# Evaluation of the impact of one round of seasonal malaria chemoprevention on resistance markers associated with sulfadoxine-pyrimethamine and amodiaquine in Karamoja, Uganda, March 2022.

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## Key message

Routine monitoring of markers of parasite resistance should form part of the implementation and scale-up of SMC with SPAQ in eastern and southern African countries that, historically, have widespread, high prevalence of SP and AQ resistance makers. This will allow us to assess the impact of SMC on these markers.

## Introduction

Malaria remains a priority public health concern in several sub-Saharan African countries, including Uganda. Seasonal malaria chemoprevention (SMC) has been found to prevent approximately 75 percent of malaria episodes in children, including severe episodes, and can prevent deaths. However, due to the high prevalence of markers associated with sulfadoxine-pyrimethamine and amodiaquine (SPAQ) resistance, SMC has not been implemented at scale in East and southern Africa. This study assessed the impact of one round of SMC using SPAQ on the potential emergence and spread of drug-resistant malaria in Karamoja, which is located in northeastern Uganda. Malaria Consortium collaborated with the Ministry of Health to pilot five monthly rounds of SMC using SPAQ between May and September 2021.

## Methods

- We conducted health facility-based, cross-sectional surveys at baseline and endline one month before SMC delivery (April 2021) and one month after (November 2021), respectively.
- Molecular markers associated with resistance to SP (PfDHFR 164L, PfDHPS 581G, PfDHFR 51I, 59R, 108N, PfDHPS 437G and 540E) and AQ (PfCRT and PfMDR1 including copy number) were analysed on 300 blood samples, taken as dry blood spots, from symptomatic children 3–59 months who had a positive malaria test (confirmed by malaria rapid diagnostic test or microscopy) in both intervention (Moroto and Kotido) and control (Nabilatuk) districts.

## Results

- The five mutations of concern (PfDHPS 437G, 540E and DHFR 51I, 59R 108N) that mediate moderate SP resistance were prevalent, but remained unchanged between baseline and endline.
- DHFR 164L and DHPS 581G mutations, which mediate high-level SP resistance, were rare at both baseline and after one round of SMC administration.
- Key mutations associated with 4-aminoquinolone resistance were rare in comparison to PfDHPS with PfDHFR mutations associated with sulfadoxine-pyrmimethamine resistance.

**Table 1: Prevalence of antifolate and transporter mutations associated with SP and AQ resistance**

| | Control group | | | | | | Intervention group | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Baseline | | | Endline | | | Baseline | | | Endline | | |
| | Wild type | Mixed | Mutant | Wild type | mixed | Mutant | Wild type | Mixed | Mutant | Wild type | Mixed | Mutant |
| | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| PfDHFR N51I | 1 (0.3) | 2 (0.7) | 227 (99) | 7 (2.4) | 3 (1) | 271 (94.4) | 0 | 0 | 248 (100) | 4 (1.4) | 20 (7.2) | 254 (91.4) |
| PfDHFR C59R | 39 (17) | 21 (9) | 176 (75) | 14 (5) | 15 (6) | 233 (89) | 63 (26.7) | 10 (4.3) | 163 (70) | 12 (4) | 14 (5) | 241 (90) |
| PfDHFR I164L | 261 (99) | 3 (0.01) | 0 | 271 (100) | 0 | 0 | 288 (100) | 0 | 0 | 277 (99.3) | 2 (0.7) | 0 |
| PfDHFR S108T/N | 0 | 7 (2.4) | 281 (97.6) | 4 (1.4) | 24 (8.9) | 241 (89.6) | 0 | 7 (2) | 283 (98) | 0 | 18 (6) | 262 (94) |
| PfDHPS A437G | 7 (4) | 35 (20) | 137 (77) | 1 (0.4) | 21 (7.6) | 253 (92) | 5 (2) | 64 (25) | 182 (73) | 2 (1) | 16 (6) | 255 (93) |
| PfDHPS A581G | 219 (100) | 0 | 0 | 266 (98.5) | 3 (1.1) | 1 (0.4) | 252 (100) | 0 | 0 | 280 (99.7) | 1 (0.3) | 0 |
| PfDHPS A613S | 203 (100) | 0 | 0 | 275 (100) | 0 | 0 | 236 (100) | 0 | 0 | 277 (100) | 0 | 0 |
| PfDHPS K540E | 0 | 1 (0.5) | 203 (99.5) | 1 (0.4) | 19 (6.8) | 258 (92.8) | 3 (1.15) | 3 (1.15) | 255 (97.7) | 2 (0.73) | 6 (2.2) | 266 (97.1) |
| PfMDR1 D1246Y | 237 (99) | 1 (0.4) | 1 (0.4) | 273 (99.6) | 0 | 1 (0.4) | 223 (99.1) | 1 (0.4) | 1 (0.4) | 263 (97) | 2 (0.7) | 1 (0.4) |
| PfMDR1 N86Y | 248 (94) | 3 (1) | 13 (5) | 268 (97) | 3 (1.2) | 4 (1.8) | 183 (84) | 9 (0.4) | 25 (12) | 260 (99) | 3 (0.1) | 0 |
| PfMDR1 Y184F | 78 (29) | 82 (0.3) | 111 (41) | 73 (27) | 55 (20) | 147 (53) | 49 (22) | 65 (29) | 109 (49) | 53 (19) | 74 (27) | 149 (54) |
| PfCRT K76T | 205 (90.0) | 2 (0.9) | 20 (8.9) | 253 (93.7) | 5 (1.9) | 12 (4.4) | 206 (89.5) | 2 (0.9) | 22 (9.5) | 253 (95.1) | 7 (2.5) | 9 (3.2) |

## Conclusion

One round of SMC with SPAQ does not appear to select for an observable change in resistance markers for SP and AQ.

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Anthony Nuwa is a medical doctor and health specialist with a PhD in public health and a master's in international health. He has over twenty years' experience in strengthening health systems in clinical and public health settings. He also holds several postgraduate qualifications related to health systems from international universities. Currently, he is the Senior Country Technical Coordinator at Malaria Consortium, and a member of its global and senior technical teams. He is a Principal Investigator in several studies, including the current study. Anthony's vast expertise in health systems and community health is compounded by a deep understanding of the social context of Uganda. Along with experience in programme management, health services research, monitoring and evaluation, operational research on malaria prevention, diagnostics, and case management, Anthony has expertise in primary healthcare, communicable disease control, integrated vector control and child survival. He has an in-depth knowledge of the latest evidence in malaria prevention, diagnosis and treatment. Anthony is chairperson of the Uganda National Malaria Partner's Coordination Committee and of the Malaria Case Management Technical Working Group (TWG). He is also a member of the National COVID-19 Task Force and other TWGs on malaria and child, maternal and newborn care at the national level.

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