Global research agenda on malaria vaccine introduction and implementation

Technical report

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Copy photo: ©WHO/Fanjan Combrink, Margaret and her 10-month-old daughter Stella stand outside Homa Bay County Teaching and Referral Hospital, Kenya, where Stella was just vaccinated against malaria and other diseases.

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Abbreviations

COVID-19	coronavirus disease
CSO	civil society organization
EPI	Expanded Programme on Immunization
IFRC	International Federation of Red Cross and Red Crescent Societies
IRS	indoor residual spraying
ITN	insecticide-treated net
MVCT	Malaria Vaccine Coordination Team
MVIP	Malaria Vaccine Implementation Programme
NMP	national malaria programme
PMC	perennial malaria chemoprevention
R21	R21/Matrix-M malaria vaccine
RTS,S	RTS,S/AS01 malaria vaccine
SMC	seasonal malaria chemoprevention
TAC	technical advisory committee
UNICEF	United Nations Children's Fund
WHO	World Health Organization

Overview and terminology

Overview

The main objective of this process was to develop a research agenda that identifies and serves to address key operational challenges and knowledge gaps as they pertain to the design, implementation and scale-up of malaria vaccines. The scope of the research agenda includes implementation and operational research questions related to the deployment of malaria vaccines, organized according to the following broad themes: (i) safety, (ii) implementation feasibility, (iii) acceptability of and demand creation for the malaria vaccine, (iv) integration of the malaria vaccine with other health interventions, (v) impact and effectiveness of the vaccine, and (vi) the economics, costing and cost-effectiveness of the vaccine. The final agenda is intended to serve as a global resource that can help facilitate a more coordinated and efficient approach to address the identified priority research areas.

Terminology

Definitions of the key terms used for this research agenda are provided in this section to enable a common understanding of the purpose and scope.

Implementation research

The World Health Organization (WHO) defines implementation research as the scientific study of the processes used in the implementation of health initiatives (e.g., interventions, strategies and policies) as well as the contextual factors that affect these processes. The main purpose of implementation research is to understand and address barriers to effective and quality implementation of health interventions, strategies and policies *(1, 2)*.

Operational research

WHO defines operational research as "the use of systematic research techniques for programme decision-making to achieve a specific outcome. Operations research provides policy-makers and managers with evidence that they can use to improve programme operations. It is a type of social science research, distinguished from other kinds of research by the following characteristics:

- It addresses specific problems within specific programmes, not general health issues;
- It addresses those problems that are under control of managers, such as programme systems, training, pricing, and provision of information;
- It utilizes systematic data collection procedures, both qualitative and quantitative, to accumulate evidence supporting decision-making;
- It requires collaboration between managers and researchers in identification of the research problem, development of the study design, implementation of the study, and analysis and interpretation of results; and
- It succeeds only if the study results are used to make programme decisions; publication alone is not a valid indicator of successful [operational research]" *(3)*.

Executive summary

Background

In October 2021, the World Health Organization (WHO) recommended the first malaria vaccine, RTS,S/AS01 (RTS,S), following decades of research to develop a safe and effective vaccine. Between 2019 and 2023, RTS,S was piloted in Ghana, Kenya and Malawi to further assess the feasibility, safety and impact of delivering the vaccine to children in the target population *(4)*. Two years later, WHO recommended a second vaccine, R21/Matrix-M (R21), based on pre-clinical and clinical trial data showing a good safety and efficacy profile *(5)*. With these advances, there has been unprecedented demand for the malaria vaccine. At least 30 countries in Africa plan to introduce the malaria vaccine as part of their national malaria control plan, and wider roll-out beyond the pilot countries started in 2024 *(6)*. It is estimated that malaria vaccine introduction could result in an additional half a million lives saved over the next 12 years. A Malaria Vaccine Coordination Team (MVCT) was established to advise and assist in defining the conditions for successful implementation of the malaria vaccine. The MVCT, co-chaired by WHO and Gavi, the Vaccine Alliance, consists of representatives from the United Nations Children's Fund (UNICEF), The Global Fund to Fight AIDS, Tuberculosis and Malaria, United States Agency for International Development/United States Centers for Disease Control and Prevention, World Bank, PATH, Clinton Health Access Initiative, Africa Centres for Disease Control and Prevention, and Bill & Melinda Gates Foundation.

As a means to guide the introduction and scale-up of the malaria vaccine, WHO, Gavi and the MVCT, identified the need to develop a research agenda to inform implementation. The research agenda aims to facilitate a more coordinated approach across funders and partners to address key knowledge gaps and information needs identified by countries taking up the vaccine. The agenda builds upon existing research and other ongoing research efforts for RTS,S and R21. This report describes the scope and objectives of the agenda, the process and methods used for developing the research agenda, the key findings from the consultation process and the final ranked list of research topics.

Research agenda development process

The research agenda was developed using a mixed methods approach consisting of a document review and a consultation process with key stakeholders from national immunization and malaria control programmes, civil society organizations, global and regional bodies, research institutions, and technical partners working in malaria or immunization programming, policy and/or research. A technical advisory committee (TAC) was established to provide

input to WHO on the design of the stakeholder consultation and the outcomes of the research prioritization process. Stakeholders were engaged to provide input into the research agenda through a mix of in-depth interviews, online surveys and virtual engagement sessions. The scope of the research agenda encompassed six key thematic areas: (i) safety of the vaccine, (ii) implementation feasibility, (iii) acceptability of and demand creation for the vaccine, (iv) integration of the vaccine with other health interventions, (v) impact and effectiveness of the vaccine, and (vi) economics, costing and cost-effectiveness of the vaccine.

In total, 132 stakeholders provided input to define the agenda. Research topics identified through the consultation process were subsequently ranked by stakeholders according to the following criteria: (i) broad relevance of the topic across malaria-endemic settings; (ii) urgency of addressing the topic to inform vaccine roll-out and scale-up; and (iii) feasibility of undertaking the research. Scores were calculated for each research topic based on the stakeholder rankings across the three criteria.

Findings

During the consultation process, stakeholders highlighted several operational challenges anticipated in the deployment of the vaccine, and pertinent knowledge gaps to address to help guide effective roll-out. Taking these challenges and knowledge gaps into consideration, 32 research topics emerged. WHO and Gavi reviewed and further refined the preliminary list of topics, which resulted in a final list of 28 topics. The breakdown of topics by thematic area was as follows: safety (three topics), implementation feasibility (eight topics), acceptability of and demand creation for the vaccine (two topics), integration of the vaccine with other health interventions (five topics), impact and effectiveness of the vaccine (seven topics), and economics, costing and cost-effectiveness (three topics). Topics on the agenda mainly focused on aspects related to the optimal delivery strategy (e.g., age-based or seasonal administration) or delivery platform (e.g., routine immunization, campaign) for the vaccine; safety, feasibility and effectiveness of using RTS,S and R21 in the same dosing schedule; co-deployment of the vaccine with other health interventions and the broader health system impacts from the roll-out of the vaccine; effective strategies to strengthen key components of the health system required for effective vaccine delivery; effectiveness of the vaccines over time and in different settings; and the economic impact of the vaccine and costs associated with different delivery approaches.

Conclusion

This research agenda development process engaged a broad group of malaria and immunization stakeholders to develop a prioritized list of 28 topics that are important for guiding the roll-out and scale-up of malaria vaccines. This research agenda is timely, given that many countries have already begun or will begin to introduce malaria vaccines in 2024 and 2025. Research questions related to implementation feasibility and vaccine acceptability may be particularly urgent to guide national programmes with plans to introduce the vaccine in the next several years. As malaria vaccine programmes mature, addressing knowledge gaps related to impact, effectiveness, economics and cost is expected to become increasingly important to guide scale-up, but may require longer evaluation timelines. A number of research priorities identified extend beyond malaria vaccines to encompass broader health system challenges, including pharmacovigilance, monitoring of vaccine coverage, supply and cold chain logistics, and health worker training, which can also help to inform other childhood immunization programmes.

The priority research list should be used to inform future investment decisions in malaria vaccine operational and implementation research. As ongoing and new research is completed, it will be critical to ensure timely and targeted dissemination of the evidence to key stakeholders supporting the introduction and roll-out of the vaccine in order to facilitate the uptake of the findings to guide programming. Given the rapid pace at which the malaria vaccine landscape is changing, it will be important to track progress against this agenda and review it periodically to ensure its continued relevance and to capture new topics that may emerge.

Malaria vaccine vials, amongst other vaccination vials, stored in a container to remain cold in rural Lilongwe, Malawi.

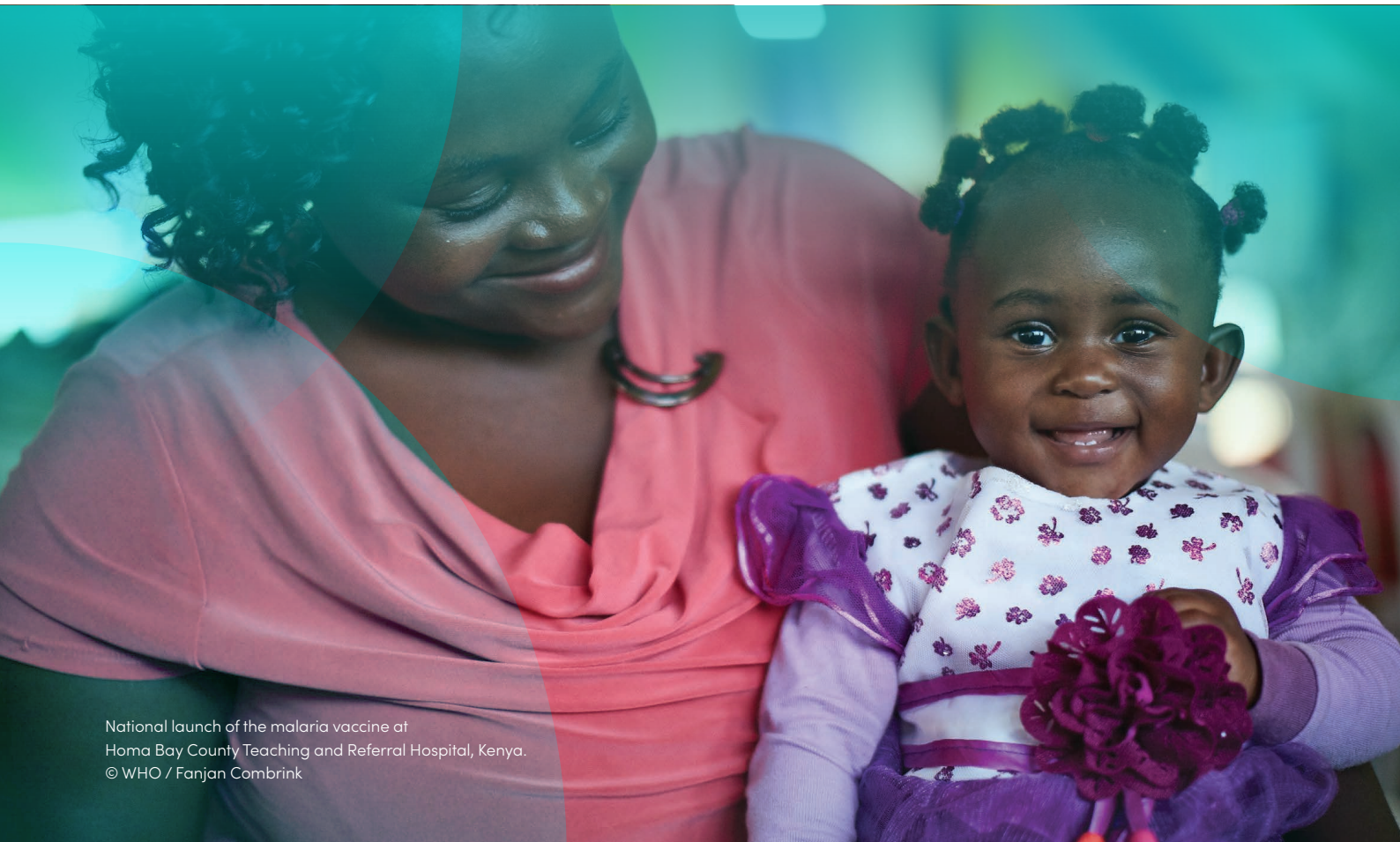
1 Background

The World Health Organization (WHO) recommends the use of malaria vaccines for the prevention of *Plasmodium falciparum* malaria in children living in malaria-endemic areas, prioritizing areas with moderate and high malaria transmission *(4, 5)*. There are two WHO-prequalified malaria vaccines: RTS,S/AS01 (RTS,S) and R21/Matrix-M (R21), which are similar with regards to vaccine construct, indication for use and administration. RTS,S was prequalified in July 2022 and R21 was subsequently prequalified in December 2023. Both vaccines have been evaluated in multi-centre phase 3 clinical trials. In addition, the introduction of RTS,S provided through routine immunization programmes was evaluated in large subnational pilot implementations in Ghana, Kenya and Malawi from 2019 through 2023 as part of the Malaria Vaccine Implementation Programme (MVIP). The recommendation for the malaria vaccine is the result of decades of research to develop a safe and effective vaccine. In addition to RTS,S and R21, a number of malaria vaccine candidates with different vaccine constructs and antigens are currently in the pipeline at various stages of clinical development *(7)*.

More than 30 malaria-affected countries have expressed interest in introducing the approved malaria vaccines, and Gavi, the Vaccine Alliance, has approved support for the introduction of the vaccine in over 20 countries as of December 2024. In 2022, Gavi and WHO established a Malaria Vaccine Coordination Team (MVCT) to advise and assist in defining the conditions for successful implementation of the malaria vaccine per Gavi's mission. To help guide the introduction and scale-up of the malaria vaccine, WHO, Gavi and the MVCT identified the need to develop a malaria vaccine research agenda to inform implementation. The overarching aim for the development of the agenda was to facilitate a more coordinated approach across funders and research and implementation partners to address key knowledge gaps and information needs identified by countries taking up the malaria vaccine in order to enable a more effective and efficient roll-out of the vaccine.

To develop the research agenda, a broad and inclusive stakeholder consultation process was conducted with five key groups: (i) national immunization and malaria programmes, (ii) research institutions, (iii) civil society organizations (CSOs), (iv) global and regional bodies, and (v) other technical experts in immunization and malaria programming and research. Stakeholders were engaged to provide their perspectives on key operational challenges in the deployment of the vaccine, existing knowledge gaps, and priority implementation and operational research questions to address the identified challenges and gaps. A technical advisory committee (TAC) was established to provide input into the design and implementation of the process. The agenda was developed with the intention of building upon existing research and lessons learned from the MVIP and other recent and ongoing research efforts for RTS,S and R21 *(8)*. Given the quickly changing malaria vaccine landscape, the intention is to periodically review and update the research agenda.

The consultation process and identification of research topics was guided by a protocol detailing the objective, scope and approach to developing the malaria vaccine research agenda *(9)*. This report summarizes the process and methods used for developing the research agenda, discusses the key audiences and intended uses of the agenda, presents the key findings from the consultation process and the final ranked list of research topics, and concludes with a summary of the key themes that emerged from the agenda and consultation process.



National launch of the malaria vaccine at
Homa Bay County Teaching and Referral Hospital, Kenya.
© WHO / Fanjan Combrink

Grace carries her daughter Beauty home from a health facility in rural Lilongwe, Malawi after Beauty received her 3rd dose of the malaria vaccine.

2 Malaria vaccine implementation research agenda objectives and scope

2.1 Objective

The main objective of this process was to develop a research agenda that identifies and serves to address key operational challenges and knowledge gaps as they pertain to the design, implementation and scale-up of the malaria vaccine. The final agenda is intended to serve as a global resource that can facilitate a more coordinated and efficient approach to address the identified priority research areas.

The research agenda development process was designed to be inclusive and widely consultative. It was informed by substantive input from malaria-affected country perspectives through the participation of representatives of government ministries (e.g., Expanded Programme on Immunization (EPI), national malaria programmes (NMPs)), research institutions in malaria-affected countries, and other in-country partners and stakeholders, including CSOs.

2.2 Scope of research agenda

The scope of the research agenda includes implementation and operational research questions related to the deployment of malaria vaccines, organized according to the following broad themes: (i) safety, (ii) implementation feasibility, (iii) acceptability of and demand creation for the vaccine, (iv) integration of the malaria vaccine with other health interventions, (v) impact and effectiveness of the vaccine, and (vi) economics, costing and cost-effectiveness of the vaccine. Table 1 provides a description of the thematic areas, with examples of the topics or subthemes classified under each respective area.

The research agenda focuses on the evidence needed to develop improved and more detailed policies, strategies and implementation guidance for malaria vaccines at the national or subnational level that may complement broader WHO policy and guidance documents. By

engaging stakeholders across multiple countries affected by malaria, the activity aimed to identify research that can provide evidence to inform multiple national governments' strategies, policies and implementation guidelines, and the global malaria and immunization communities more broadly.

The geographical scope of the research agenda focused on Gavi-eligible countries in sub-Saharan Africa with moderate and high transmission of *P. falciparum* malaria. Countries that had been approved for the first round of Gavi funding for the malaria vaccine were prioritized for inclusion in the consultations, given their experiences with the pilot implementation or initial preparations for the introduction of the vaccine.

Table 1. Thematic areas for the research agenda

THEMATIC AREA	DEFINITION
Safety	Encompasses aspects related to the safety of the vaccine, such as national regulation and vaccine registration, monitoring of adverse events following immunization, safety of the vaccine in vulnerable populations, safety of different dosing schedules, and the safe deployment and co-administration of the malaria vaccine with other vaccines or drugs
Implementation feasibility	Encompasses aspects related to the overall feasibility of implementation of a malaria vaccine programme, such as the vaccine's delivery strategy or platform (including leveraging existing delivery platforms for other health interventions), dosing regimen and schedule, equitable coverage of the vaccine, supply chain considerations, demand forecasting, processes/systems related to loss to follow-up for each vaccine dose and missed opportunities for vaccination, subnational implementation, expansion or scale-up planning, human resources planning and capacity/training to support implementation of the vaccine, and strategies and approaches for the delivery of the vaccine in humanitarian or conflict settings

THEMATIC AREA	DEFINITION
Acceptability of and demand creation for the vaccine	Encompasses aspects related to the perception and acceptability of the vaccine among the target populations, health care workers and community members, as well as strategies that influence adoption/uptake, including effective health communication, social and behaviour change, community engagement, and social mobilization approaches or interventions in different settings, including hard-to-reach populations
Integration of the vaccine with other health interventions	Encompasses aspects related to synergies and/or constraints in deploying or co-administering the malaria vaccines with other health interventions, including other malaria interventions (chemoprevention, insecticide-treated nets (ITNs), indoor residual spraying (IRS), etc.), non-malaria vaccines, additional malaria vaccines (e.g., acceptability and feasibility of concurrent availability of multiple products, country product preferences, interchangeability of multiple products in a schedule), and broader health system impacts (benefits and costs) of the deployment of the vaccine (e.g., benefits and costs of delivering the vaccine during the child's second year of life)
Impact and effectiveness of the vaccine	Encompasses the overall effectiveness of the vaccine (including the added value of a fourth dose and the potential for malaria rebound[1]), impact of the vaccine on malaria burden and all-cause mortality (directly measured or modelled), and the impact of the malaria vaccine on antimalarial resistance and vaccine escape/resistance
Economics, costing and cost-effectiveness of the vaccine	Encompasses aspects related to the broader economics, costing and cost-effectiveness of the vaccine, such as the long-term financial implications of the vaccine, the economic impact in terms of costs averted with the implementation of the vaccine, cost-effectiveness of the malaria vaccine as part of a package of interventions, societal perspectives on cost-effectiveness, and changes in the cost-effectiveness of the vaccine as vaccine costs change or malaria transmission within a country or setting declines

1 Malaria rebound can be defined as a period of increased malaria risk after time-limited protection from malaria (e.g., after chemoprevention, vaccination or vector control), relative to individuals of the same age from the same population who did not receive the intervention *(10)*.

9-month-old Favor Ruth waiting for her mother at the Chemelil Gok Health Centre in western Kenya, where the malaria vaccine was being administered as part of the Malaria Vaccine Implementation Programme.

3 Methodology for development of the research agenda

The research agenda was developed using a mixed methods approach consisting of a document review and a consultation process with key stakeholder groups who served as key informants for identifying and prioritizing topics for the research agenda *(9)*. Individuals from the following five key stakeholder groups were initially mapped and engaged to provide input into the process:

- **government representatives** from malaria-affected countries in sub-Saharan Africa, serving within the national EPI or NMP;
- **CSOs** working in community health, malaria and/or immunization;
- **regional and global bodies** that support vaccine policy and implementation guidelines and/or provide technical support to ministries of health in preparing for the introduction of the malaria vaccine, such as WHO, UNICEF, Gavi, International Federation of Red Cross and Red Crescent Societies (IFRC), and Africa Centres for Disease Control and Prevention;
- **research institutions** that have been engaged in malaria vaccine-related research or the MVIP, or that have substantial experience in implementation research for other non-malaria vaccines;
- **technical partners** working in or providing support to vaccine programming and vaccine operational or implementation research.

This section summarizes the key steps in the process for developing the agenda. Further details on the methodology and process can be found in the detailed protocol *(9)*. Fig. 1 illustrates the five-step process used to develop the research agenda.

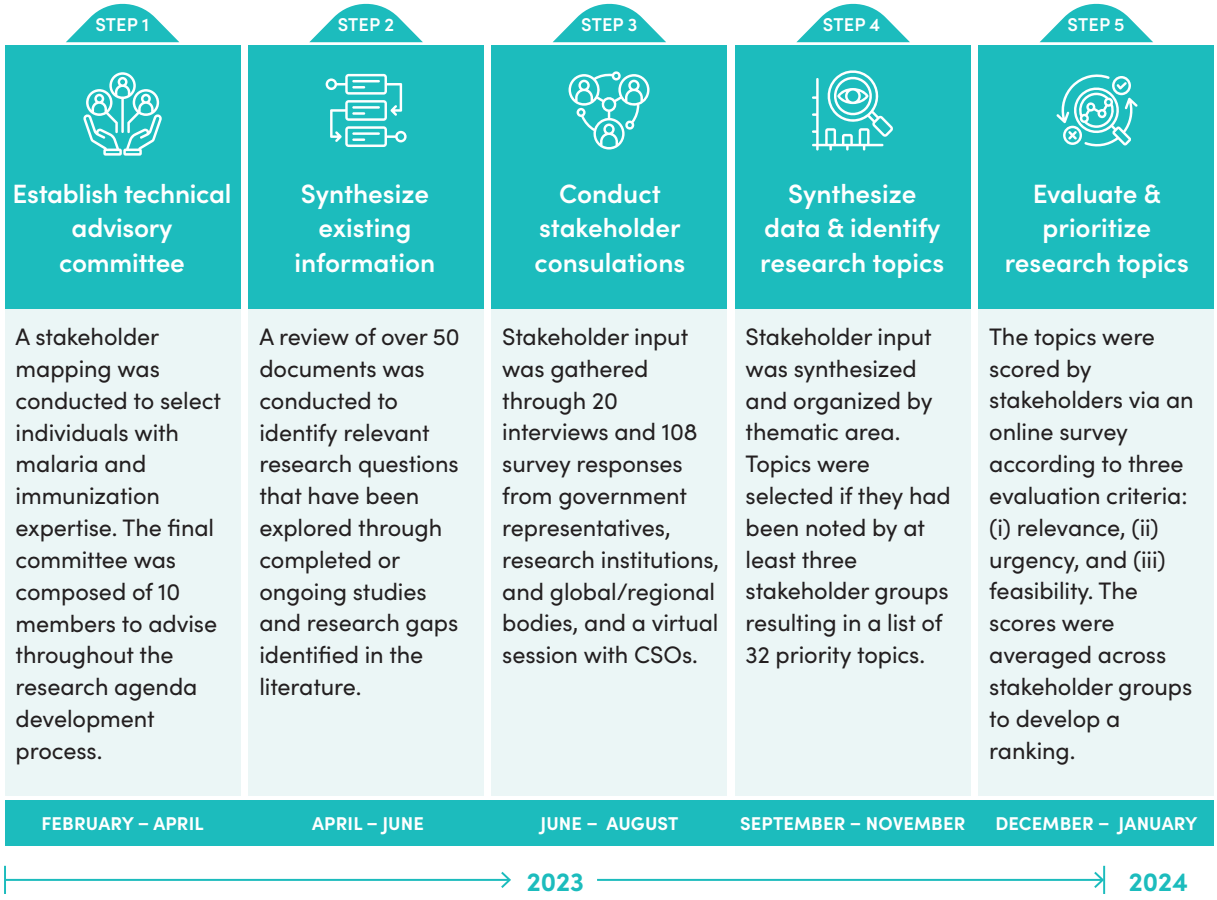


Fig. 1. Summary of the approach for developing the malaria vaccine implementation research agenda

3.1 Step 1: Establish Technical Advisory Committee

The TAC was established to support the development of the research agenda. To form the TAC, a stakeholder mapping was conducted to identify malaria and immunization experts with background in the areas of operational and implementation research, evidence synthesis, programme implementation or programme leadership, and stakeholders from research and government institutions and other global and regional bodies. Ten members were selected to serve on the committee; the selection of committee members was done to ensure diversity by member background and demographics, including geography and gender, technical or subject matter area of expertise, and institutional representation. The full list of TAC members is available in Annex 1. The TAC was convened four times throughout the development of the research agenda to advise on and provide input to the protocol and stakeholder mapping; review and refine the preliminary list of research topics to go through the ranking process; and to support the finalization of the ranked list of topics.

3.2 Step 2: Synthesize existing information

In step 2, a document review was conducted to identify relevant research questions that have been explored through completed or ongoing studies and research gaps highlighted in the literature. The scope of the document review was guided by the thematic areas defined for the research agenda and limited to documents published between 2015 and 2023. Over 50 documents were reviewed, including published and grey literature, programme documents, research databases, meeting reports, and requests for proposals or award notices (see Annex 2 for a full list of documents). The information extracted from the document review was organized into the key thematic areas to illustrate what research has been completed or is ongoing, as well as what knowledge gaps have been identified. Insights from the review were summarized in a report and used to inform the refinement of the interview guides for the stakeholder consultations. Identified research gaps from the review were also synthesized with the inputs gathered from the stakeholder consultations in Step 3 to establish priority knowledge gaps.

3.3 Step 3: Conduct stakeholder consultations

Stakeholder input was captured through a mix of interviews, online surveys and a virtual engagement session. A stakeholder mapping was conducted initially to identify relevant stakeholders to engage in the consultation process across the five stakeholder groups. Interviews were conducted with government representatives from ministries of health and NMPs, research institutions, and global and regional organizations, such as the WHO Regional Office for Africa, Gavi and UNICEF, using a structured interview guide. The aim of the interviews was to gather stakeholder perspectives on implementation challenges and barriers experienced or anticipated in introducing the malaria vaccine, pertinent knowledge gaps, and priority implementation and operational research questions to inform the introduction and roll-out of the vaccine. Participants were purposively selected based on their direct experience with malaria vaccine introduction and/or research, and to ensure diversity across geographical areas and malaria transmission settings. Interviews were conducted via Zoom and audio-recorded if consent was provided, and notes were taken. Interviews lasted approximately one hour and were conducted in both English and French. A total of 20 interviews were conducted with stakeholders across the three targeted stakeholder groups. Table 2 summarizes the interviews completed across the stakeholder groups.

Table 2. Stakeholder consultations completed

STAKEHOLDER GROUP	INSTITUTIONS REPRESENTED	# OF INTERVIEWS CONDUCTED
Government representatives	Benin (NMP), Burkina Faso (EPI), Ghana (NMP), Kenya (EPI), Sierra Leone (NMP), South Sudan (EPI and NMP), Uganda (EPI)	7
Research institutions	Faculty of Health Sciences at University of Abomey-Calavi, Benin; Research Institute of Health Sciences, Burkina Faso; Kenya Medical Research Institute; Manhiça Health Research Centre/Farmacias de Mozambique; Noguchi Memorial Institute for Medical Research at University of Ghana; University of Health and Allied Sciences, Ghana; Kamuzu University of Health Sciences, Malawi; University of Sciences, Techniques, and Technologies and Malaria Research and Training Center, Mali	8
Global and regional bodies	Gavi, IFRC, UNICEF, WHO Regional Office for Africa, WHO Global Malaria Programme, WHO Immunization, Vaccines and Biologicals	5
Total		20 interviews

To complement the interviews, an online survey was sent to an additional 117 stakeholders who were identified through the stakeholder mapping to gather similar information on anticipated challenges and barriers, knowledge gaps, and research priorities. A total of 53 stakeholders responded to the survey. A separate tailored survey was sent out to members of CSOs. CSOs that were part of the Civil Society for Malaria Elimination and the Amref Health Africa networks were targeted as part of the consultation. In total, 55 CSO members across the two CSO networks completed the survey. Finally, a virtual engagement session was held with the CSOs to present synthesized survey findings and get additional feedback.

3.4 Step 4: Synthesize data and identify research topics

The data from the interviews, online survey and CSO engagement session were synthesized and organized across the three main areas of inquiry – operational barriers and challenges, knowledge gaps, and priority research questions – and by thematic area. Within each thematic

area, subthemes were identified. Emergent themes were drawn out around operational barriers and challenges and knowledge gaps, and synthesized by thematic area and subtheme. Research topics were included in the preliminary list of priority research topics if they were noted by at least three stakeholders. Research gaps and priority research questions identified through the document review were also included if they were referenced by at least two stakeholder groups from the consultation process. The preliminary research topics were reviewed by the TAC, WHO and Gavi for clarity, specificity and alignment with the thematic areas. The aim was to determine priority knowledge gaps and research questions to help guide effective malaria vaccine implementation. A total of 32 topics across the six thematic areas were identified through the stakeholder consultations and document review.

3.5 Step 5: Evaluate and prioritize research topics

An online survey was created for stakeholders and TAC members to score the priority research topics according to three key criteria: (i) relevance of the topic across multiple country settings; (ii) urgency of addressing the topic to inform the vaccine introduction and roll-out; and (iii) feasibility of carrying out a research study to address the topic (taking into account the methodology, budget, time required and ethical considerations). All stakeholders who were initially identified during the stakeholder mapping were invited to participate in the scoring of the topics through the online survey. In total, 94 stakeholders participated in the online survey, of which 21 were government representatives, 17 from CSOs, 19 from global and regional bodies, 26 from research institutions, and 11 from technical partners.

Participants were asked to score each topic against the three criteria using a five-point Likert scale. Scores were assigned to the responses (e.g., "strongly agree" received five points, whereas "strongly disagree" received one point). For each topic, a score was calculated for each criteria by summing the total scores received and dividing by the total possible score. To calculate the overall score for a topic, an average was taken across the scores for the three criteria. The summed scores were then used to rank the research topics from highest to lowest priority, overall, and within the six thematic areas. Scores were also calculated for the research topics within each of the five stakeholder groups to identify any differences in the rankings across the groups. The TAC was convened to review the ranking scores and provide suggestions for how best to present the overall agenda to the broader immunization and malaria community.

The 32 research topics that emerged from the stakeholder consultation process were then further refined by WHO and Gavi as part of an effort to keep the list up to date and relevant, informed by updates to ongoing research studies taking place during or after the stakeholder consultation process. The result of this process was 28 research topics across the six thematic areas.

A health worker fills a syringe from a malaria vaccine vial at Kawale health center in rural Lilongwe, Malawi. The centre provides malaria vaccinations to young children as part of routine childhood vaccinations.

4 Findings

4.1 Overview

The main findings from the stakeholder consultations are summarized in this section across the three central themes covered: (i) operational challenges and barriers experienced or anticipated in the roll-out of the vaccine; (ii) pertinent knowledge gaps identified; and (iii) a prioritized list of implementation and operational research questions from the consultation process. During the consultations, stakeholders were first asked to reflect on what they perceived to be key operational barriers and knowledge gaps related to the introduction of the malaria vaccine. Subsequently, they were asked to prioritize what they saw as the priority research questions, reflecting on what they had previously identified as key barriers and knowledge gaps. The operational challenges/barriers and knowledge gaps identified by stakeholders were then synthesized into emergent themes and cross-walked with the identified priority research questions to help inform and refine the topics.

4.2 Operational challenges and barriers

Stakeholders were asked to discuss the operational challenges and barriers that were experienced in the initial roll-out of the vaccine in countries that had already piloted the vaccine, or to provide their perspectives on the key challenges and barriers anticipated when the malaria vaccine is introduced in their country or more broadly based on the country's previous experience with other vaccine introductions. Table 3 summarizes the commonly reported challenges highlighted in the consultations. The full list of operational challenges reported in the consultations is provided in Annex 3.

Key challenges highlighted by stakeholders related to safety included lack of robust systems to monitor adverse events following immunization or to monitor risk of rebound over time. Implementation feasibility issues commonly noted were challenges with delivering additional doses outside of routine schedules, ensuring completion of the four-dose vaccine regimen, maintaining vaccine cold chains, training health workers, coordination across programmes, and reaching vulnerable groups in areas with poor health care access. Addressing vaccine hesitancy and sustaining strong advocacy and community sensitization efforts over time were also highlighted as common challenges. Lastly, ensuring government commitment to co-financing of the vaccine was also identified as a challenge facing country malaria vaccine programmes.

Table 3. Summary table of common challenges and barriers

THEMATIC AREA	SUBTHEME	CHALLENGE OR BARRIER
Safety	**Monitoring of adverse events**	Challenges with monitoring adverse events in the context of less robust systems and limited funding
		Monitoring for waning immunity or malaria rebound[1] over time as vaccine protection decreases
Implementation feasibility	**Delivery strategy/ platform**	Challenges with delivering vaccine doses outside of the routine EPI schedule
	Dosing regimen/ schedule	Challenges with lower uptake/coverage of the fourth dose of the vaccine when delivered in the second year of life
	Supply chain	Challenges with cold chain and storage for outreach deployment; some facilities lack a fully functioning cold chain
	Human resources planning/capacity	Inadequate training and re-training of staff before and after vaccine introduction
	Coordination/ integration	Collaboration/integration of vaccine programme across different government implementing programmes/departments, including having clearly defined roles for different programmes and levels (national, subnational)

THEMATIC AREA	SUBTHEME	CHALLENGE OR BARRIER
Implementation feasibility (continued)	**Equitable coverage of the vaccine**	Challenges with achieving easy and equitable access to all vaccine doses for the most at-risk populations, particularly in areas with poor access to childhood immunization services
		Challenges with funding and transport to provide outreach/mobile vaccination centres in hard-to-reach areas
Acceptability of and demand creation for malaria vaccines	**Perception and acceptability of the vaccine among the target populations, health care workers and community members**	Vaccine hesitancy due to the high number of doses required, misinformation and mistrust among the target population, particularly in countries where there was resistance to coronavirus disease (COVID-19) vaccination
	Strategies that influence adoption/ uptake, including effective health communication, social and behaviour change, community engagement, and social mobilization approaches or interventions in different settings	Advocacy/community sensitization around the need to continue use of other malaria interventions
Economics, costing and cost-effectiveness of the vaccine	**Economics/costing of the vaccine**	Government ownership and commitment to co-financing for the vaccine

4.3 Knowledge gaps

Stakeholders were asked to reflect on pertinent knowledge gaps for which research or guidance would be useful to inform the introduction and broader roll-out of the vaccine. Table 4 summarizes the more commonly reported gaps highlighted in the consultations (noted by more than one stakeholder group). The full list of knowledge gaps noted in the consultations is provided in Annex 4.

Several gaps were identified under the thematic area of implementation feasibility and speak to the need for better understanding and guidance on how to target and deploy the vaccine subnationally, what human resources and training are required, and how best to leverage partnerships and other sectors to support the delivery of the vaccine. In addition, stakeholders noted the need for a framework or guidance specifically for strategic communication and community engagement that countries can use to plan for vaccine sensitization efforts, a better breakdown or understanding of the full costs of vaccine delivery, and guidance on effective strategies for delivering the vaccine in hard-to-reach areas. They also highlighted the need to address information gaps related to safety of the vaccine in vulnerable populations, how to ensure that surveillance systems can be strengthened to enable the monitoring of vaccine effectiveness over time, and how missed doses or delayed delivery of the vaccine impacts the overall effectiveness of the vaccine.

Table 4. Summary table of knowledge gaps

THEMATIC AREA	SUBTHEME	KNOWLEDGE GAP
Safety	**Safe deployment among vulnerable populations**	Safety of the malaria vaccine in vulnerable populations (e.g., individuals with pre-existing conditions) and measures to prevent harm
Implementation feasibility	**Subnational implementation**	Framework or guidance for how to target and deploy the vaccine subnationally
	Human resources planning and capacity	National government or ministry of health capacity and resources needed to lead the introduction and roll-out of the malaria vaccine
		Understanding whether the current human resources capacity in country is adequate to accommodate the addition of the malaria vaccine and information on what the workload will be for health care workers at the different levels of the system to support the delivery of the vaccine
		Understanding the core competencies and training required for health worker cadres to deliver the malaria vaccine
	Coordination and integration of the vaccine programme across government agencies and partners	Information on how best to leverage partnerships and collaboration across sectors and with the private sector to support implementation of the vaccine
	Equitable coverage of the vaccine	Understanding the best delivery strategies for the vaccine in hard-to-reach areas/populations, particularly for the fourth dose of the vaccine

THEMATIC AREA	SUBTHEME	KNOWLEDGE GAP
Acceptability of and demand creation for the vaccine	**Strategies that influence adoption/uptake, including effective health communication, social and behaviour change, community engagement, and social mobilization approaches or interventions in different settings**	Framework for strategic communication and community engagement on vaccine safety, efficacy and benefits to promote vaccine demand, with guidance on tailoring communication to specific contexts and target groups
Impact and effectiveness of the vaccine	**Effectiveness of the malaria vaccine**	Guidance on effective surveillance systems for monitoring vaccine effectiveness and identifying the potential for increased malaria risk after vaccine protection wanes
		Understanding how delayed or missed doses affect the effectiveness of the vaccine
Economics, costing and cost-effectiveness of the vaccine	**Economics/costing of the vaccine**	Understanding the costs of producing and distributing the vaccine and how best to manage those costs

4.4 Malaria vaccine implementation research priorities

In total, 28 research topics were identified through the research priority setting process (see Table 5). The original list of 32 topics that emerged from the stakeholder consultation process is included in Annex 5. The breakdown of the topics by thematic area is as follows: safety (three topics), implementation feasibility (eight topics), acceptability of and demand creation for the vaccine (two topics), integration of the vaccine with other health interventions (five topics), impact and effectiveness of the vaccine (seven topics), and economics, costing and cost-effectiveness of the vaccine (three topics). The overall evaluation scores across the topics ranged from 68.0 to 88.3, with 16 topics receiving an overall score of 80 or higher (Annex 5). The relatively small range in the scores indicates that stakeholders perceived most topics to be of broad relevance, an important priority to inform the roll-out of the vaccine, and feasible to undertake. Overall, the scores and rankings of the topics across the different stakeholder groups did not vary substantially and showed good consensus across the five groups. Only slight differences in rankings were observed across the groups, mainly within the thematic area related to integrating the vaccine with other health interventions. Through consultation with WHO, Gavi and the TAC, it was decided not to present the final list of topics ranked by their evaluation scores due to the overall high scores and relatively narrow range in scores.

Eunice brings her 1-year-old daughter Scovia to receive the malaria vaccine at the Chemelil Gok Health Centre in western Kenya.
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The topics covered in the research agenda are mainly focused across the following themes:

- exploring the safety, feasibility and effectiveness of using RTS,S and R21 in the same dosing schedule;
- addressing several delivery-related questions, including how best to deliver the vaccine in seasonal settings, and strategies for how to optimize coverage of the vaccine, particularly for doses delivered in the second year of life and among vulnerable and hard-to-reach populations;
- gaining better understanding of the acceptability of the vaccine among caregivers, community members and health care workers, and how acceptability may change over time, as well as effective community engagement and social and behaviour change strategies or interventions to promote vaccine uptake;
- assessing co-deployment of the vaccine with malaria and other health interventions, as well as understanding any broader health system impacts from the roll-out and scale-up of the vaccine;
- identifying effective strategies to strengthen key components of the health system required for effective vaccine delivery, including information systems for monitoring adverse events and vaccine coverage and effectiveness, supply chain and logistics, cold chain management, and health worker training and supervision;
- assessing the level and duration of vaccine effectiveness when delivered in different settings, dosing schedules and populations not currently targeted for the vaccine;
- measuring the economic impact of the vaccine and assessing the costs associated with different delivery approaches.

The final list of malaria vaccine implementation research priorities included in Table 5 were identified through the stakeholder consultation process and then further refined by WHO to reflect the latest available evidence related to the topics.

Table 5. Final list of malaria vaccine implementation research priorities

During the refinement process, WHO reviewed and summarized the evidence available on the identified research priorities. Topics that have been sufficiently addressed with available evidence (and are therefore no longer considered to be high-priority research topics) have been written in grey font and denoted by an asterisk (*). Topics that have been partially addressed, such that evidence is available but important questions remain, have been written in black font and denoted by an asterisk (*). The evidence available for topics denoted by an asterisk is summarized in Annex 6. Research questions that apply to multiple thematic areas are repeated under each relevant heading.

RESEARCH TOPICS
Safety
▸▸ Explore the safety of using RTS,S and R21 vaccines in the same dosing schedule (e.g., interchangeability of the two vaccines).
▸▸ Identify and evaluate approaches to strengthen key components of the pharmacovigilance system during the introduction and scale-up of vaccines.
▸▸ Assess the safety of the co-administration of the malaria vaccine with other relevant childhood vaccines (e.g., measles, pentavalent vaccines (DTP-HepB-Hib), rotavirus, and pneumococcal conjugate vaccines).[2]*
Implementation feasibility
▸▸ Explore the feasibility of using RTS,S and R21 vaccines in the same dosing schedule (e.g., interchangeability of the two vaccines).
▸▸ Assess (through quantitative and qualitative methods) different schedules for malaria vaccine delivery to achieve the highest coverage in perennial and seasonal settings, including additional doses beyond the first three doses.
▸▸ Assess feasibility and coverage achieved through different delivery approaches.
▸▸ Identify and evaluate effective strategies for ensuring equitable access to the vaccine among hard-to-reach and vulnerable populations, including conflict, humanitarian, urban poor or slum settings.

2 Data are available for RTS,S on the co-administration with these common childhood vaccines and studies are currently under way for R21.

RESEARCH TOPICS

Implementation feasibility (continued)

- Identify and evaluate strategies to improve uptake of malaria vaccines during the second year of life, such as aligning the delivery of the malaria vaccine with other childhood interventions (e.g., vitamin A, deworming, growth monitoring, ITNs, seasonal malaria chemoprevention (SMC) or perennial malaria chemoprevention (PMC)) and methods for improving service utilization (e.g., child care centre- or school-based vaccination, Periodic Intensification of Routine Immunization, other extended outreach, defaulter tracing systems).
- Evaluate approaches to improve the collection and reporting of vaccine coverage data in routine surveillance systems to inform programmatic decision-making.
- Identify and evaluate strategies to strengthen the existing supply chain, cold chain and logistics systems during the introduction and scale-up of vaccines.
- Evaluate approaches to optimize training, re-training and supervision of health service managers and health care workers to deliver malaria vaccines according to recommended guidelines.

Acceptability of and demand creation for the vaccine

- Evaluate social and behaviour change and community engagement strategies to address challenges with vaccine acceptability and demand.[3*]
- Assess how community, caregiver and health worker perception, acceptance and uptake of the vaccine change over time, considering factors such as the partial protection of the vaccine, the four-dose schedule and availability of other malaria interventions.[3*]

3 A large longitudinal qualitative study was conducted in Ghana, Kenya and Malawi assessing social and behaviour change and community engagement strategies and community, caregiver and health worker perceptions. These findings have been published and presented in different forums, and therefore are not listed as outstanding priority research questions. Such questions, however, are context-specific, and additional studies in different settings and contexts would be beneficial.

RESEARCH TOPICS

Integration of the vaccine with other health interventions

- Evaluate the combined impact of malaria vaccination with other malaria control interventions in perennial and seasonal transmission areas and in other important settings (e.g., emergency and hard-to-reach settings).[4]*
- Assess the feasibility, acceptability and coverage of different models of combining or linking the vaccine with SMC or PMC delivery (co-administration, parallel administration or sequential administration).
- Assess strategies to leverage malaria vaccine visits to increase uptake of other child health interventions (e.g., delivery of other vaccines, vitamin A supplementation, deworming, promotion of ITN use).
- Evaluate the effectiveness and impact of leveraging the four-dose malaria vaccine schedule to deliver catch-up doses and reach zero-dose children for routine EPI vaccines.[5]*
- Monitor the impact of malaria vaccination on coverage and use of other EPI vaccines and malaria interventions.[6]*

4 Evidence is available on the impact of the malaria vaccine combined with ITNs and case management and the combination of seasonal vaccination and SMC, and an ongoing study is exploring the co-deployment of RTS,S and PMC. Outstanding questions remain on the effectiveness when vaccination is provided with PMC or SMC, or with other interventions in emergency or hard-to-reach settings.

5 This research question has been partially addressed in Ghana, Kenya and Malawi, where a minimal increase in catch-up doses was measured with the introduction of the malaria vaccine. Too few zero-dose children were identified in the survey population to assess the potential to reach zero-dose children. Developing and assessing innovations to fully utilize the additional vaccine visits to increase catch-up and to reach zero-dose children remains a priority research question.

6 Impact of malaria vaccination on the coverage and use of other EPI vaccines and malaria interventions was assessed in serial household surveys conducted in Ghana, Kenya and Malawi. In each country, no impact of vaccination was observed on the coverage and use of EPI vaccines or other malaria interventions. This is therefore not listed as an outstanding priority research question.

RESEARCH TOPICS

Impact and effectiveness of the vaccine

- Assess the effectiveness of using RTS,S and R21 vaccines in the same dosing schedule (e.g., interchangeability of the two vaccines).
- Monitor coverage as a key driver of the impact of the malaria vaccine under programmatic conditions in different settings (e.g., hard-to-reach areas, humanitarian or conflict settings, varying levels of health system functioning or strength).
- Measure R21 vaccine effectiveness following three vs. four doses.[7]
- Assess the level and duration of vaccine effectiveness following the fourth dose and additional annual doses in areas of seasonal or perennial transmission.[8]*
- Measure the efficacy of the vaccine in populations not currently targeted for the vaccine, specifically school-aged children.
- Evaluate the impact of the malaria vaccine on the broader health system (e.g., reduction in outpatient visits, inpatient visits[9]* for malaria, health care costs).
- Measure the impact of the vaccine in routine use across different delivery approaches (e.g., age-based vs. seasonal delivery)[10]* and contexts (e.g., areas with low EPI coverage or that are hard to reach).

7 In the R21 phase 3 trial, the protocol was to provide four doses to all participants in the R21 study arm; the efficacy of a three-dose vs. four-dose schedule was not evaluated.

8 The efficacy of RTS,S up to dose 7 has been studied in a seasonal vaccination schedule in Burkina Faso and Mali, but has only been evaluated in an age-based vaccination schedule up to dose 4. The efficacy of a fifth and sixth dose of R21 in seasonal and age-based vaccination schedules is currently being evaluated in the ongoing phase 3 trial.

9 The impact of the introduction of the RTS,S vaccine on inpatient visits for malaria has been well documented in Ghana, Kenya and Malawi. The impacts on outpatient visits and overall health care costs have yet to be studied.

10 This research topic has been partially addressed. The impact of the vaccine using an age-based approach in areas with functional EPI programmes has been studied in Ghana, Kenya and Malawi.

RESEARCH TOPICS

Economics, costing and cost-effectiveness of the vaccine

- Measure the costs associated with the introduction and scale-up of the vaccine through different delivery platforms (e.g., routine EPI or campaign-based) for seasonal or hybrid vaccination schedules.[11]*
- Measure the economic impact of the vaccine on work absenteeism, productivity, labour force and health care expenditures.
- Measure the cost–benefit and cost-effectiveness of the malaria vaccine as part of a mix with other malaria prevention interventions.[12]*

11 The costs associated with vaccine introduction and scale-up through routine EPI have been investigated in Ghana, Kenya and Malawi. The costs associated with seasonal and hybrid schedules have also been estimated, using Mali and Burkina Faso as examples. Therefore, this is not listed as a research priority, but countries may want to conduct additional costing studies using local data.

12 Cost–benefit and cost-effectiveness of the RTS,S malaria vaccine as part of a mix with other malaria prevention interventions have been modelled. Mathematical modelling is also under way to look at the impact and cost-effectiveness of different mixes of interventions including malaria vaccines.

Six months old Susana Atta is the first child to receive the malaria vaccine in Ghana, administered during the national launch of the Malaria Vaccine Implementation Programme (MVIP) held in Cape Coast, Ghana.
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5 Key takeaways and conclusions

This research agenda development process engaged a broad group of malaria and immunization stakeholders to develop a prioritized list of operational and implementation research topics that are important for guiding the roll-out and scale-up of malaria vaccines. The agenda builds upon ongoing and existing research in this space. Decisions to invest resources to address topics from the prioritized list should be made with careful consideration of research that may have been completed or is ongoing to address these priority topics. This research agenda is timely, given that many countries have already begun or will begin to introduce the vaccine in 2024 and 2025 and are thinking about what operational challenges may arise or what information gaps they may want to address to help guide their programming. As ongoing and new research is conducted, it will be critical to ensure timely and targeted dissemination of the evidence to the national EPI and NMP and other stakeholders providing support to the vaccine roll-out in order to facilitate the uptake of the findings for guiding those programmes.

The generally narrow range in the scores across the topics and broad alignment across the stakeholder groups suggest that all the topics identified through the stakeholder consultation process are important for guiding the broader introduction and scale-up of the vaccine. Some topics, particularly under the thematic areas of implementation feasibility and acceptability of/demand creation for the vaccine, are more urgent, as addressing them will help national programmes to introduce the vaccine more effectively and efficiently. Several of the topics under these themes will likely be very context-specific and important to address across different settings.

Several topics on the agenda are not malaria-specific, but speak to broader health system challenges, which are relevant across all vaccines. These include questions related to strengthening systems for pharmacovigilance, information systems for tracking data on coverage of vaccines among eligible populations and the effectiveness of vaccines over time, supply chain and logistics systems, cold chain management, and implementation of effective training and supervision for health care workers. Investment in these research areas has the potential to provide relevant learning and impact, not only for malaria vaccine introduction, but also for country EPI efforts more broadly.

The malaria vaccine landscape is quickly changing with the recommendation of the second malaria vaccine, R21, which occurred during the development of this research agenda. Given the rapidly changing landscape and the ongoing and planned investments in research on malaria vaccines, it will be important to track progress against this agenda and review it periodically to ensure its continued relevance and to capture new topics that may emerge.

A poster about the malaria vaccine on the wall at Homa Bay County Teaching and Referral Hospital in western Kenya.
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Annex 1. List of Technical Advisory Committee members

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Robert Bednarczyk	Emory University	United States of America
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Perpetua Uhomoibhi	National Malaria Elimination Programme	Nigeria

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Annex 3. Full list of operational challenges and barriers from stakeholder consultations by thematic area

During the consultation process, stakeholders were asked to provide their perspectives on operational challenges and barriers to implementation of the malaria vaccine and key evidence gaps. Stakeholders were then asked to prioritize what they saw as the priority research questions, reflecting upon what they had previously identified as key operational challenges/barriers and knowledge gaps. Stakeholders' perspectives on the operational challenges/barriers and knowledge gaps were then analysed and organized by thematic area to inform the emergent list of priority research topics. The table below includes the full list of operational challenges and barriers, organized by thematic area and stakeholder group, that were identified through the stakeholder consultation process. The operational challenges and barriers reflect stakeholders' perspectives and should not be seen as a standalone list. Importantly, some of these operational challenges and barriers may already be sufficiently or partially addressed by available evidence, and this has been taken into account in the final prioritization.

Theme 1: Safety

SUBTHEME	CHALLENGES, BARRIERS AND OTHER IMPLEMENTATION CONSIDERATIONS	SOURCE(S)
Monitoring of adverse events	Inadequate training of health workers on how best to deal with adverse events in order to alleviate anxiety of families/communities	Gov, RI
	Setting up and/or adapting a pharmacovigilance system to identify and assess adverse side effects	Gov, RI
	Challenges with monitoring adverse events in the context of less robust systems and limited funding	Gov, RI, GRB, TP, CSO
	Monitoring for waning immunity or malaria rebound over time as vaccine protection decreases	Gov, GRB, RI

Gov: government representative; RI: research institution; GRB: global or regional body; TP: technical partner; CSO: civil society organization

Theme 2: Implementation feasibility

SUBTHEME	CHALLENGES, BARRIERS AND OTHER IMPLEMENTATION CONSIDERATIONS	SOURCE(S)
Delivery strategy/ platform	Challenges with delivering vaccine doses outside of the routine EPI schedule	Gov, GRB, TP, CSO
	Challenges with identifying eligible children at health facilities in the community or identifying missed communities	Gov, TP
	Long wait times at vaccination centres and limited number of vaccination centres	Gov, CSO
Dosing regimen/ schedule	Challenges with drop-out for the fourth dose of the vaccine delivered in the second year of life	Gov, RI, TP, CSO
	Challenges with the multi-dose nature of the vaccine and planning out the dosing schedule to ensure that all doses are given	Gov, CSO
Coverage/ reach of the vaccine among eligible populations	Inadequate sensitization leading to challenges with coverage of the target population	RI, CSO
	Challenges with improving defaulter tracing	CSO
Supply chain	Challenges with cold chain and storage for outreach deployment; some facilities lack a fully functioning cold chain	Gov, RI, TP, CSO
	Challenges with year-round availability of vaccines or sustained availability of the vaccine over time	RI, GRB
Demand forecasting	Insufficient planning period incorporated into timelines	CSO

Human resources planning/ capacity	Inadequate training and re-training of staff before and after vaccine introduction	Gov, RI, CSO
	Competing tasks for programmes (e.g., delivering catch-up doses for HPV vaccines, COVID-19 vaccines, etc.) and inadequate number of health staff to implement new vaccines	Gov, CSO
Coordination/ integration	Challenges with collaboration/integration of vaccine programme across different government implementing programmes/departments, including having clearly defined roles for different programmes and levels (national, subnational)	Gov, GRB, TP, CSO
Equitable coverage of the vaccine, with particular attention to vulnerable and hard-to-reach populations	Challenges with achieving easy and equitable access to all vaccine doses for the most at-risk population groups, particularly in areas with poor access to EPI services	RI, GRB, TP
	Challenges with restocking the vaccine in conflict areas due to inconsistent flights/transport to the area	Gov, RI
	Difficulty reaching people in high security risk areas or humanitarian areas, especially to deliver a four-dose vaccine	Gov, RI
	Challenges with obtaining health history, including vaccine history, among people who are internally displaced	Gov
	Challenges with funding and transport to set up outreach/mobile vaccination centres in hard-to-reach areas	Gov, RI, CSO

Gov: government representative; GRB: global or regional body; TP: technical partner; CSO: civil society organization; RI: research institution

Note: No challenges were identified under the subtheme of subnational implementation.

Theme 3: Acceptability of and demand creation for malaria vaccines

SUBTHEME	CHALLENGES, BARRIERS AND OTHER IMPLEMENTATION CONSIDERATIONS	SOURCE(S)
Perception and acceptability of the vaccine among the target populations, health care workers and community members	Vaccine hesitancy due to the high number of doses required, misinformation and mistrust among the target population, particularly in countries where there was resistance to COVID-19 vaccination	Gov, RI, TP, CSO
	Communication challenges around effectively conveying that the vaccine offers partial protection and dealing with refusals due to rumours or safety concerns	GRB, CSO
	Sociocultural norms, religious beliefs, socioeconomic status, gender roles in decision-making, opinions of community leaders and opinion shapers negatively affecting vaccine acceptability	CSO
	Poor satisfaction with health services received at health facilities negatively affecting acceptability	CSO
	Preference for traditional local remedies over Western medicine	CSO
Strategies that influence adoption/uptake, including effective health communication, social and behaviour change, community engagement, and social mobilization approaches or interventions in different settings	Limited advocacy/sensitization materials due to funding constraints	Gov, RI
	Inadequate systems to sensitize communities and engage local leaders/ champions in sensitization efforts	Gov, RI
	Advocacy/community sensitization around the need to continue use of other malaria interventions after vaccination	Gov, RI, CSO

Gov: government representative; RI: research institution; TP: technical partner; CSO: civil society organization; GRB: global or regional body

Theme 4: Integration of the vaccine with other health intervention

SUBTHEME	CHALLENGES, BARRIERS AND OTHER IMPLEMENTATION CONSIDERATIONS	SOURCE(S)
Co-administration/ deployment with other malaria interventions	Coordination of malaria vaccine introduction with NMP activities	RI, TP
	Malaria vaccine should be complementary to other malaria interventions, not replace them.	Gov
Co-administration/ deployment with other vaccines	Challenges with building synergies between zero-dose initiatives and malaria vaccine introduction	TP
	Competing priorities with other vaccines and health interventions	Gov
Broader health system impacts (benefits or costs) from deployment of vaccine	Confusion with introducing a new vaccine alongside the COVID-19 vaccines	RI
Co-administration/ deployment with additional malaria vaccine products	In the event a country selects one of the malaria vaccine products over the other, continuous availability of the selected vaccine needs to be ensured.	Gov

RI: research institution; TP: technical partner; Gov: government representative

Theme 5: Impact and effectiveness of the vaccine

SUBTHEME	CHALLENGES, BARRIERS AND OTHER IMPLEMENTATION CONSIDERATIONS	SOURCE(S)
Impact on malaria burden and all-cause mortality	Insufficient data on the impact of the malaria vaccine on the health system	GRB
	Challenges with monitoring the impact of the malaria vaccine through routine delivery	GRB
Effectiveness of the malaria vaccine	Delivery through EPI might mean that some children receive the vaccine outside of the peak/high malaria transmission season. (Note: vaccine efficacy can be optimized by vaccinating just before peak malaria transmission season).	RI
	Additional data required on how much the fourth dose adds to protection against severe malaria and mortality	TP, RI

GRB: global or regional body; RI: research institution; TP: technical partner

Theme 6: Economics, costing and cost-effectiveness of the vaccine

SUBTHEME	CHALLENGES, BARRIERS AND OTHER IMPLEMENTATION CONSIDERATIONS	SOURCE(S)
Economics/costing of the vaccine	Government ownership and commitment to providing the required co-financing for the vaccine	Gov, GRB, TP
	Lack of or insufficient data on full delivery costs of the malaria vaccine	TP
Cost-effectiveness of the vaccine (e.g., in different transmission settings, in comparison to other interventions, over the long term)	Cost-effectiveness of administering the fourth dose of the malaria vaccine	TP
	Lack of or insufficient data on different vaccine deployment strategies	RI

Gov: government representative; GRB: global or regional body; TP: technical partner; RI: research institution

Annex 4. List of identified knowledge gaps by thematic area

During the consultation process, stakeholders were asked to provide their perspectives on challenges and barriers to implementation of the malaria vaccine and key evidence gaps. Stakeholders were then asked to identify priority research questions, considering what they had previously identified as key operational challenges/barriers and knowledge gaps. Stakeholders' perspectives on the operational challenges/barriers and knowledge gaps were then analysed and organized by thematic area to inform the emergent list of priority research topics. The table below includes the full list of knowledge gaps, organized by thematic area and stakeholder group, that were identified through the stakeholder consultation process. The knowledge gaps reflect stakeholders' perspectives and should not be seen as a standalone list. Importantly, some of these knowledge gaps may already be sufficiently or partially addressed by available evidence, and this has been taken into account in the final prioritization.

Theme 1: Safety

SUBTHEME	KNOWLEDGE GAPS	SOURCE(S)
Monitoring of adverse events	How best to influence caregivers to report on adverse events	RI
Safety of different dosing schedules and long-term safety	Long-term safety of the R21 antigen and Matrix-M adjuvant in the target population	TP
Safe deployment among vulnerable populations	Safety and efficacy of the vaccines in older populations, including school-aged children and pregnant women	TP
	Safety of malaria vaccines in vulnerable populations (e.g., individuals with pre-existing conditions) and measures to prevent harm	RI, TP
Safe deployment/ co-administration with other vaccines or drugs	Assessment of the side effects and interactions between the malaria vaccines and SMC drugs (Note: this has been assessed in clinical trials to have no interaction and a good safety profile)	RI

SUBTHEME	KNOWLEDGE GAPS	SOURCE(S)
National regulation and vaccine registration	Guidance around the process for vaccine registration and regulation, including the mechanisms for scientific review of vaccine data prior to approval and licensing decision	TP

RI: research institution; TP: technical partner

Theme 2: Implementation feasibility

SUBTHEME	KNOWLEDGE GAPS	SOURCE(S)
Delivery strategy or platform	How best to create a service delivery platform for malaria vaccine doses that are outside of the routine EPI schedule (e.g., at 7 or 8 months of age).	TP
	How best to identify children at 7, 8 and 9 months of age and track them over time to complete the full four-dose series of the vaccine	TP
Coverage/reach of the vaccine among eligible populations	Understanding the eligibility criteria, including availability of the vaccine for pregnant women and adults (Note: currently recommended malaria vaccines are only indicated for use in children)	TP
	Assessing the coverage or reach of the vaccine among the target population	Gov
	Understanding the key barriers to accessing the vaccine among the target population	Gov
Supply chain/logistics considerations	Understanding the necessary health infrastructure in the subnational areas that are targeted for the malaria vaccine, including storage conditions and capacity requirements	TP
	Guidance on what to do in the face of supply challenges with a malaria vaccine that has already been introduced in a country	TP

SUBTHEME	KNOWLEDGE GAPS	SOURCE(S)
Demand forecasting	Current levels of demand for the malaria vaccine in malaria-endemic countries	GRB
Subnational implementation	Framework or guidance for how to target and deploy the vaccine subnationally	Gov, RI, TP
Expansion or scale-up planning	Lack of clarity on co-financing of the vaccine	Gov
Human resources planning and capacity/ training to support implementation of the vaccine	Capacity and resources of national governments/ministries of health to lead the introduction and roll-out of the malaria vaccine	Gov, GRB, TP
	Understanding whether current human resources capacity is adequate in the country to accommodate the addition of the malaria vaccine and information on the workload for health care workers at the different levels of the system to support delivery of the vaccine	GRB, TP
	Understanding the core competencies and training required for health worker cadres to deliver the malaria vaccine	RI, TP
	Knowledge of vaccine providers and recipients on the profile of the vaccine, including the benefit of receiving all recommended doses, partial protection provided by the vaccine, and the need for continued use of other malaria prevention interventions	RI
	Health care worker training implications or requirements with two malaria vaccine products available and the potential for a product switch or that both products are used within a single country	GRB

SUBTHEME	KNOWLEDGE GAPS	SOURCE(S)
Coordination/ integration of the vaccine programme across government agencies and partners	How best to leverage partnerships and collaboration across sectors and with the private sector to support implementation of the vaccine	GRB, TP
	How to strengthen integration of the immunization programme within primary health care	GRB
Equitable coverage of the vaccine, with particular attention to vulnerable and hard-to-reach populations	How limited resources can be allocated to ensure equitable access to the vaccine	TP
	Understand the best delivery strategies for the vaccine in hard-to-reach areas, particularly for the fourth dose of the vaccine	RI, TP
	Understand how different delivery strategies influence equitable access to the vaccine	TP
	Understand how gender influences vaccine acceptance and use	TP

TP: technical partner; Gov: government representative; GRB: global or regional body; RI: research institution

Theme 3: Acceptability of and demand creation for malaria vaccines

SUBTHEME	KNOWLEDGE GAPS	SOURCES(S)
Perception and acceptability of the vaccine among the target populations, health care workers and community members	Policy-makers' receptivity to moderate efficacy levels of the malaria vaccines, given the high level of efficacy of most (but not all) routine EPI vaccines	RI
	How product characteristics affect acceptability and demand for the malaria vaccines (e.g., liquid versus lyophilized, thermostability of the vaccine)	TP
	Extent to which perceived effectiveness of malaria doses 1–3 impact adherence or non-adherence to dose 4	TP
	How the difference in vaccine product characteristics and perceived differences in efficacy will impact providers' and recipients' perception of the effectiveness of the malaria vaccines	RI
Strategies that influence adoption/uptake, including effective health communication, social and behaviour change, community engagement, and social mobilization approaches or interventions in different settings	Framework for strategic communication and community engagement on vaccine safety, efficacy and benefits to promote vaccine demand, with guidance on tailoring communication to specific contexts and target groups	Gov, GRB, TP

RI: research institution; TP: technical partner; Gov: government representative; GRB: global or regional body

Theme 4: Integration of the vaccine with other health interventions

SUBTHEME	KNOWLEDGE GAPS	SOURCE(S)
Co-administration/ deployment with other malaria interventions	When monoclonals become available, guidance on use and targeting in the context of malaria vaccines	RI
	Comparative effectiveness of malaria vaccines and monoclonals when they become available	RI
	How best to mitigate declines in uptake of other malaria control interventions with the deployment of the vaccine	RI
Co-administration/ deployment with additional malaria vaccine products	Understanding the drivers affecting vaccine product preference and how having more than one vaccine product affects implementation and health worker and community acceptance	GRB

RI: research institution; GRB: global or regional body

Note. No topics were identified under the subtheme of broader health system impacts.

Theme 5: Impact and effectiveness of the vaccine

SUBTHEME	KNOWLEDGE GAPS	SOURCE(S)
Impact on malaria burden and all-cause mortality	Impact of the malaria vaccine in other (non-African) geographical areas	TP
	Perceived impact of the vaccine among communities and health workers	GRB
Effectiveness of the malaria vaccine	Effective surveillance systems for monitoring vaccine effectiveness and identifying increased malaria risk after vaccine effectiveness wanes	Gov, RI
	Effectiveness of the vaccines in children who are immunocompromised or have comorbidities	RI
	Long-term effectiveness of the vaccines	RI
	How delays in the schedule or missed doses affect the effectiveness of the vaccines	RI, TP
	Effectiveness of the vaccines without the use of other malaria prevention measures (e.g., ITNs)	TP
	Whether there is any age shift effect of clinical or severe malaria cases in immunized children after ceasing vaccination (Note: this has been studied for RTS,S and is currently being monitored in the R21 phase 3 trial)	RI
Other health impact of the malaria vaccine	Impact of the vaccine on other health conditions (e.g., anaemia, malnutrition) and cognitive development	TP

TP: technical partner; GRB: global or regional body; Gov: government representative; RI: research institution

Note. No topics were identified under the subtheme of impact on antimalarial resistance and vaccine escape.

Theme 6: Economic, costing and cost-effectiveness of the vaccine

SUBTHEME	KNOWLEDGE GAPS	SOURCE(S)
Economics/costing of the vaccine	Sustainable financing mechanisms in low-income countries	TP
	Understanding the cost of producing and distributing the vaccines and how best to manage the costs	GRB, TP
	Co-financing of strategies to reach hard-to-reach populations	TP
	How the cost of the vaccine will change over time as demand increases and supply improves	Gov
	Costs of delivering the vaccine during the second year of life	GRB
	Factors influencing government commitment to the vaccine and how this compares to other routine EPI vaccines	GRB
	Local manufacturing impact on accelerating the uptake of/demand for the vaccine	TP
Cost-effectiveness of the vaccine (e.g., in different transmission settings, in comparison to other interventions, over the long term)	Cost-effectiveness of integrating the malaria vaccine with other health interventions (e.g., immunization, health, nutrition, water and sanitation and hygiene)	GRB
	Cost-effectiveness of the fourth dose in perennial settings and additional annual doses up to age 5	RI

TP: technical partner; GRB: global or regional body; Gov: government representative; RI: research institution

Annex 5. Research priority rankings and scores across thematic areas, overall and by stakeholder group

This table includes the original set of ranked research topics that emerged from the stakeholder consultation process prior to WHO's review and refinement of the topics.

Topics that have been partially or fully addressed with available evidence have been denoted by an asterisk (*).

RANK	RESEARCH TOPIC	OVERALL SCORE	SCORE BY STAKEHOLDER GROUP				
			CSO	GOV	GRB	RI	TP
Safety							
1	**Assess the safety of the co-administration of the malaria vaccine with other relevant childhood vaccines***	86.7	76.8	86.3	87.4	91.0	89.4
2	**Evaluate approaches to monitoring adverse events following malaria vaccination across different delivery strategies (age-based vs. seasonal) and contexts (e.g., emergency/humanitarian/hard-to-reach areas)***	83.5	81.0	83.0	80.4	87.7	82.4

RANK	RESEARCH TOPIC	OVERALL SCORE	SCORE BY STAKEHOLDER GROUP				
			CSO	GOV	GRB	RI	TP
Implementation feasibility							
1	Assess the optimal schedule for the malaria vaccine to achieve the highest coverage and effectiveness, particularly for the timing of the fourth dose*	88.3	87.9	86.3	86.7	92.3	85.5
2	Assess feasibility and coverage achieved through different delivery schedules/ platforms in areas where delivery of the vaccine will be seasonal	87.9	88.7	82.2	89.3	92.8	83.6
3	Identify and evaluate effective strategies for ensuring equitable access to the vaccine among hard-to-reach / vulnerable populations (e.g., conflict, humanitarian, urban poor/slum areas)	84.0	82.4	83.7	80.7	87.8	83.0
4	Identify and evaluate strategies to improve uptake of malaria vaccines during the second year of life*	83.8	82.7	80.3	87.4	86.4	80.0
5	Evaluate approaches to improve the collection and reporting of vaccine coverage data to inform programmatic decision-making	83.2	82.2	83.9	74.4	90.0	82.4
6	Identify and evaluate strategies to strengthen the supply chain and logistics to ensure a continuous supply of the malaria vaccine	75.9	76.8	80.0	63.2	84.4	68.5
7	Evaluate approaches to optimize training, re-training and supervision of health service managers and health care workers in delivery of the malaria vaccine*	75.7	82.0	72.3	74.4	75.1	76.4

RANK	RESEARCH TOPIC	OVERALL SCORE	SCORE BY STAKEHOLDER GROUP				
			CSO	GOV	GRB	RI	TP
Acceptability of and demand creation for the vaccine							
1	Evaluate social and behaviour change and community engagement strategies to address challenges with vaccine acceptability and demand*	83.0	80.4	81.7	80.0	87.2	84.2
2	Assess how community acceptance and uptake of the vaccine change over time, considering factors such as the partial protection of the vaccine, the four-dose schedule, and availability of other malaria interventions	82.9	81.4	80.6	81.1	88.2	80.0
3	Assess caregivers', community members' and other relevant populations' understanding and perceptions of the vaccine over time and how these influence vaccine acceptability and uptake*	80.1	84.4	80.6	77.4	84.4	80.6
4	Assess attitudes, perceptions and acceptability of the malaria vaccine over time among health care workers*	79.0	76.7	76.8	73.3	84.8	82.4
Integration of the vaccine with other health interventions							
1	Assess the interchangeability of the RTS,S and R21 vaccines with regard to feasibility, safety and effectiveness	81.6	71.7	80.7	85.9	82.2	86.5
2	Evaluate the combined impact of malaria vaccination with other malaria control interventions in perennial and seasonal transmission areas and in other important settings (e.g., emergency and hard-to-reach areas)*	81.5	75.8	83.9	79.6	85.3	78.1

RANK	RESEARCH TOPIC	OVERALL SCORE	SCORE BY STAKEHOLDER GROUP				
			CSO	GOV	GRB	RI	TP
Integration of the vaccine with other health interventions (continued)							
3	Assess the feasibility, acceptability and coverage of different models of combined or linked vaccine and SMC and PMC delivery (co-administration, parallel administration, sequential administration)*	79.5	77.1	75.8	76.5	84.7	82.0
4	Evaluate the impact of the malaria vaccine programme and malaria vaccination on coverage and use of other malaria interventions*	79.1	70.9	78.6	77.0	84.8	79.7
5	Assess the feasibility and acceptability of the integration of the delivery of the malaria vaccine with other child health interventions in the first and second year of life	79.0	78.2	77.9	71.9	85.3	80.0
6	Assess the impact of the malaria vaccination programme on the coverage of other childhood immunization vaccines*	78.7	74.9	77.9	73.3	86.9	74.0
7	Assess feasibility and impact of integrating the four-dose malaria vaccine schedule to deliver catch-up doses and reach zero-dose children for other routine childhood immunization vaccines*	77.9	74.7	77.9	81.9	81.4	67.9
8	Identify and evaluate approaches to strengthen key components of the health system critical for vaccine delivery, including information systems, supply chain, cold chain management, and pharmacovigilance, to support the introduction and scale-up of vaccines	77.1	77.1	74.4	67.8	85.6	77.6
9	Evaluate what the broader health system impacts are in terms of health service utilization (e.g., reduction in outpatient visits, inpatient visits for malaria) from the deployment of the malaria vaccine*	76.3	74.7	75.1	73.0	80.3	77.0

RANK	RESEARCH TOPIC	OVERALL SCORE	SCORE BY STAKEHOLDER GROUP				
			CSO	GOV	GRB	RI	TP
Impact and effectiveness of the vaccine							
1	Measure the impact of the malaria vaccine on malaria transmission, malaria burden and malaria mortality	83.9	82.4	86.0	78.1	88.9	80.6
2	Measure vaccine effectiveness depending on the receipt of different number of doses, with a particular focus on the differences between receiving three vs. four doses, for R21 in particular	81.9	77.3	78.2	85.5	88.6	72.0
3	Assess the level and duration of vaccine efficacy following the fourth dose of the malaria vaccine and additional annual doses	81.5	79.5	82.1	79.3	86.4	75.6
4	Measure the impact of the malaria vaccine under programmatic conditions in different settings (e.g., differing transmission settings, hard-to-reach areas, humanitarian or conflict settings, varying levels of health system functioning or strength)*	76.5	76.8	71.9	77.6	77.8	79.4
5	Measure the effectiveness of the vaccine in populations not currently targeted for the vaccine (e.g., school-aged children, pregnant women)*	73.2	75.3	73.3	69.2	73.9	75.0
6	Evaluate the impact of clearing malaria parasites prior to vaccination on vaccine effectiveness	69.2	74.5	68.8	62.0	72.8	65.0

RANK	RESEARCH TOPIC	OVERALL SCORE	SCORE BY STAKEHOLDER GROUP				
			CSO	GOV	GRB	RI	TP
Economics, costing and cost-effectiveness of the vaccine							
1	Measure costs associated with the introduction and scale-up of the vaccine through different delivery platforms or strategies	80.8	81.1	79.6	79.6	84.2	77.0
2	Measure the cost–benefit and cost-effectiveness of the malaria vaccine compared to or in combination with other malaria prevention interventions*	79.2	76.6	75.8	74.1	85.3	83.2
3	Measure the cost-effectiveness of the vaccine across different delivery schedules (e.g., age-based vs. seasonal)* or platforms (routine immunization, campaigns) and contexts (e.g., areas with low childhood immunization coverage, hard-to-reach areas)	78.2	77.0	75.3	79.5	82.8	72.1
4	Measure the economic impact of the vaccine on work absenteeism, productivity, labour force, and health care expenditures*	68.0	79.9	70.8	59.6	68.1	64.0

CSO: civil society organization representatives; Gov: government representatives; GRB: global and regional body representatives; RI: research institution representatives; TP: technical partner representatives

Annex 6. Malaria vaccine implementation research priorities with available evidence

The final list of malaria vaccine research priorities included in Table 5 were identified through the stakeholder consultation process and then further refined by WHO to reflect the latest available evidence related to the topics. During the refinement process, WHO reviewed and summarized the evidence available on the identified research priorities. Topics that have been sufficiently addressed with available evidence (and are therefore no longer considered to be high-priority research topics) have been written in grey font and denoted by an asterisk (*). Topics that have been partially addressed, such that evidence is available but important questions remain, have been written in black font and denoted by an asterisk.

RESEARCH TOPICS	AVAILABLE EVIDENCE
Safety	
Assess the safety of the co-administration of the malaria vaccine with other relevant childhood vaccines (e.g., measles, pentavalent vaccines (DTP-HepB-Hib), rotavirus, and pneumococcal conjugate vaccines).*	Data are available for RTS,S on the co-administration with these common childhood vaccines *(1, 2)*, and studies are currently under way for R21 *(3)*.
Acceptability of and demand creation for the vaccine	
Evaluate social and behaviour change and community engagement strategies to address challenges with vaccine acceptability and demand.*	A large longitudinal qualitative study was conducted in Ghana, Kenya and Malawi assessing social and behaviour change and community engagement strategies and community, caregiver and health worker perceptions. These findings have been published *(4, 5)* and presented in different forums, and therefore are not listed as outstanding priority research questions. Such questions, however, are context-specific, and additional studies in different settings and contexts would be beneficial.
Assess how community, caregiver and health worker perception, acceptance and uptake of the vaccine change over time, considering factors such as the partial protection of the vaccine, the four-dose schedule and availability of other malaria interventions.*	

RESEARCH TOPICS	AVAILABLE EVIDENCE
Integration of the vaccine with other health interventions	
Evaluate the combined impact of malaria vaccination with other malaria control interventions in perennial and seasonal transmission areas and in other important settings (e.g., emergency and hard-to-reach settings).*	Evidence is available on the impact of the malaria vaccine combined with ITNs and case management *(6–8)* and the combination of seasonal vaccination and SMC *(9, 10)*, and an ongoing study is exploring the co-deployment of RTS,S and PMC *(11)*. Outstanding questions remain on the effectiveness when vaccination is provided with PMC or SMC, or with other interventions in emergency or hard-to-reach settings.
Evaluate the effectiveness and impact of leveraging the four-dose malaria vaccine schedule to deliver catch-up doses and reach zero-dose children for routine EPI vaccines.*	This research question has been partially addressed in Ghana, Kenya and Malawi, where a minimal increase in catch-up doses was measured with the introduction of the malaria vaccine *(4, 7)*. Too few zero-dose children were identified in the survey population to assess the potential to reach zero-dose children. Developing and assessing innovations to fully utilize the additional vaccine visits to increase catch-up and to reach zero-dose children remains a priority research question.
Monitor the impact of malaria vaccination on coverage and use of other EPI vaccines and malaria interventions.*	Impact of malaria vaccination on the coverage and use of other EPI vaccines and malaria interventions was assessed in serial household surveys conducted in Ghana, Kenya and Malawi *(4, 7)*. In each country, no impact of vaccination was observed on the coverage and use of EPI vaccines or other malaria interventions. This is therefore not listed as an outstanding priority research question.

RESEARCH TOPICS	AVAILABLE EVIDENCE
Impact and effectiveness of the vaccine	
Assess the level and duration of vaccine effectiveness following the fourth dose and additional annual doses in areas of seasonal or perennial transmission.*	The efficacy of RTS,S up to dose 7 has been studied in a seasonal vaccination schedule in Burkina Faso and Mali *(6)*, but has only been evaluated in an age-based vaccination schedule up to dose 4. The efficacy of a fifth and sixth dose of R21 in seasonal and age-based vaccination schedules is currently being evaluated in the ongoing phase 3 trial.
Evaluate the impact of the malaria vaccine on the broader health system (e.g., reduction in outpatient visits, inpatient visits* for malaria, health care costs).	The impact of the introduction of the RTS,S vaccine on inpatient visits for malaria has been well documented in Ghana, Kenya and Malawi *(4, 7)*. The impacts on outpatient visits and overall health care costs have yet to be studied.
Measure the impact of the vaccine in routine use across different delivery approaches (e.g., age-based vs. seasonal delivery)* and contexts (e.g., areas with low EPI coverage or that are hard-to-reach).	This research question has been partially addressed. The impact of the vaccine using an age-based approach in areas with functional EPI programmes has been studied in Ghana, Kenya and Malawi *(4, 7)*.
Economics, costing and cost-effectiveness of the vaccine	
Measure the costs associated with the introduction and scale-up of the vaccine through different delivery platforms (e.g., routine EPI or campaign-based) for seasonal or hybrid vaccination schedules.*	The costs associated with vaccine introduction and scale-up through routine EPI have been investigated in Ghana, Kenya and Malawi *(12, 13)*. The costs associated with seasonal and hybrid schedules have also been estimated, using Mali and Burkina Faso as examples *(14)*. Therefore, this is not listed as a research priority, but countries may want to conduct additional costing studies using local data.

RESEARCH TOPICS	AVAILABLE EVIDENCE
Measure the cost–benefit and cost-effectiveness of the malaria vaccine as part of a mix with other malaria prevention interventions.*	Cost–benefit and cost-effectiveness of the RTS,S malaria vaccine as part of a mix with other malaria prevention interventions have been modelled *(4, 15–22)*. Mathematical modelling is also under way to look at the impact and cost-effectiveness of different mixes of interventions including malaria vaccines.

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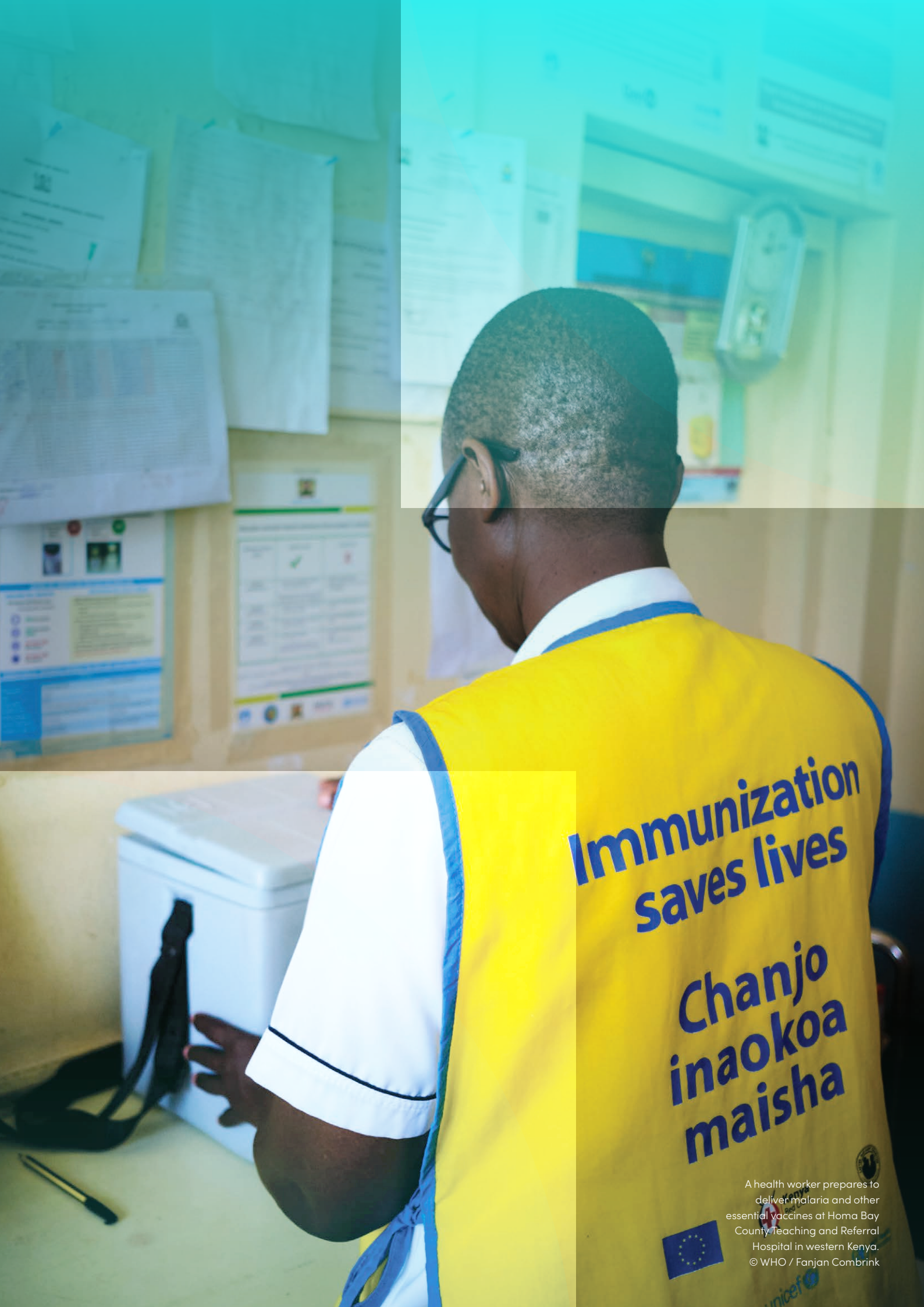
Annex 7. Declarations of interests

Declarations of competing interests were received from eight members of the technical advisory committee. Five members declared potential competing interests. This included participation in WHO working groups by Matthew Coldiron (member of Defeating Meningitis 2030 Technical Taskforce, SAGE Working Group on Meningococcal Vaccines, Guideline Development Group for meningitis diagnosis, treatment and care), Margaret Gyapong (Chair of WHO/TDR Scientific and Technical Advisory Committee), Terri Hyde (member of the Pneumonia and Rotavirus Working Group), and Eusebio Macete (member of SAGE/MPAG Working Group on Malaria Vaccines). All working group memberships declared were assessed as either unrelated to malaria vaccines and/or non-significant due to lack of financial renumeration. Terri Hyde is also a member of the Malaria Vaccine Coordination Team and the Gavi HPV sub-team; these are not WHO working groups and the malaria vaccine expertise was deemed valuable input for the technical advisory committee. Abraham Hodgson declared receiving income from WHO for the nationwide STEPS survey in Ghana on major non-communicable diseases, which was considered financially significant but unrelated to malaria vaccines. All members were not considered by WHO to have declared any interest that may be perceived as a potential conflict with regards to the objectives of the technical advisory committee.



A health worker prepares to deliver malaria and other essential vaccines at Homa Bay County Teaching and Referral Hospital in western Kenya.
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