Protecting those most at risk

Children under the age of 5, who have developed little or limited immunity to malaria, are most at risk of the disease. In 2018, this group accounted for 67% of all malaria deaths worldwide, most of which occurred in sub-Saharan Africa.¹ In the absence of an effective vaccine to protect children against malaria, the World Health Organization (WHO) recommends seasonal malaria chemoprevention (SMC), whereby full antimalarial treatment courses are administered to children at regular intervals during periods of high malaria transmission (typically the rainy season, which lasts 3–4 months). MMV and its partners are working hard to maximize supply security and access to currently available medicines for SMC, to support the generation of evidence that could justify an age-range expansion of SMC, and to develop new alternatives that could expand the geographical reach of SMC to other areas of seasonal transmission in Africa.

Seasonal malaria chemoprevention (SMC)

In 2012, the WHO recommended monthly administration of the medicine sulfadoxine-pyrimethamine plus amodiaquine (SPAQ) for SMC in the Sahel region of sub-Saharan Africa. In clinical trials, SPAQ has been shown to reduce cases of uncomplicated and severe malaria by 75% in children under 5,² and post-implementation data from Mali and Burkina Faso have shown it reduces the chance of testing positive for malaria during the season by 44–62%³. However, coverage is not universal. In 2018, about 12 million children who could have benefited from SMC were not covered,¹ so continued efforts are needed to reach more children.

MMV’s partner Fosun Pharma is the only WHO-prequalified supplier of SPAQ. To increase the number of quality-assured suppliers, MMV has been supporting a second manufacturer, S Kant Healthcare Ltd. (India) to develop a second child-friendly, dispersible SPAQ product (Supyra⁴). In July 2018, S Kant submitted a dossier to the WHO prequalification (PQ) programme,⁵ and subsequently to the Global Fund Expert Review Panel (ERP) in September 2018. The ERP issued a positive opinion in February 2019, allowing countries to purchase Supyra with international donor funds until February 2020, while the WHO-PQ review was ongoing.⁶ Market authorization of Supyra has now been achieved in two countries and review is ongoing in a further five.⁷ Since the launch of SMC in 2014, the number of protected children has increased from 3 million in 2015 to over 20 million in 2019. This dramatic scale-up has been achieved in part by the distribution of 96 million treatment courses of SPAQ (Fosun Pharma and S Kant products combined) in 13 countries in 2019, bringing the total number of courses distributed since 2014 to 357 million.

The WHO recommends SMC in children aged 3–59 months. However, data from Senegal, which has implemented SMC in children up to 10 years, suggest that SMC is as effective, and cost-effective, in the higher age group (5–10 years) as in children under 5. As a result, four countries⁸ are now considering increasing the age range for SMC. MMV’s SEAMACE² programme will explore ways to expand coverage of SMC in the coming years, by extending the target age range, expanding geographic coverage within the Sahel, and increasing the duration of coverage where warranted by local transmission patterns (from 3–4 to 3–5 months). Given the threat of sulfadoxine-pyrimethamine (SP) resistance in eastern and southern Africa, MMV also intends to develop new combinations of existing antimalarials that can provide long-duration protection, including intramuscular injectable formulations of prodrugs⁹ (p. 33), as well as new therapies based on monoclonal antibody technology.¹⁰

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5. Set up in 2001, the WHO’s prequalification programme is designed to “facilitate access to medicines that meet unified standards of quality, safety and efficacy for HIV/AIDS, malaria and tuberculosis.”
6. WHO-PQ for S Kant’s SPAQ is targeted for year-end 2020.
7. Registered in Nigeria and Cameroon; review ongoing in Guinea, Ghana, Niger, Burkina Faso and Mali.
9. Seasonal Malaria Chemoprevention Extension.
10. Prodrugs: a precursor of a drug that must undergo chemical conversion by metabolic processes in the body before becoming an active pharmacological agent.
11. This was the subject of a recent review paper authored by a team of MMV’s in-house scientific Macintyre F et al. “Injectable anti-malarials revisited: discovery and development of new agents to protect against malaria.” Malar J 17, 402 (2018).

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Source: Medicines for Malaria Venture | Annual report 2019
Since the WHO issued its SMC recommendation in 2012, what kind of impact has it had on the Sahel region of Africa?

In most countries that have implemented SMC, malaria incidence initially reduced by 25–60%, and malaria-related mortality by 40–45%. The intervention is therefore having a significant protective effect against uncomplicated and severe malaria. This is great news, but we will have to confirm these reductions over the coming years, and during the 2020 COVID-19 pandemic in particular. Senegal, Burkina Faso and Ghana are among the countries that have seen the most significant benefits from SMC so far, and we hope that other countries in the region will benefit as we look to increase SMC coverage. It’s really important that we apply robust and consistent methodology to assess the impact of SMC on the burden of malaria in the Sahel region, and evaluate its benefits continuously.

How are countries mobilizing national resources to increase uptake of SMC?

Some countries are seeking financial support from the World Bank and other regional banks to complement the funding they receive through multinational mechanisms such as the Global Fund and the US President’s Malaria Initiative. In addition, governments in some countries, such as Mali and Ghana, are increasingly contributing towards SMC campaigns and allocating more of their malaria funds towards SMC. However, the proportion of resources that comes from national sources is still negligible, and most countries are largely dependent on international donor funding.

What are the logistical challenges associated with implementing an SMC campaign?

In the early days of implementation, forecasting the supply of SMC was a major challenge as it was based on census data that were often old and inaccurate. With updates to census data, countries are now much better able to predict their SMC supply needs. Social and political migration in some countries also makes forecasting difficult. Countries generally have an extra 10% stock of SPAQ as a buffer to cover any additional needs, but thanks to improved coordination between countries, rapid movement of stock from areas of low to high demand is now possible.

Compliance to SMC is also a challenge. The first dose of SPAQ is administered by a healthcare worker, but ensuring adherence to the second and third doses of AQ alone, which are usually given by caregivers (parents or guardians), is challenging (see pp. 22–23 for one solution). Supervised administration of the full course of SMC would be beneficial but would also increase costs. Several countries are currently exploring this option.

How has MMV helped to diversify the supplier base for SPAQ?

• Only one WHO-prequalified, child-friendly SPAQ product is currently available, and so MMV is supporting a second supplier, S Kant Healthcare, to bring forward a new child-friendly, dispersible formulation. However, demand for SMC is likely to increase in the coming years due to the extension of the age range to include children up to 10 years of age, and an increased duration of coverage (up to 5 months based on changing epidemiological patterns). Ensuring a steady supply of SPAQ will therefore be crucial.

What is MMV’s mid- to long-term strategy for SMC?

• Should the efficacy of SPAQ be compromised by resistance, new medicines will be needed. To increase the options for SMC, MMV is looking at new molecules, as well as repurposing existing antimalarial medicines. While exploring possible alternatives to SPAQ, we are keeping a close eye on the cost of a potential new product and trying to keep it within a similar price range as the currently approved medicines. Last year, we tested a new co-formulation of atovaquone-proguanil and amodiaquine in a drug-drug interaction study, which has the potential to achieve the same preventive efficacy as SPAQ. Unfortunately, this combination presented an unacceptable safety risk in healthy volunteers and the study was stopped.

SMC is classified as a protective intervention aimed at decreasing the number of malaria cases and deaths. However, in the long run, MMV would like to complement SMC with transmission-blocking interventions that can be administered either before or at the same time as SMC, thus contributing to an overall reduction in malaria in the community. One possible avenue could include the addition of endectocides (e.g. ivermectin), which kill mosquitoes, in combination with SPAQ; another approach could be to add a low dose of primaquine to kill gametocytes (the parasite stage that causes transmission from infected humans to mosquitoes). These approaches could help reduce rates of re-infection significantly in areas of high transmission.

Ensuring a steady supply of SPAQ will therefore be crucial.

With SMC:

Malaria incidence reduced by 25–60%

Malaria-related mortality reduced by 40–45%
Drocas Dako knows how to multitask. During Mali’s seasonal malaria chemoprevention campaign, she’s out of the door by 7 am to distribute free pills that protect children from malaria. She goes from one household to the next, carrying her baby on her back.

At one of the first homes, Drocas is welcomed with friendly greetings and chatter as she and the household’s grandmother, Assitar, collect the young children and sit down together in the shade of a nearby tree.

Thinking back to the training she received from a nurse at the closest health clinic, Drocas administers the pills to a 4-year-old boy, Alou, and speaks kindly as she reminds Assitar of the importance of checking off on Alou’s SMC card that the second and third doses were indeed given later at home.

That afternoon, Drocas emerges from visiting another household in the Segou region and makes a mark with chalk next to the home’s door to signal that she has visited the house and distributed medicine, as is the custom during SMC campaigns. Drocas managed to reach all six of the eligible children living there.

During the first campaign cycle in July, Drocas reminded Assitar and other caregivers that she would be back almost exactly one month later to administer another dose and would return again in both September and October.

For young children in Mali and other countries across Africa’s Sahel region, Drocas is a life saver.

“During Mali’s seasonal malaria chemoprevention (SMC) campaign, she’s out of the door by 7 am to distribute free pills that protect children from malaria.”
Karotumay holds her son, Bedy, age 2, and the card that shows he has just received an antimalarial through Mali's SMC campaign. As a mother of six, she knows the importance of protecting children from malaria. “When children get malaria, they vomit and have such a bad fever that they can convulse and die. It’s very serious and treatment at the health centre can be very expensive,” says Karotumay. “In the past, Bedy’s older sister and brothers received SMC to prevent malaria. I know it works.”