
Malaria vaccines update

Eastern and Southern Africa National Malaria
Programmes and Partners Annual Meeting 2023

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World Health
Organization



Credit: WHO/F.Combrink

Updated WHO recommendation, including R21/Matrix-M as a second malaria vaccine



WHO press briefing on SAGE meeting outcomes, 2 October



As a malaria researcher, I used to dream of the day we had a safe and effective vaccine against malaria. Now we have two.”

WHO Director-General's [opening remarks](#)

WHO Press release: <https://www.who.int/news/item/02-10-2023-who-recommends-r21-matrix-m-vaccine-for-malaria-prevention-in-updated-advice-on-immunization>

WHO recommendation: malaria vaccines

WHO recommends the programmatic use of malaria vaccines for the prevention of *P. falciparum* malaria in children living in malaria endemic areas, prioritizing areas of moderate and high transmission

- The malaria vaccine should be provided in a schedule of 4 doses in children from around 5 months of age¹ for the reduction of malaria disease and burden
- A 5th dose, given one year after dose 4, may be considered in areas where there is a significant malaria risk remaining in children a year after receiving dose 4
- Countries may consider providing the vaccine using an age-based, seasonal, or a hybrid of these approaches in areas with highly seasonal malaria or areas with perennial malaria transmission with seasonal peaks
- Countries should prioritize vaccination in areas of moderate and high transmission, but may also consider providing the vaccine in low transmission settings
- Vaccine introduction should be considered in the context of comprehensive national malaria control plans

This recommendation now includes two malaria vaccines:

- **RTS,S/AS01**
WHO prequalified in 2022
- **R21/Matrix-M**
Currently under WHO pre-qualification review

WHO recommendation: malaria vaccine dose schedule and delivery

- In areas of perennial malaria transmission, the malaria vaccine should be provided as a 3-dose primary series, starting from around 5 months of age, with a minimal interval of 4 weeks between doses
- The fourth dose should be given to prolong protection. There can be flexibility to optimize delivery for dose 4:
 - Alignment with other second year of life vaccines
 - Administration prior to seasonal peaks in malaria transmission to optimize efficacy
 - The optimal interval between dose-3 and 4 has not been established
- If malaria remains a significant public health problem in children a year after the fourth dose, then a fifth dose might be considered, depending on a local assessment of feasibility and cost-effectiveness

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WHO recommendation based on full evidence review of R21/Matrix-M by expert advisory bodies SAGE and MPAG on 27 September 2023¹

R21/Matrix-M Phase 3 trial design:

Seasonal administration (n=2,400), ages 5-36 months at first vaccination

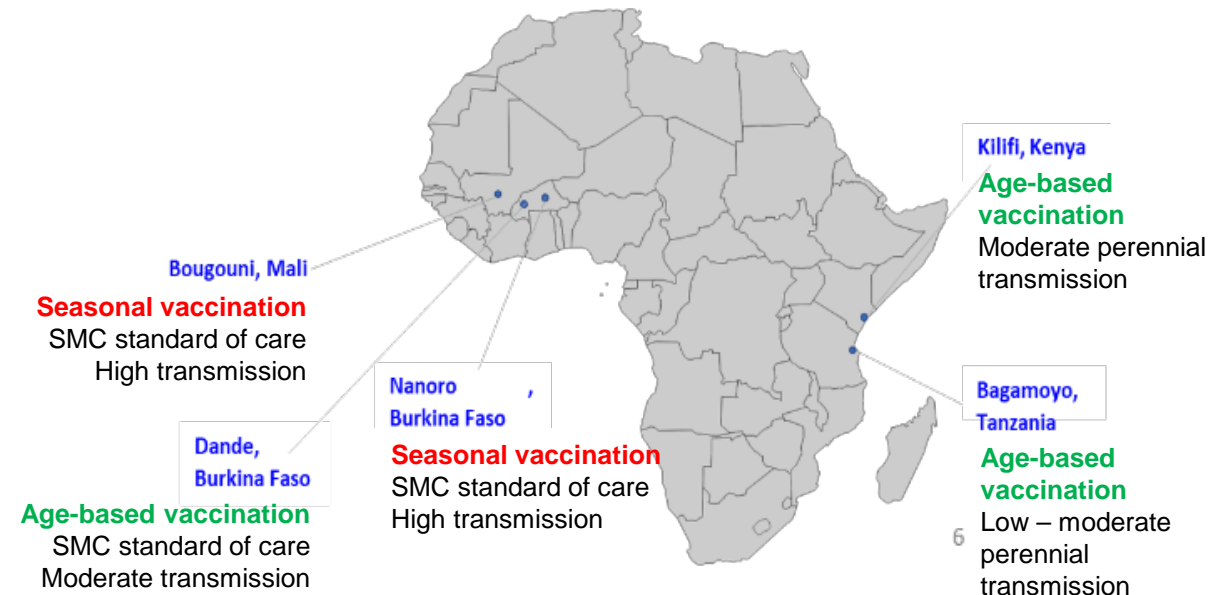
- 2 sites: Nanoro, Burkina Faso and Bougouni, Mali

Age-based (“standard”) administration (n=2,400), ages 5-36 months at first vaccination

- 3 sites: Dande, Burkina Faso; Kilifi, Kenya and Bagamoyo, Tanzania

Primary endpoint: 12 months post dose-3

Data available and reviewed through 18-months follow-up post dose 3



Evidence on R21/Matrix-M (R21) malaria vaccine

- **High efficacy when given just before the high transmission season:** In areas with highly seasonal malaria transmission (where malaria transmission is largely limited to 4 or 5 months per year), the R21/Matrix-M vaccine was shown to reduce symptomatic cases of malaria by 75% during the 12 months following a 3-dose series. A fourth dose given a year after the third maintained efficacy
 - **This high efficacy is similar to the efficacy demonstrated when RTS,S is given seasonally (73% during 12 months follow-up)**
- **Good efficacy when given in an age-based schedule:** The vaccine showed good efficacy (66%) during the 12 months following the first 3 doses in moderate to low perennial transmission settings. A fourth dose a year after the third maintained efficacy
 - Although it has not been tested in areas of high perennial transmission, R21 expected have similar high impact as that seen with RTS,S
 - No data are available to directly compare the performance of R21 and RTS,S when given in an age-based strategy.
- **High impact:** Mathematical modelling estimates indicate the public health impact of the R21 vaccine is expected to be high in a wide range of malaria transmission settings, including low transmission settings
- **Cost effectiveness:** At price assumption of US\$ 2 – US\$ 4 per dose, the cost-effectiveness of the R21 vaccine would be comparable with other recommended malaria interventions and other childhood vaccines
- **Safety:** The R21 vaccine was shown to be safe in clinical trials. As with other new vaccines, safety monitoring will continue
- **Similarity of R21 and RTS,S vaccines:** The R21 vaccine is similar to RTS,S in construct, target population, and delivery strategy. There is no evidence that one vaccine performs better than the other
- **Price:** The initial price of R21/Matrix-M vaccine is expected to be considerably lower than that for RTS,S/AS01

Implications and next steps

Outlook of key next steps

- **Ongoing WHO pre-qualification review for R21/Matrix-M**
 - WHO PQ is a pre-requisite for UNICEF to procure and for Gavi to fund the vaccine
- **UNICEF to finalize supply agreement with Serum Institute of India (SII), manufacturer of R21/Matrix-M**
 - SII indicates to have established production capacity for 100 million doses per year
- **Cumulative supply availability of two malaria vaccines expected to meet the demand, starting in 2024**
 - Enabling more countries to introduce and scale up faster

Further information

- **WHO Press release on R21/Matrix-M recommendation:** <https://www.who.int/news/item/02-10-2023-who-recommends-r21-matrix-m-vaccine-for-malaria-prevention-in-updated-advice-on-immunization>
- **SAGE meeting materials:** https://www.who.int/news-room/events/detail/2023/09/25/default-calendar/sage_meeting_september_2023
 - Full evidence report on R21/Matrix-M and additional background documents available in the SAGE «Yellow Book»; Session highlights; Presentation
- **Updates will be made to incorporate the updated WHO recommendation in materials available to support country vaccine introductions, including:**
 - Q4 2023: Update to *WHO Guidelines for Malaria (incl. MAGICApp)*
 - Q4 2023: Implementation Guidance for Malaria Vaccines
 - Guide to introducing a malaria vaccine
 - Generic training modules for health workers
 - WHO webpage on malaria vaccines and dedicated TechNet-21 page on the malaria vaccine (forthcoming)
 - Q1 2024: Revision to the Gavi application guidelines

Thank you



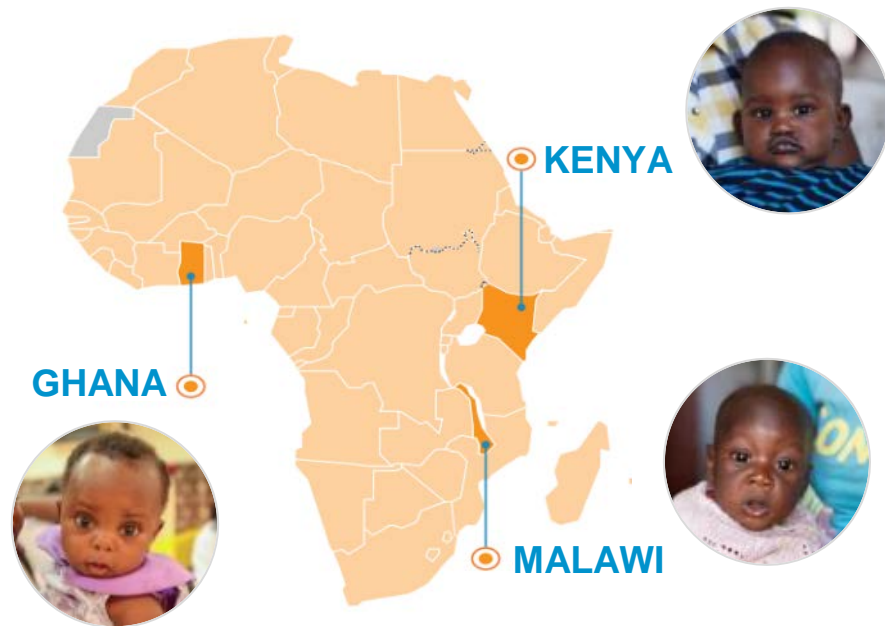
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Back-up slides

Summary findings from the Malaria Vaccine Implementation Programme (RTS,S/AS01 implementation since 2019) helped inform R21/Matrix-M vaccine consideration

Since 2019, over 1.8 million children vaccinated with RTS,S/AS01, over 5.4 million doses administered



- **Feasible to introduce with high uptake**
- **High demand** by community and acceptability by health workers
- **Vaccine confirmed to be safe**
- **High impact:** Vaccine introduction resulted in a substantial reduction in severe malaria and all cause mortality in children age-eligible to receive the vaccine, even when introduced in areas with good ITN use and access to care
- **Equity:** Vaccine delivery is equitable by gender or socioeconomic status and is reaching children who are not using other forms of prevention

Estimated public health impact of R21/Matrix-M¹



MRC Centre for
Global Infectious
Disease Analysis

Imperial College
London

Use the fitted, validated model to predict impact in non-seasonal and seasonal settings with different levels of transmission, over a 15-year time horizon.

Seasonal setting	Perennial		Seasonal	
Implementation method	Age-based	Age-based	Seasonal	Hybrid
Proportion of clinical cases averted in children younger than 5 years	41.6% [46.0; 30.6]	41.4% [47.2; 29.3]	43.4% [49.8; 29.4]	41.8% [47.4; 29.4]
Proportion of malaria deaths averted in children younger than 5 years	34.3% [44.6; 21.4]	34.4% [45.3; 20.2]	35.0% [47.8; 18.9]	33.6% [45.9; 20.3]
Clinical cases averted per 100,000 fully vaccinated children	190,602 [42,236; 330,866]	210,616 [32,428; 398,620]	225,428 [37,117; 391,277]	211,369 [32,324; 398,726]
Malaria deaths averted per 100,000 fully vaccinated children	632 [268; 633]	663 [216; 719]	689 [236; 709]	672 [217; 733]

Estimates represent median values at 20% $PfPr_{2-10}$ and intervals median values at 3% and 65% $PfPr_{2-10}$ for a four-dose schedule.

¹ For full draft manuscript, see addition Background Document 7.7 (The public health impact and cost-effectiveness of the R21/Matrix-M malaria vaccine: a mathematical modelling study) included the “SAGE Yellow Book” for the September 2023 meeting, accessible here: https://www.who.int/news-room/events/detail/2023/09/25/default-calendar/sage_meeting_september_2023

Estimated cost effectiveness of R21/Matrix-M¹



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- Use the fitted, validated model to predict cost effectiveness in non-seasonal and seasonal settings over a range of transmission levels.

Seasonal setting	Perennial		Seasonal	
Implementation method	Age-based	Age-based	Seasonal	Hybrid
Cost per clinical case averted (USD)				
\$2 per dose	\$5 [33, 3]	\$5 [43, 2]	\$7 [58, 4]	\$6 [52, 3]
\$3 per dose	\$7 [42, 4]	\$6 [56, 3]	\$9 [69, 5]	\$8 [65, 4]
\$4 per dose	\$10 [55, 6]	\$9 [73, 4]	\$12 [83, 6]	\$10 [82, 5]
Cost per DALY averted (USD)				
\$2 per dose	\$25 [97, 23]	\$23 [122, 17]	\$38 [169, 38]	\$29 [146, 23]
\$3 per dose	\$36 [126, 34]	\$33 [158, 27]	\$48 [202, 47]	\$40 [181, 32]
\$4 per dose	\$50 [165, 48]	\$46 [205, 40]	\$61 [246, 59]	\$53 [228, 43]

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