Seasonal targeting of the RTS,S/AS01 malaria vaccine: a complementary tool but sustained funding is required

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In October 2021, WHO recommended the RTS,S/AS01 (RTS,S) malaria vaccine for widespread use for children living in regions with moderate to high *Plasmodium falciparum* malaria transmission.[1] The recommendation received a positive reception worldwide as, despite being both preventable and treatable, malaria continues to affect the poorest nations, hampering population health, economic growth, and social wellbeing. The vaccine itself is not a silver bullet for malaria burden, offering only a 30% reduction in severe malaria disease when implemented in routine settings.[1] However, the vaccine adds another tool to the malaria reduction toolbox to complement drug therapy, vector control, and other health-system-specific measures. RTS,S further increases equity in malaria intervention: evidence from pilot countries (Ghana, Kenya, and Malawi) showed that more than 90% of children were benefitting from at least one of two preventative measures (bednets and vaccination).[1]

Phase 3b clinical trials in Mali and Burkina Faso showed that seasonally targeted vaccination was non-inferior to seasonal malaria chemoprevention (SMC) at reducing clinical disease in children aged 5–17 months for 3 years following vaccination.[2] Needing to explore general applicability of these findings, mathematical modelling is a powerful tool to incorporate the findings of the clinical trial with individual dynamics to estimate the suitability of seasonally targeted vaccination across several seasonal, transmission, and operational settings.

In *The Lancet Global Health*, Hayley Thompson and colleagues used a mathematical model to explore whether RTS,S vaccination would have a greater effect if implemented seasonally to children aged 5–17 months at the time of first vaccination than an age-targeted approach (age 6, 7·5, 9, and 27 months for the four doses respectively) in two seasonal settings.[3] The authors found that seasonally targeted vaccination was predicted to lead to greater absolute reductions in malaria cases and deaths compared with an age-targeted vaccination: relative to an age-based strategy in which there was an average of 44 000 cases averted, seasonal vaccination averted an additional 14 000–39 000 (32–88%) cases. When seasonally targeted vaccination was modelled with SMC, the joint effect on cases and deaths was substantial compared with each intervention in isolation. Although the addition of SV-RTS,S was predicted to prevent a further 42 000–67 000 (38–60%) clinical cases in children younger than 5 in seasonal settings compared with SMC alone (111 000 cases), the superiority of seasonally targeted vaccination over age-targeted vaccination was reduced.

Thompson and colleagues show the potential epidemiological benefit that RTS,S vaccination and, in particular, seasonally targeted vaccination can have when paired with SMC. For countries to consider incorporating vaccination into current malaria policy, the economic implications need to be considered. Age-targeted vaccination could result in cost savings if administered alongside other age-appropriate vaccinations according to the country's Essential Programme on Immunisation schedule. Seasonally targeted vaccinations might require different delivery platforms in which such cost sharing might not be possible. Future research needs to include cost-effective analyses for different implementation scenarios, to guide individual country planning and support funding applications.

Beyond gains in health and reduced health-care costs, it is equally important for future research to consider the broader benefits of vaccination such as herd protection effects, effect on equity, and macroeconomic consequences.[2]

Countries seeking to adopt and deploy seasonally targeted intervention packages should customise the recommended vaccination schedule and social and behaviour change communication efforts to their local context. Differences in seasonal patterns across ecological zones within some countries will mean such tailoring is required at the subnational level. These requirements reinforce the need for robust and broad surveillance systems to monitor trends in cases, vaccine coverage, deployment of vector control activities, and health and demographic data. Scientists with expert knowledge of climate forecasting and its effect on future malaria seasons should also be consulted.

With the study estimating that largest gains are to be realised when seasonally targeted vaccination is paired with SMC, it becomes more important than ever that funding for vaccination, vaccine development, and supporting malaria interventions be sustained to realise the full value of vaccination. Vaccine development during the COVID-19 pandemic presented a paradigm shift in the global health financing model. US investment in COVID-19 vaccine development in 2020 exceeded US$ 11 billion compared with $7 million for malaria between 2007 and 2018.[5] The pandemic also showed that even minor disruptions in access to treatment can undo much of the health gains from the last decade. Eliminating malaria in all countries requires reignited efforts in research and development and health-systems strengthening so that the global aim of malaria elimination by 2030 is not only met, but sustained through future exogenous shocks.

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1 WHO. WHO recommends ground-breaking malaria vaccine for children at risk. 2021. https://www.who.int/news/item/06-10-2021-who-recommends-groundbreaking-malaria-vaccine-for-children-at-risk (accessed Oct 29, 2022).

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3 Thompson HA, Hogan AB, Walker PGT et al. Seasonal use case for the RTS,S/AS01 malaria vaccine: a mathematical modelling study. *Lancet Glob Health* 2022; **10:** e1782–92.

4 Hutubessy RC, Lauer JA, Giersing B, et al. The Full Value of Vaccine Assessments (FVVA): a framework to assess and communicate the value of vaccines for investment and introduction decision making *SSRN* 2021; published online May 19. https://dx.doi.org/10.2139/ssrn.3841999 (preprint).

5 Tetteh K. Malaria vaccine: not perfect but life-saving. 2021. https://www.lshtm.ac.uk/research/centres/malaria-centre/news/336171/malaria-vaccine-not-perfect-life-saving (accessed Oct 29, 2022).