Rapid assessments for the deployment of seasonal malaria chemoprevention in new geographies of East and southern Africa

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Overview

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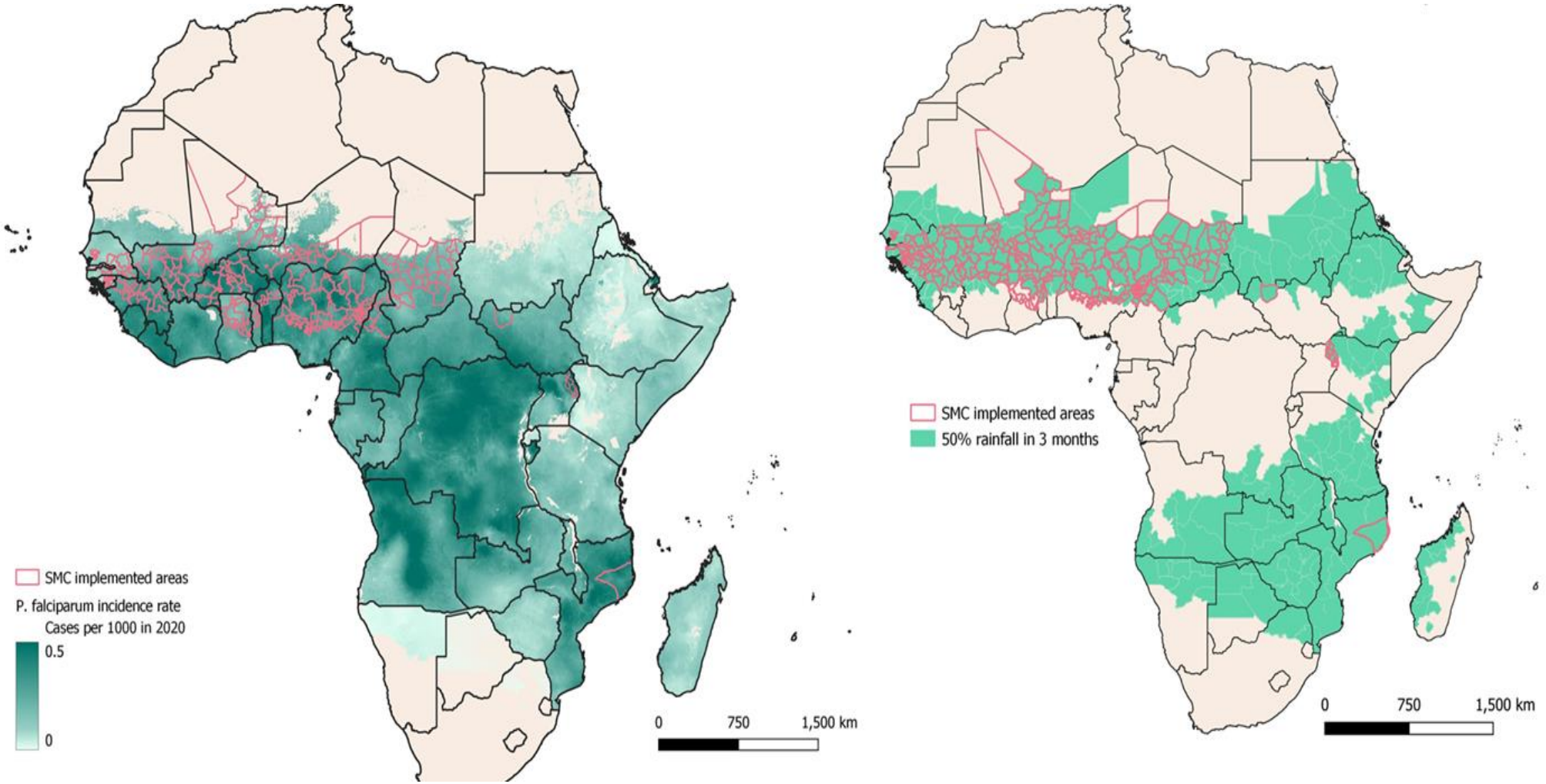
Introduction

- Seasonal malaria chemoprevention (SMC) with sulfadoxine-pyrimethamine (SP) and amodiaquine (AQ) is a highly effective community-based intervention to prevent malaria caused by *Plasmodium falciparum*.
- Updated malaria chemoprevention recommendations no longer include geographic restrictions and allow more flexibility in recognising age-based risk among children.
- The guidelines could enable SMC in previously untreated areas of East and southern Africa with seasonal malaria transmission patterns.
- Particularities of East and southern Africa include potentially high resistance profiles, malaria transmission and prevalence, population immunity and efficacy of SPAQ.
- Malaria Consortium plans to conduct rapid assessments in new geographies of East and southern Africa over the next two years to inform decisions about the potential scale-up of the intervention in those locations.

Potential SMC-eligible areas

Figure 1:



Unpublished figure. The raster file for P. falciparum incidence rates values was downloaded from the Malaria Atlas Project. The annual rainfall map is based on the model developed by Cairns et al.(2012). The figure was generated by Maria Suau Sans.

Selection of locations for rapid assessments

Seasonal malaria transmission:
- 60% of malaria cases within four months
- 60% of rainfall within a period of four months

Resistance markers profile:
- Existing data on prevalence of molecular markers associated with resistance to SP and AQ

Potential beneficiaries:
- Children aged 3–59 months

Operational considerations:
- SMC priority in the malaria strategic plan
- Supportive National Malaria Control Programme/Ministry of Health
- Feasibility of coordinating implementation and drug importation, including security and operational costs

Shortlisted geographies:
- Mozambique (Niassa province)
- Malawi (Dowa District)
- Democratic Republic of the Congo (Haut Katanga province)
- Madagascar (West Coast and southern region)
- Tanzania
- Angola
- Zambia
- Zimbabwe
- Djibouti

Methods

Seasonal malaria chemoprevention rapid assessment

- **Rapid assessment:** involves the administration of only one cycle of SMC. A period of 42 days of data collection per location will be required for the completion of all study components, followed by data management, analysis and results write-up per location.
- **Aim:** to estimate the effectiveness, chemoprevention efficacy, potential deployment impact, acceptability and feasibility of SMC using sulfadoxine-pyrimethamine and amodiaquine (SPAQ) in new geographies of East and southern Africa.
- **Study design:** type 2 hybrid effectiveness-implementation study protocol, including five different components.
- **Study components:**
  1. A cluster randomised controlled trial to estimate the effectiveness of SPAQ
  2. A two-arm trial to estimate the chemoprevention efficacy of SPAQ
  3. A cross-sectional study to estimate the prevalence of molecular markers associated with the resistance to SP and AQ
  4. Dynamic modelling to estimate the potential impact of SMC implementation and prioritise areas for scale-up
  5. A qualitative study to evaluate the feasibility and acceptability of the intervention
- **Study setting:** rural community settings with highly seasonal malaria transmission.

Methods: Cluster randomised controlled trial

Key question: How effective is SMC with SPAQ at preventing **clinical malaria** among children aged 3–59 months in these new locations?

Design:

- Cluster randomised controlled trial

Outcome:

- Clinical rapid diagnostic test-confirmed malaria cases occurring over 42 days following a receipt of the first dose of SPAQ

Measurement method:

- Surveys at timepoints 0, 14, 28 and 42 post-SMC distribution
- Optimised surveillance system

Methods: Chemoprevention efficacy study

Key question: What is the chemoprevention efficacy of SMC with SPAQ at preventing **malaria infections** among children aged 3–59 months in these new locations?

Design:

- A two-arm intervention trial

Outcome:

- Chemoprevention failure (presence of parasites in blood samples anytime before day 28 post-SMC administration)
- Prevalence of antimalarial resistance markers among chemoprevention failures
- Drug concentrations among chemoprevention failures.

Measurement methods:

- qPCR
- Sequencing

Methods: Resistance markers component

Key question: What is the prevalence of the molecular markers associated with SPAQ resistance in these new geographies?

Design:

- Cross-sectional study

Outcomes:

- Prevalence of resistance-associated molecular markers in blood samples collected from symptomatic children under five years with a positive RDT attending the study health facilities
- SP: mutations in the dihydrofolate reductase gene (***dhfr***) in the dihydropteroate synthetase gene (***dhps***) and *P. falciparum* chloroquine resistance transporter gene (***pfcrt***)
- AQ: *P. falciparum* multidrug resistance gene 1 (***pfmdr1***)

Measurement method:

- PCR

Methods: Dynamic modelling

Key question: What model can best predict the suitability of SMC in these new geographies?

Design:

- Dynamic modelling

Outcome:

- Estimates of the proportion of clinical malaria cases that could be averted using SMC across a broader geographic scale, allowing for factors such as varying transmission intensity, seasonality and drug resistance, as part of the body of evidence to inform on areas suitable for further scale-up of SMC in nearby geographies

Measurement methods:

- Collation of data from other components and historic data

Methods: Qualitative component

Key question: How feasible and acceptable is SMC with SPAQ in these new geographies?

Design:

- Qualitative study

Outcome:

- Experiences, opinions and perceptions surrounding SMC

Measurement methods:

- Focus group discussions
- In-depth interviews with key informants (KIIs) using interview guides, audio records and transcripts

Strengths

- **Multifaceted approach:** The study design is comprehensive, covering efficacy, effectiveness, molecular analysis, modelling and qualitative aspects. This allows for a well-rounded understanding of the intervention.
- **Cross-validation:** The different components can serve to cross-validate each other, supporting the findings between components and increasing their relevance.
- **Randomised controlled trial design:** This type of study design allows for a high level of control over variables through randomisation providing strong evidence of causality.
- **Geographical diversity:** Given the similarity of our findings across countries, our results may be generalisable across other settings where SMC may be implemented.
- **Analysis plan:** The intention-to-treat analysis approach, enables the estimation effect of SMC in real-world conditions.

Limitations

- **Dynamic modelling:** The use of historic data may not accurately reflect current conditions; however, modelling will also include data collected just before the start of the study.
- **Open-label:** Both the cluster randomised controlled trial and the chemoprevention efficacy study groups are not blinded. This can introduce bias both from participants, who may alter their behaviour in ways that can affect the study outcomes, and from researchers, who may unconsciously alter the way they interact with participants.

Implementation plan

Mozambique (Niassa)

- Protocol approved by national ethical review board (ERB)
- Timeline: February–March 2024.

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Malawi (Dowa)

- Protocol under revision by the Malawi National Malaria Control Programme
- Submission to the ERB
- Timeline: January–February 2024.

2

Democratic Republic of Congo (Haut Katanga)

- Reviewing data
- Protocol adaptation
- Tentative timeline: December 2023.

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Ministry of Health

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Thank you

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