Malaria vaccines indicator

Benefits of the intervention

Serogroup or serotype coverage by vaccines considered (for serogroup- or serotype-specific vaccines)

RTS,S/AS01 and R21/Matrix-M are pre-erythrocytic vaccines that target the central repeat amino acid sequence Asn-Ala-Asn-Pro (NANP) region of the *P. falciparum* circumsporozoite protein (CSP). 1
Protection extends across diverse *P. falciparum* strains circulating in Africa. 2, 3

Given the species-specific design of these vaccines and the substantial sequence divergence of CSP across malaria parasites, meaningful protection against non-*falciparum* species is not expected, although this has not been directly evaluated.

Efficacy and effectiveness estimates (e.g. against infection, disease, hospitalization, death), including in different populations

Clinical trials of age-based delivery of RTS,S and R21 vaccines showed more than 50% reduction in malaria cases over the first year of follow up, and prolonged protection with the fourth dose. 1, 4, 5, 6 WHO re-affirmed its recommendation for the 4-dose schedule after a case-control study showed the fourth dose provides 30% incremental effectiveness against severe malaria compared to three doses. 7

An independent evaluation of RTS,S/AS01 pilot implementation in childhood immunization in three African countries during a 46-month period showed a 13% drop in mortality from all causes among children age-eligible for vaccination, and a substantial reduction (22%) in hospitalizations for severe malaria. [8]

About 75% reduction of malaria cases was achieved over the first year of follow up when malaria vaccines were given seasonally, just prior to the start of the high transmission season, and prolonged protection with annual seasonal doses. [9]

The WHO recommendation for R21/Matrix-M was based on the similar vaccine construct as RTS,S/AS01 and results from an ongoing trial that showed similar high vaccine efficacy across sites using age-based and seasonal vaccination approaches. There is no evidence to date showing that one vaccine performs better than the other. [5]

Duration of protection and waning of immunity in general and risk groups

Four doses of RTS,S/AS01 or R21/Matrix-M malaria vaccines provide added protection through early childhood, the period of highest risk of severe malaria in moderate-to-high-transmission settings.

Data show RTS,S/AS01 efficacy against clinical and severe malaria is highest in the first six months after the third dose, then wanes over time until a fourth dose is given 18 months later. [1, 4] The fourth dose extends protection but does not restore to highest efficacy. Protection against clinical malaria persists for up to seven years in children who received three or four doses, whereas sustained protection against severe malaria requires all four doses. [10] There is no evidence of severe malaria rebound in children who received only three doses. [11] When administered seasonally with Seasonal Malaria Chemoprevention (SMC), RTS,S/AS01 (up to seven doses) confers substantial and sustained protection against clinical and severe malaria for over five years. [12]

Data show R21/Matrix M demonstrates high efficacy against clinical malaria the first six months after the third dose, with minimal waning observed until the fourth dose was given 12 months

later. Long term follow up of Phase-3 study sites using age-based and seasonal approaches is ongoing. 5

Sources

1.
World Health Organization (2024). Malaria vaccines: WHO position paper, May 2024. Wkly Epidemiol Rec. 99(19):225–248 (https://www.who.int/publications/i/item/who-wer-9919-225-248, accessed 13 May 2026).

2.
RTS,S Clinical Trials Partnership. Efficacy and safety of RTS,S/AS01 malaria vaccine. N Engl J Med. 2015;372(17):1605–1615. doi:10.1056/NEJMoa1415447.

3.
Datoo MS, Dicko A, Tinto H, Ouédraogo JB, Hamaluba M et al. Safety and efficacy of malaria vaccine candidate R21/Matrix-M in African children: a multicentre, double-blind, randomised, phase 3 trial. Lancet. 2024;403(10426):533–544. doi:10.1016/S0140-6736(23)02511-4.

4.
RTS,S Clinical Trials Partnership. Efficacy and safety of RTS,S/AS01 malaria vaccine with or without a booster dose in infants and children in Africa: final results of a phase 3, individually randomised, controlled trial. Lancet. 2015;386(9988):31–45. doi:10.1016/S0140-6736(15)60721-8.

5.
World Health Organization (2024). Full evidence report on the R21/Matrix-M malaria vaccine. Geneva: World Health Organization (https://zenodo.org/records/10908560, accessed 19 January 2026).

6.
Datoo MS, Dicko A, Tinto H, Ouédraogo JB, Hamaluba M et al. Safety and efficacy of malaria vaccine candidate R21/Matrix-M in African children: a multicentre, double-blind, randomised, phase 3 trial. Lancet. 2024;403(10426):533–544. doi:10.1016/S0140-6736(23)02511-4

7.
World Health Organization (2025). Meeting of the Strategic Advisory Group of Experts on Immunization, September 2025: conclusions and recommendations, 5 December 2025. Wkly Epidemiol Rec. 100(49):661–700 (https://iris.who.int/handle/10665/384559, accessed 20 May 2026).

8.
Mwapasa V, Asante KP, Milligan P, Akech S, Oduro A et al. Impact of introducing the RTS,S/AS01E malaria vaccine on mortality in young children in Ghana, Kenya, and Malawi: an observational evaluation of a cluster randomised implementation programme. Lancet. 2026;407(10541):1796–1808. doi:10.1016/S0140-6736(26)00248-5.

9.
Chandramohan D, Zongo I, Sagara I, Cairns M, Yerbanga RS et al. Seasonal malaria vaccination with or without seasonal malaria chemoprevention. N Engl J Med. 2021;385(11):1005–1017. doi:10.1056/NEJMoa2026330.

10.
Tinto H, Otieno W, Gesase S, Sorgho H, Otieno L et al. Long-term incidence of severe malaria following RTS,S/AS01 vaccination in children and infants in Africa: an open-label 3-year extension study of a phase 3 randomised controlled trial. Lancet Infect Dis. 2019;19(8):821–832. doi:10.1016/S1473-3099(19)30300-7.

11.
World Health Organization (2025). Meeting of the Strategic Advisory Group of Experts on Immunization, September 2025: conclusions and recommendations, 5 December 2025. Wkly Epidemiol Rec. 100(49):661–700 (https://iris.who.int/handle/10665/384559, accessed 13 May 2026).

12.
Dicko A, Ouedraogo J-B, Zongo I, Sagara I, Cairns M et al. Seasonal vaccination with RTS,S/AS01E vaccine with or without seasonal malaria chemoprevention in children up to the age of 5 years in Burkina Faso and Mali: a double-blind, randomised, controlled, phase 3 trial. Lancet Infect Dis. 2024;24(1):75–86. doi:10.1016/S1473-3099(23)00368-7.