



Perspective

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R21/Matrix-M malaria vaccine three years on: Progress, challenges and implications for malaria control in Africa

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Three years after the World Health Organization (WHO) recommended the R21/Matrix-M malaria vaccine in October 2023, substantial progress has been made in its deployment across Africa, yet malaria remains a major public-health and socio-economic challenge[1]. In 2024, an estimated 282 million malaria cases and 610 000 deaths occurred globally, with the African Region continuing to bear the overwhelming burden. Kenya alone accounted for approximately 4.2 million estimated cases and 11 700 deaths[1]. Despite gains from long-lasting insecticidal nets, indoor residual spraying, artemisinin-based combination therapies and intermittent preventive treatment, the disease continues to claim hundreds of thousands of young lives each year, underscoring the need for additional tools.

By mid-2026, malaria vaccines, both R21/Matrix-M and RTS,S/AS01, had been introduced in 25 African countries (five nationally and 20 sub-nationally), including Kenya[2]. More than 58 million doses had been delivered through United Nations Children's Fund (UNICEF) and Gavi, the Vaccine Alliance, with an annual target population exceeding 10 million children[2]. R21/Matrix-M, developed by the University of Oxford and manufactured by the Serum Institute of India, is a pre-erythrocytic subunit vaccine that targets the circumsporozoite protein of *Plasmodium (P.) falciparum*. It is administered intramuscularly in a three-dose primary series (usually four weeks apart) to children aged 5–36 months, followed by a booster approximately 12 months later. Both R21/Matrix-M and RTS,S/AS01 are WHO-recommended and prequalified; they have not been compared head-to-head. WHO advises that country choice should be guided by programmatic suitability, supply and cost rather than claims of superiority[3].

Serum Institute of India's large production capacity to produce up to 100 million doses annually plus a negotiated price of approximately US\$3 per dose (from late 2026) have largely resolved the severe supply constraints that existed during 2023–2024[4]. This

has enabled countries to scale up. For instance, Ethiopia's October 2025 launch, targeting 91 000 children in 58 high-burden districts, exemplifies the scale now achievable. Real-world data are now showing reductions in clinical malaria and hospitalisations when the vaccine is combined with other interventions[2].

However, the optimism surrounding the vaccines is tempered by accelerating biological threats. First, both vaccines primarily target *P. falciparum* offering limited or no protection against other malaria species, including *P. vivax*, whose presence in Africa has increased[5]. To exacerbate the problem, insecticide resistance, and partial artemisinin resistance is now confirmed in Eritrea, Rwanda, Uganda, and Tanzania, with modelling showing rapid expansion and entrenchment in East Africa[1]. Additionally, the invasive urban vector *Anopheles stephensi* which has established itself across the Horn of Africa, including in Kenya, with 424 confirmed locations by 2024 and more than 90% of detections occurring after 2020, further complicates control efforts[6]. Unlike native vectors, *Anopheles stephensi* thrives in urban environments and is resistant to multiple insecticide classes, fundamentally altering transmission dynamics in cities previously spared from endemic malaria[6,7].

The most troubling development is financial. Funding shortfalls now limit scale-up more than vaccine availability; many countries implement the vaccine below national targets[2]. Competing

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health priorities, cold-chain capacity and the need for sustained domestic financing remain critical. On the other hand, recent cuts to international health aid have disrupted surveillance, procurement, and campaign delivery. For instance, global malaria funding in 2024 was less than half the target, leaving a substantial shortfall that could have contributed to a slight increase of deaths from 2023[2].

The availability of two complementary malaria vaccines represents a genuine milestone. However, evidence strongly supports an integrated approach combining other malaria control interventions including insecticide-treated nets, indoor residual spraying, prompt diagnosis and treatment, and chemoprevention, alongside strengthened local manufacturing capacity and species-specific surveillance, rather than relying on vaccination as a substantive standalone solution. For example, Médecins Sans Frontières (MSF)'s rollout in Ethiopia's Kule refugee camp, the first full R21 implementation in a humanitarian setting, reported nearly 50% fewer malaria-related deaths in 2025 compared to 2024 when vaccination was combined with insecticide-treated nets, indoor residual spraying, and preventive treatment[8].

The R21 vaccine has moved from promise to practice in dozens of countries within three years, but its impact is threatened by resistance, invasion, and, most critically, inadequate financing. The remaining task is to ensure sustained and scaled investment so that the promise of these vaccines translates into fewer malaria deaths among African children.

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