any increase in resistance prevalence after one annual round of SMC
- Determine whether receipt of SPAQ associated with reduction in odds of clinically significant malaria outcomes
- Assess the change in reported malaria morbidity indicators through routine data
- Document adaptation of SMC implementation to the Mozambican context
- Explore feasibility/acceptability of SMC among stakeholders
- Evaluate process of SMC implementation in terms of distribution quality/coverage.

Research methods

Objective	Design/method	Population	Sample size	Timing
1. Process documentation	Documentation of the adaptation process	N/A	0	August – November
2. Evaluation of coverage and quality	Quantitative: End-of-round survey	Children 3–119 months	1,800	March 2021
3. Acceptability assessment	Qualitative: Key informant interviews and focus group discussions	Health workers, caregivers, community leaders, implementers, policy makers	120	March/April 2021
4. Data quality audit, SMC and impact	Quantitative: 4.1 Data quality assessment	Cases of children <5 years	26 HFs in all three districts	August 2019 – March 2021
	4.2 DHIS2/SISMA data analysis	Cases of children <5 years	26 HFs in all three districts	November 2020 – May 2021
5. SPAQ protective effect	Quantitative: 5.1 Non-randomised controlled trial	Children aged 3–59 months	800	October 2020 – May 2021
	5.2 Resistance marker study	Children aged 3–59 months	600	October 2020 – May 2021

Adaption results

- Eleven SMC training tools translated from English to Portuguese
- Rumour management approach developed
- SMC leader appointed by each community
- Additional Training-of-Trainers for SMC implementors and supervisors conducted in Portuguese
- Face-to-face meetings/trainings adapted according to national COVID-19 guidelines
- Daily basis monitoring in each cycle (analysing daily administrative data) introduced
- Electronic database for daily data entry created and data clerk allocated.

Acceptability results

Benefits/importance of SMC

- SMC was widely accepted as it was preceived to help prevent malaria transmission.

Facilitators of SMC adherence

- Good coordination between local authorities and implementing partner
- Good engagement of local and religious leaders in community mobilisation.

Challenges during SMC implementation

- Some fear and mistrust in the intervention remained.

"… Overall, this strategy is quite impactful and we feel that even children under five years of age in particular have had reduced malaria incidence by about 40, 50, 60 percent in the district…" **Stakeholder**

"….In the past, all children used to get sick due to malaria, but from November until now, I can see that malaria has already decreased in my community due to the pills that they were distributing to homes in the area; I see the pills made us happy…" **Caregiver**

Coverage results

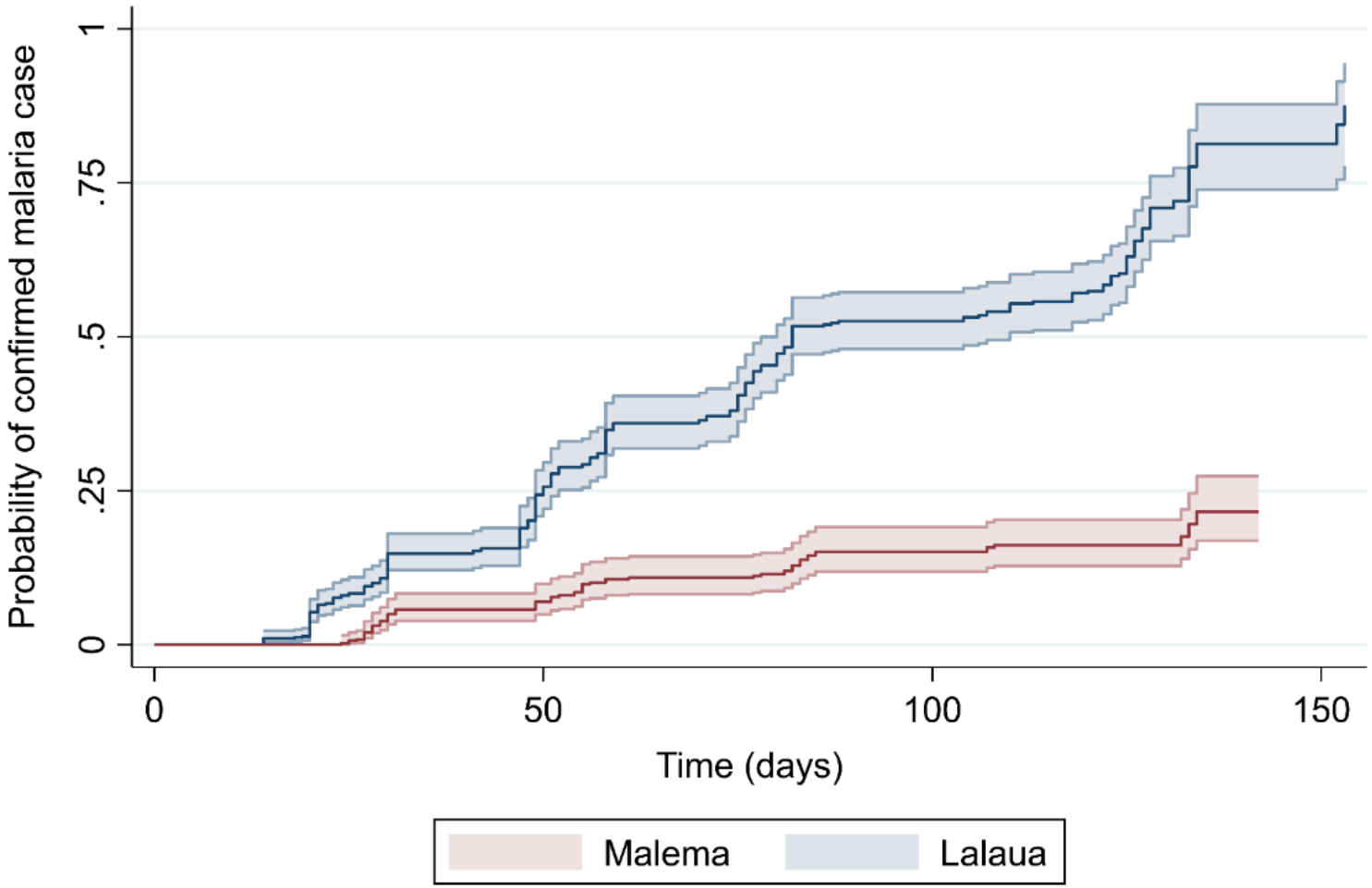
Indicator	Denominator	Proportion (%)	95% Confidence Interval (CI)
SMC knowledge			
Caregiver heard date of SMC cycle	Households with eligible children (3–59 months)	84.4	79.7–88.2
Caregiver knowledge age eligibility	Households with eligible children (3–59 months)	88.3	84.9–91.0
SMC SPAQ administration			
Household coverage	Households with eligible children (3–59 months)	89.3	85.8–92.0
Child coverage, received four cycles of day 1 SPAQ in 2020/21 round (caregiver report)	Eligible children (3–59 months)	77.0	69.7–82.9
Day 2 and 3 adherence (both days)	Eligible children received day 1 SPAQ	99.3	98.5–99.7
Evidence of receipt of SMC SPAQ			
SMC record card retention	Eligible children (3–59 months)	87.7	83.9–90.8
Child coverage (SMC record card)	Eligible children with available SMC record card	94.0	91.2–95.9
Child coverage (caregiver report)	Ineligible children (5–9 years, in household with children aged <10 years); representative sample	15.3	11.5–20.1

Data quality audit key findings

- Variability in data quality from registers to paper forms across all districts
- Overall improvement in data quality seen in summary forms to SISMA (DHIS2) in last 12 months
- Need for refresher training and ongoing support before phase 2 activity happens — health centre preparedness assessments currently being planned.

Non-randomised trial results

Kaplan-Meier plot of confirmation of malaria cases in Malema (intervention district) and Lalaua (control district)



Results of a chi-square test of the difference of the proportion of children in intervention and control districts experiencing one or more confirmed malaria cases during follow-up

χ^2=142.55; df=1, p<0.001

Odds Ratio: 0.14; 95% CI: 0.10–0.20
Estimated protective effect of 86 percent

Results of a survival analysis (with failure defined as a confirmed malaria case) employing a random-effects Cox proportional-hazards model for recurrent events

Hazard ratio: 0.17; 95% CI: 0.12–0.22, p<0.001

Estimated protective effect of 83 percent

Drug resistance

- According to 2013 WHO guidelines, traditionally '***The areas in which SMC with SP + AQ is suitable are those in which the efficacy of the combination remains >90 percent***'
- However, we know that drug resistance to sulfadoxine, pyrimethamine and amodiaquine is much higher in east and southern Africa than anywhere that SMC has previously been attempted, and that efficacy may be below 90 percent.
- Therefore, we wanted to ascertain the prevalences of SP+AQ resistance-associated genotypes and if this could impact the effectiveness of SMC:
  - dhfr: codons 108, 51 and 59
  - dhps: codons 431, 437, 540, 581 and 613
  - pfcrt: codons 72–76
  - pfmdr1: codons 86, 184 and 1246.

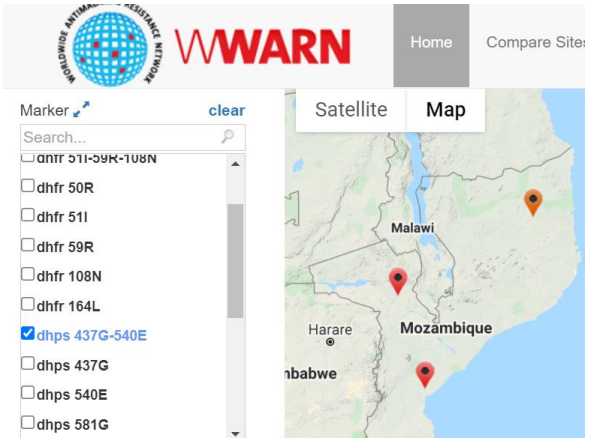


Table 3. *Plasmodium falciparum pfdhfr* polymorphism (mutated allele) *

		ALL n=50		Intervention n=31		Control n=19	
		Intervention no. (%)	Control no. (%)	Baseline , no. (%)	Endline , no. (%)	Baseline , no. (%)	Endline , no. (%)
Gene	SNP	n=31	n=19	n=20	n=11	n=12	n=7
Pfdhfr	N51I	31 (100)	19 (100)	20 (100)	11 (100)	12 (100)	7 (100)
	C59R	31 (100)	19 (100)	20 (100)	11 (100)	12 (100)	7 (100)
	S108N	31 (100)	19 (100)	20 (100)	11 (100)	12 (100)	7 (100)
	I164L	0	0	0	0	0	0

*SNP, single-nucleotide polymorphism

Table 4. *Plasmodium falciparum pfmdr1* and *pfcrt* polymorphism (mutated allele) *

		All n= 46		Intervention n= 26		Control n= 20	
		Intervention,no. (%)	Control,no. (%)	Baseline, no. (%)	Endline, no. (%)	Baseline, no. (%)	Endline, no. (%)
Gene	SNP	n= 26	n=20	n= 12	n= 14	n= 12	n= 8
	N86Y	0	0	0	0	0	0
	Y184F	20 (76.9)	14 (70.0)	11 (91.6)	9 (64.3)	8 (66.7)	6 (75.0)
pfmdr1	D1246Y	0	0	0	0	0	0

*SNP, single-nucleotide polymorphism

Pyrimethamine & Amodiaquine; Pfdhfr & Pfmdr1 + Pfcrt

Table 2. *Plasmodium falciparum pfdhps* polymorphism (mutated allele) *

		ALL n=100		Intervention n=54		Control n=46	
		Intervention no. (%)	Control no. (%)	Baseline , no. (%)	Endline , no. (%)	Baseline , no. (%)	Endline , no. (%)
Gene	SNP	n=54	n=46	n=27	n=27	n=22	n=24
Pfdhps	I431V	0	0	0	0	0	0
	A437G	49 (90.7)	42 (91.3)	23 (85.2)	26 (96.3)	18 (81.8)	23 (95.8)
	K540E	46 (85.2)	39 (84.8)	22 (81.5)	24 (88.9)	18 (81.8)	21 (87.5)
	A581G	1 (1.9)	0	0	1 (3.7)	0	0
	A613S	2 (3.7)	0	2 (7.4)	0	0	0

*SNP, single-nucleotide polymorphism

Sulfadoxine; Pfdhps

Overall key findings

- Results from phase 1 of the Mozambique SMC implementation study demonstrate that SMC with SPAQ is
  - safe
  - feasible
  - acceptable in the local context.

- The intervention was successfully delivered
  - according to schedule
  - at the anticipated scale
  - achieving high coverage.

- No serious adverse events were reported.

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Overall key findings cont'd

- Acceptability of the intervention among the population was high, with no negative rumours reported.

- The intervention appears to be highly effective: in a non-randomised controlled trial, children who lived in a district where SMC had been implemented had **86 percent lower odds** of developing clinical malaria during the peak transmission season compared with children who lived in the control district without SMC implementation.

- There were high rates of SP resistance but low AQ-associated markers. One annual round of SMC does not appear to have had a negative impact on the SP resistance profile.

Next steps

- In phase 2, more work is needed to understand the efficacy of SPAQ to clear existing infections and prevent new ones. This is what we mean by the term ‘chemoprevention efficacy’.

- To inform policy change, more robust evidence of effectiveness in the form of a randomised controlled trial is also needed.

- In addition, there is a need to better understand changes over time in SP resistance in symptomatic malaria cases. A scenario where SMC contributes towards extremely rapid selection of highly SP-resistant parasites must be avoided, as this will affect the intervention’s effectiveness in the longer term.

Acknowledgements

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Thank you

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