

Update on malaria vaccines

March 2024

Background

As of October 2023, the World Health Organization (WHO) recommends two vaccines for the prevention of *Plasmodium falciparum* malaria in children, following advice from the joint review of R21/Matrix-M by the Malaria Policy Advisory Group and the Strategic Advisory Group of Experts on Immunization (1). The two vaccines are RTS,S/AS01 (RTS,S) and R21/Matrix-M (R21). The WHO recommendation for RTS,S in 2021 was informed by findings from the Malaria Vaccine Implementation Programme (MVIP) in Ghana, Kenya and Malawi, which started in 2019. The MVIP demonstrated the feasibility, safety and substantial impact of the vaccine in routine use. Priority research questions on R21 were identified during the joint review by the Malaria Policy Advisory Group and the Strategic Advisory Group of Experts on Immunization. Accordingly, WHO has convened an internal coordination team to monitor initiation of and findings from those studies.

Demand for malaria vaccines is high, and, to date, 20 countries have been approved by Gavi, the Vaccine Alliance, to receive support for introduction. Beginning in 2024, the cumulative supply availability of the two WHO-recommended and -prequalified malaria vaccines is expected to meet this high demand, enabling more countries to introduce and scale up the vaccine in areas where malaria is a major public health risk.

Update on the MVIP

The WHO-coordinated MVIP was completed in December 2023. The programme yielded many lessons learned that were applied to the review of the R21 vaccine and will inform subsequent malaria vaccines in terms of their delivery, demand and impact. From the start of vaccination with the first malaria vaccine, RTS,S, in 2019 to December 2023, over 6.5 million doses were administered and over 2 million children reached in Ghana, Kenya and Malawi. All three pilot countries have secured support from Gavi to continue vaccine implementation following the end of the MVIP. In addition, Ghana (approved) and Kenya (pending review by Gavi's Independent Review Committee) have submitted applications to scale up malaria vaccine implementation outside the pilot areas.

Vaccine uptake has remained consistently high in all three countries, despite the challenges brought about by external factors during the MVIP, including the global coronavirus disease (COVID-19) pandemic and climatic factors, such as flooding. According to administrative data for 2023 (January to December), the estimated coverage of the first dose of RTS,S was 83% in Ghana (third dose: 81%; fourth dose: 83%), 83% in Kenya (third dose: 77%; fourth dose: 50%) and 87% in Malawi (third dose: 76%; fourth dose: 46%). Ghana reached high dose-four coverage by changing the timing of the delivery of dose four from 24 months of age to 18 months of age to coincide with the established administration of the meningococcal A conjugate vaccine and the second dose of the measles-rubella containing vaccine. This and the many other lessons learned from vaccine implementation in the MVIP countries have been documented and shared to support non-pilot countries in the planning of vaccine introduction (2).

The 46-month community mortality and sentinel hospital surveillance, which was part of the malaria vaccine pilot evaluation, was completed in Ghana and Malawi in February 2023 and in Kenya in July 2023. The results were presented to the MVIP Data Safety and Monitoring Board in October and to the

Strategic Advisory Group of Experts on Immunization/Malaria Policy Advisory Group Working Group on Malaria Vaccines in November 2023. In late 2023, the results were also presented at the annual meeting of the American Society of Tropical Medicine and Hygiene and the third International Conference on Public Health in Africa in Lusaka, Zambia.

The RTS,S malaria vaccine introduction was associated with a substantial reduction (13%; 95% CI: 3–22) in vaccine-attributable all-cause mortality in children age-eligible for vaccination and 22% (95% CI: 3–36) reduction in hospitalization with severe malaria. Use of insecticide-treated nets, coverage of other vaccines and care-seeking behaviour were balanced between the vaccinating and comparator areas. This impact was achieved during the period of vaccine scale-up (with coverage of the three primary doses of 75% in Ghana, 69% in Kenya and 63% in Malawi in 1-year-old children surveyed in 2022; and coverage of the fourth dose of 54%, 34% and 33% in children aged 30–41 months, or 28–39 months in Malawi, also surveyed in 2022). Impact is expected to increase further as vaccine coverage increases.

Following review of the results, the Strategic Advisory Group of Experts on Immunization/Malaria Policy Advisory Group Working Group on Malaria Vaccines concluded that the final MVIP results strengthen the evidence that informed the existing WHO malaria vaccine recommendation made in October 2021 and demonstrate a good safety profile and significant reduction in hospitalized severe malaria and all-cause mortality in young children.

Malaria vaccine roll-out

The demand for malaria vaccines among governments and communities in malaria-endemic countries is high. As of February 2024, 20 countries have been approved by Gavi to receive support for initial subnational malaria vaccine introduction, and six applications, including from two new countries are currently under review.¹ On 22 January 2024, Cameroon became the first country outside the pilot programme to introduce malaria vaccines into its childhood immunization programme, initially targeting 42 health districts in the country's 10 regions as part of a phased introduction (3). On 5 February, malaria vaccination in selected health districts was launched in Burkina Faso. WHO is coordinating and providing technical support, leveraging the experience from the pilots to support country introductions in 2024. Following the WHO recommendation for the R21 malaria vaccine in October 2023 and WHO prequalification of the vaccine in December, Gavi has included R21 in its malaria programme. The cumulative supply availability of the two WHO-recommended and -prequalified malaria vaccines is expected to meet the high demand, starting in 2024. Given the forecasted easing of supply constraints (4), the *Framework for allocation of limited malaria vaccine supply* (5) will no longer be applied. As a result, Gavi has developed updated guidelines for countries to submit malaria vaccine scale-up plans (6). These updated guidelines will enable countries to expand the scope of malaria vaccine introduction beyond the areas initially approved by Gavi, in line with Gavi and WHO guidance.

Gavi-supported malaria vaccine learning agenda

The Gavi Board recently approved the provision of funds for a learning agenda to help identify and address potential implementation challenges to the uptake and roll-out of the malaria vaccine. PATH has provided technical support to WHO to develop a country-driven global malaria vaccine research agenda specifically focused on operational and implementation research. The aim of this research

¹ Countries with approved Gavi applications for subnational malaria vaccine introduction include: Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Côte d'Ivoire, Democratic Republic of the Congo, Ghana, Guinea, Kenya, Liberia, Malawi, Mozambique, Niger, Nigeria, Sierra Leone, South Sudan, Sudan and Uganda.

agenda is to support a more coordinated approach across global health stakeholders and funders to address key evidence gaps for malaria vaccine scale-up. Drawing from this global malaria vaccine research agenda, WHO has worked with Gavi to identify and prioritize the evidence gaps that are particularly relevant to the scope and timeline of the Gavi learning agenda funding. The shortlisted research areas are currently being finalized and funds are expected to be awarded and spent by the end of 2025.

References

1. Meeting of the Strategic Advisory Group of Experts on Immunization, September 2023: conclusions and recommendations. *Weekly Epidemiological Record*, 98 (98), 599–620. Geneva: World Health Organization; 2023 (<https://iris.who.int/handle/10665/374994>, accessed 16 February 2024).
2. Malaria vaccine introduction – technical resources [website]. TechNet-21 (<https://www.technet-21.org/en/topics/programme-management/malaria-vaccine>, accessed 16 February 2024).
3. Cameroon kicks off malaria vaccine rollout [website]. In: News. Brazzaville: World Health Organization Regional Office for Africa; 2024 (<https://www.afro.who.int/countries/cameroon/news/cameroon-kicks-malaria-vaccine-rollout>, accessed 16 February 2024).
4. Malaria vaccine: questions and answers on supply, price and market shaping, October 2023. Copenhagen: United Nations Children’s Fund Supply Division; 2023 (<https://www.unicef.org/supply/documents/malaria-vaccine-questions-and-answers>, accessed 16 February 2024).
5. Framework for the allocation of limited malaria vaccine supply. Geneva: World Health Organization; 2022 (<https://www.who.int/publications/m/item/framework-for-allocation-of-limited-malaria-vaccine-supply>, accessed 16 February 2024).
6. Gavi Malaria Vaccine Support: Interim Guidelines, December 2023. Gavi, The Vaccine Alliance, 2023. (https://www.gavi.org/sites/default/files/support/guidelines-2023/Gavi_Interim_Guidelines_Malaria_Vaccine_Support.pdf, accessed 20 February 2024).

Contact

For more information, please contact:

Mary Hamel, Malaria Vaccine Team Lead, WHO Headquarters, Immunization, Vaccines & Biologicals, hamelm@who.int