

Malaria Vaccine Implementation Programme (MVIP) update and framework for policy decision



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MPAC, 11 April 2018

Global **Malaria** Programme



World Health
Organization

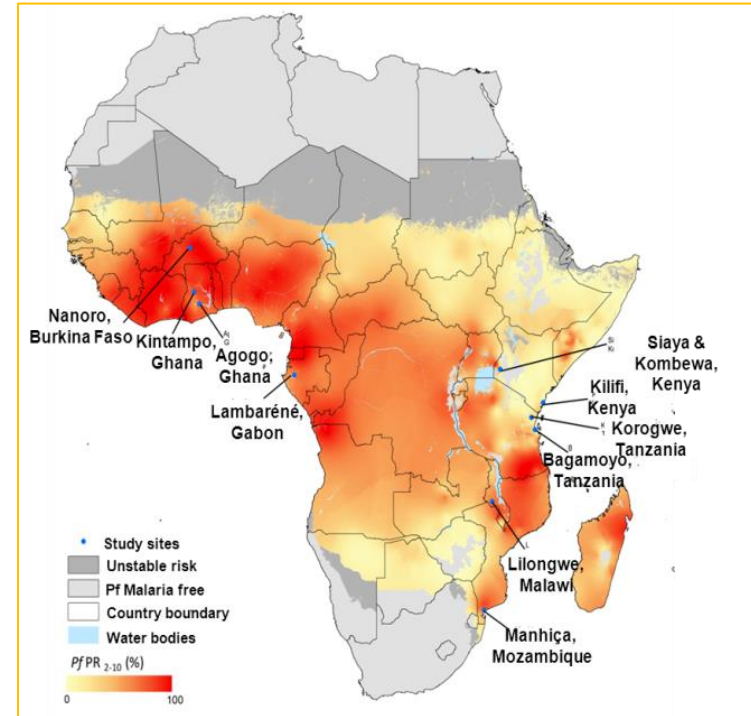
MVIP update

- Background to MVIP
- MVIP Updates
 - Regulatory
 - Vaccine introduction
 - Vaccine safety preparations
 - Evaluation
 - Governance and advisory committees
 - Partners and funding
 - Communications
- Framework for Policy Decision

Brief background to MVIP

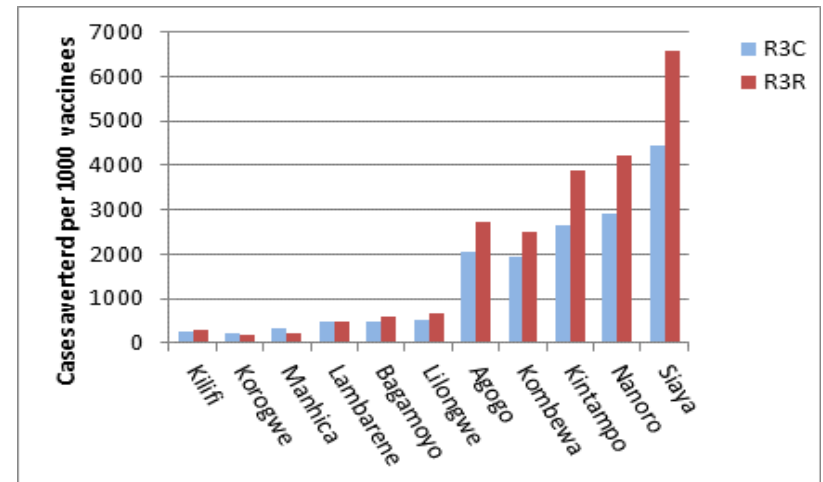
MVIP background

- RTS,S/AS01 Phase 3 trial
 - 15,499 children, 11 sites, 7 African countries
- Children 5-17 months, 4 doses over 4 years:
 - 39% reduction in clinical malaria,
 - 31% reduction in severe malaria
 - 62% reduction severe malaria anaemia
 - 29% reduction blood transfusions



MVIP background

- Potential for high impact moderate/high transmission with 4 doses
 - 6565 cases averted/1000 children vaccinated over 4 yrs
 - Modeling data from all sites: 1 life saved/ 200 vaccinated
- Potential safety signals:
 - Meningitis, cerebral malaria
 - Gender difference in all-cause mortality



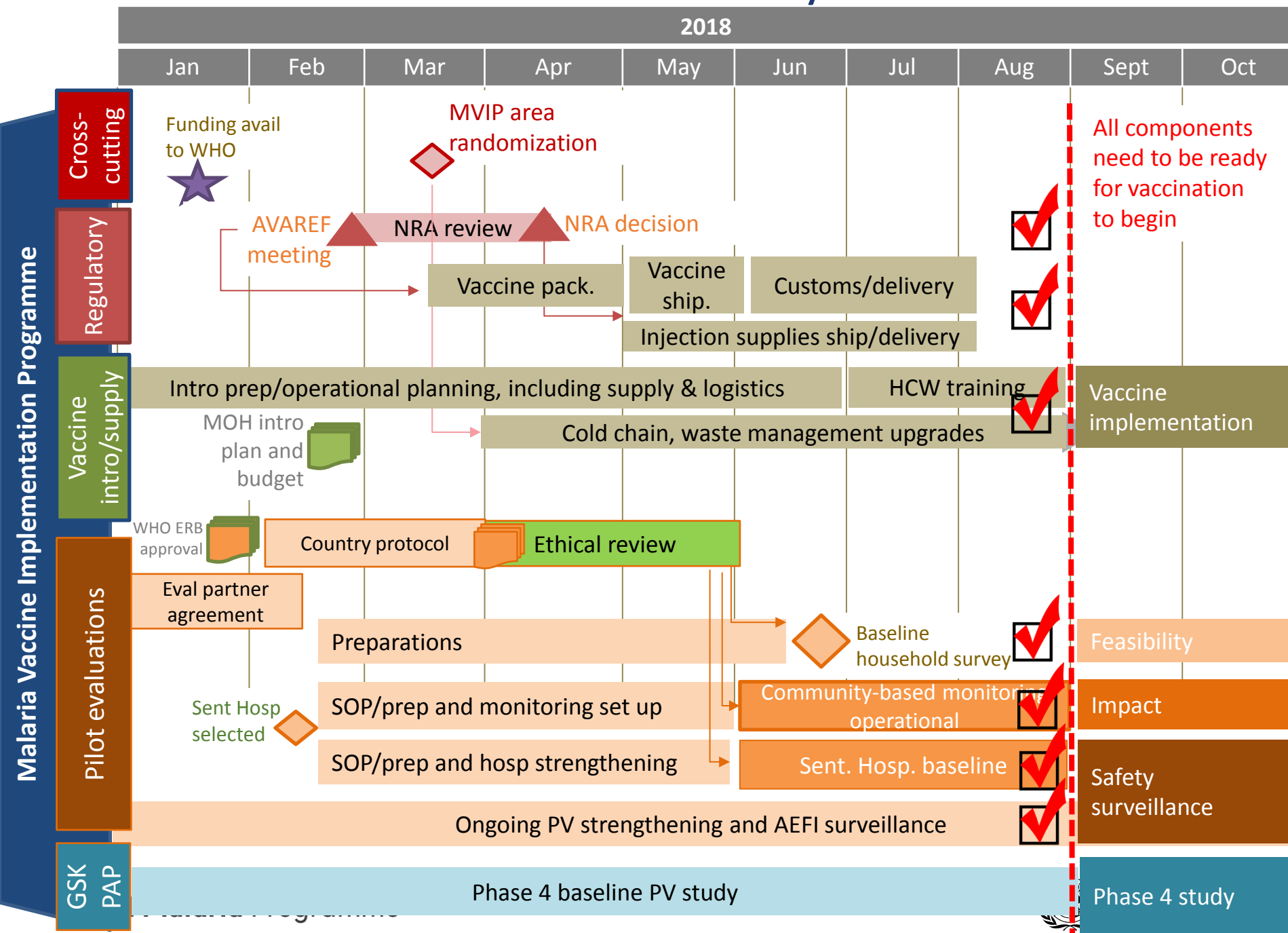
MVIP background

- European Medicines Agency positive scientific opinion
 - “Acceptable safety profile”, “benefits outweigh risks”
- SAGE/MPAC recommended
 - Phased introduction by EPI programmes and through routine systems in pilot implementations
 - Independent evaluation of
 - Feasibility of delivering 4 doses with new vaccine visits
 - Safety, emphasis on meningitis and cerebral malaria
 - Impact, on mortality (including by gender) and severe malaria
- Call for Expressions of Interest from countries
 - Ghana, Kenya, Malawi selected using pre-determined criteria

MVIP components

- Country-led sub-national RTS,S introduction
 - Areas randomized to receive the vaccine or serve as comparators
- WHO-commissioned independent evaluation of:
 - Feasibility
 - Measures of vaccine coverage - household surveys, administrative method
 - Qualitative evaluation of behaviours and barriers to vaccine uptake/delivery
 - Health economics analysis
 - Safety
 - Sentinel hospital surveillance (will also depend on routine pharmacovigilance, GSK -led phase 4 data)
 - Impact
 - Sentinel hospital surveillance, community mortality surveillance (and by gender)
- GSK-led Phase IV study
 - Safety & effectiveness; focus is capturing all AEFI/AESI
 - Home visits, increased capacity at health facilities (may affect uptake/impact)

Indicative timeline to start vaccination in first country



MVIP update

MVIP updates

- **Regulatory**
 - Joint review by the national regulatory authorities (NRA) under African Vaccine Regulatory Forum (AVAREF) in Kenya (26-28 February)
 - NRAs to consider RTS,S dossier: response by mid-May/June
- **Vaccine introduction**
 - Introduction plans and budgets finalised for all 3 countries
 - Earliest possible introductions: Ghana Sep 2018, Malawi & Kenya Oct 2018
 - Planning for vaccine delivery - WHO, UNICEF Supply Division and GSK meeting in January

MVIP updates (2)

- Vaccine Safety

- MVIP presented at the Global Advisory Committee Vaccine Safety (GACVS) meeting, Dec 2017
 - www.who.int/vaccine_safety/committee/topics/malaria_vaccine/Dec_2017/en/
- Countries improving AEFI reporting approaches
 - Good progress in Ghana and Malawi, potential risk to timeline in Kenya
- 10 Adverse Events of Special Interest (AESI) agreed by MoHs

MVIP updates (3)

- Evaluation
- Good progress in Kenya and Ghana - pending contracts
 - Potential sentinel hospital visits - deficiencies in diagnostics identified
- Evaluation master protocol approved by WHO ethics committee
 - Development/approvals of country-specific protocols - may risk timelines
- Expert group on cerebral malaria & meningitis convened 5, 19 Feb
- PATH identified investigators for qualitative research
- GSK negotiating with potential evaluation partners
 - Governance and advisory bodies
 - Programme Advisory Group (PAG) met Oct 2017 and Mar 2018
 - Data & Safety Monitoring Board (DSMB) met 6-7 March, 2018
 - WHO leadership briefed quarterly

MVIP updates (4)

- Funding
 - Donor agreements fully executed Jan 2018 (up to 2020)
 - Funding to regional & country offices, supporting vaccine introduction, staff hiring
 - Coordination/Communications
 - Regular inter-agency, country & cross-WHO calls
 - Generic IEC and Training materials developed with countries, available for adaptation
 - Creation and update of MVIP websites
 - Fact sheets, key messages, Q and A

Framework for policy decision (For guidance)

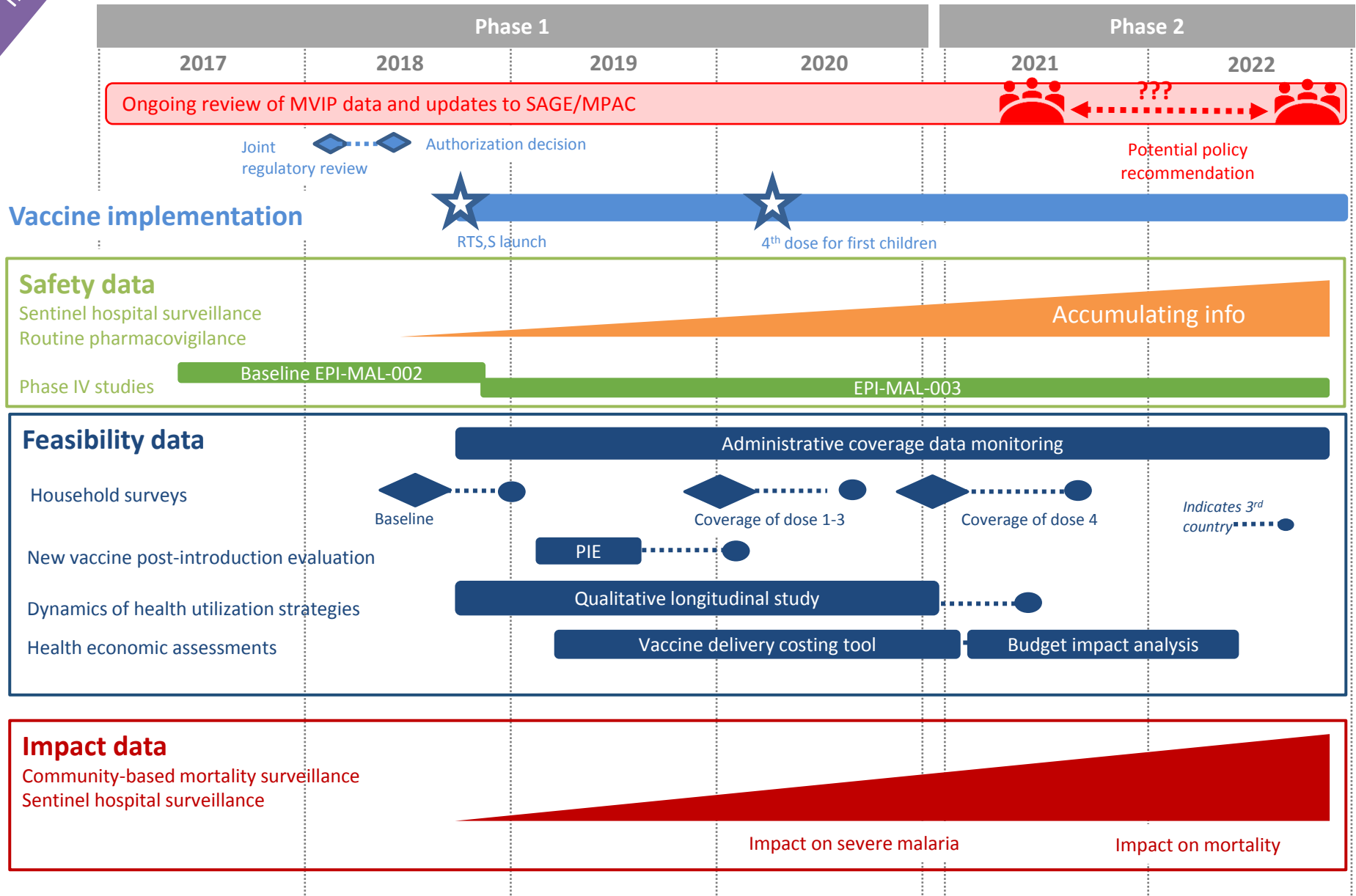
Questions for MPAC on the framework for policy decision

- Does MPAC agree with the approach?
- Are the suggested outcomes and matrices useful for policy decision?
- Does MPAC agree on the following suggested next steps?
 - Additional SAGE and MPAC members join the PAG to create a working group to consider and deliberate on the questions posed within the Framework (2 from each?)
 - The working group develops a report of those considerations and present to MPAC and SAGE at future meeting, aiming for Oct 2018
 - Next step for Chairs of MPAC and SAGE to provide to the MVIP secretariat the names of those available to participate on such a working group

Framework for policy decision for RTS,S

- MPAC and SAGE requested data be collected through the pilot implementations to answer questions on feasibility, safety, impact to inform a policy decision on wider use of RTS,S
- Framework for Policy Decision aims to describe how data will inform policy at the end of the pilots, in 2022
- Also will describe how data could inform
 - Expansion of vaccinations into pilot comparator areas
 - Broader country-wide implementation prior to 2022 should emerging findings show¹:
 - Concerns about safety resolved
 - Implementation data favorable
 - Fourth dose coverage high

Overview of MVIP timelines: data accumulating over time...



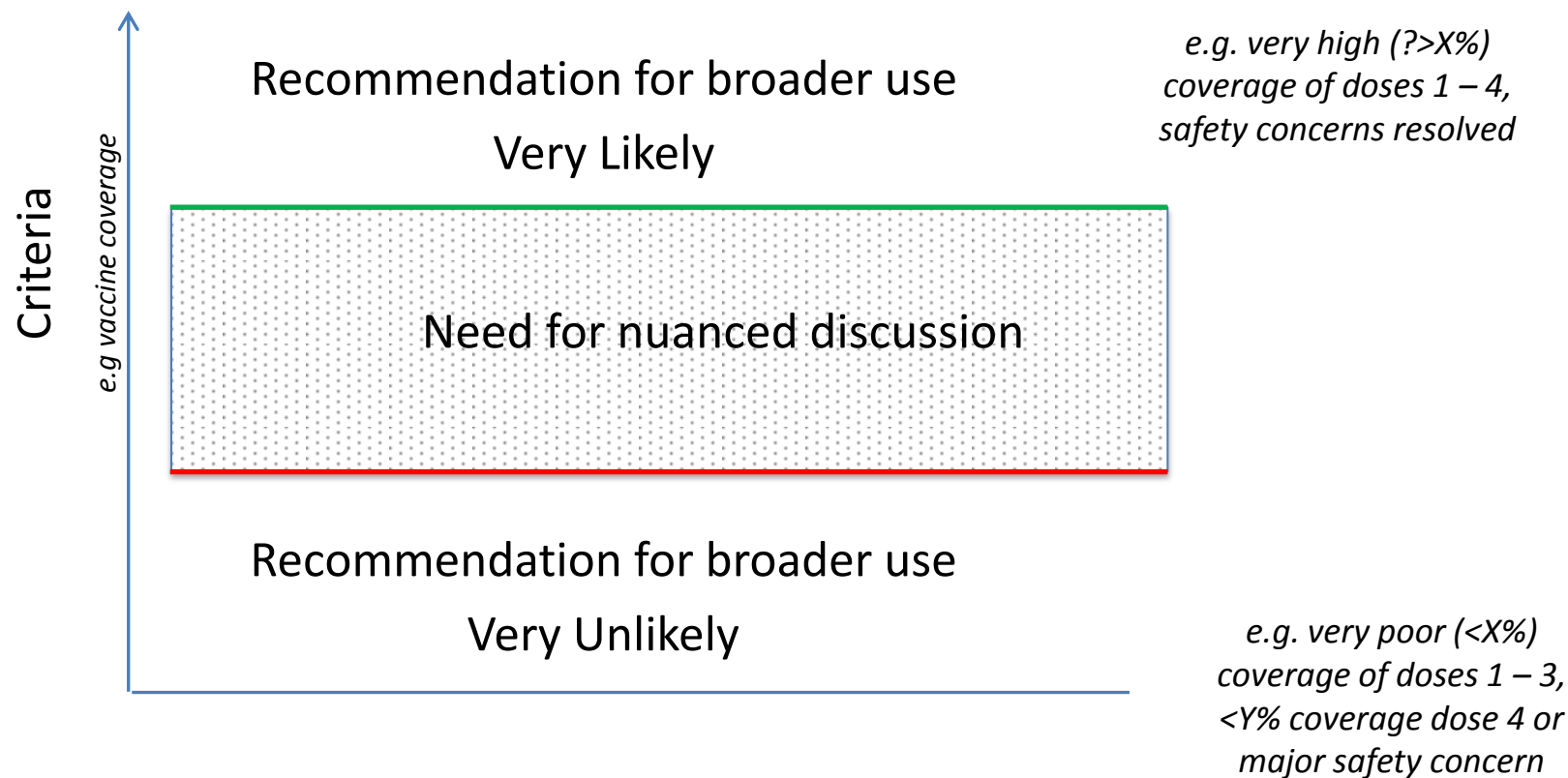
Questions to be considered for the framework for policy decision

- What criteria, if met, would likely lead to a recommendation for vaccine use at the end of the pilot programme?
 - Is evidence of impact on mortality required for policy recommendation
 - What to do if conflicting findings from different countries
 - Or if data availability lags considerably from one country
- Is it conceivable that there could be an earlier policy recommendation, prior to pilot end
 - If yes, what data would support such a decision?
- What criteria, if met, would likely lead to a recommendation not to implement the vaccine

Questions to be considered for the framework for policy decision: broader implementation before study end

- What criteria would support “favorable implementation data”, and broader country-wide implementation of RTS,S?
 - High coverage dose 4, safety signals resolved and:
 - No or little adverse effect on other vaccines?
 - Continued malaria control use, or impact data suggesting no negative effect of lower use?
 - Cost effectiveness?
- What would be considered “high fourth dose coverage”?
 - Can data-driven thresholds of vaccine coverage be used to guide decisions on country-wide use before pilot end?

MVIP framework for decision making



Modelers engaged to estimate thresholds of vaccine coverage that predict impact

- Through PATH, engaged modellers from Swiss Tropical Institute and Imperial College, London
 - Generating estimates for a range of vaccine coverage that will estimate impact on severe malaria, malaria mortality or cost effectiveness
- Modelling methods presented to the WHO Immunization and Vaccine-related Implementation Research Advisory Committee (IVIR-AC) March 2018

Modelers will consider two scenarios for vaccine impact and cost-effectiveness (CE) estimates

- Impact estimates for MVIP pilot areas:
 - Estimates of impact and CE will be generated with parasite prevalences that correspond to those in the pilot areas
 - Area-specific assumptions on vaccination coverage, costs, and coverage of malaria preventive/curative interventions based on publicly available data
- Impact estimates for a range of malaria transmission settings where the RTS,S vaccine may be recommended/implemented should there be a policy recommendation:
 - Estimates will be generated for parasite prevalence levels representative of those found in sub-Saharan Africa (e.g. 10% to 65%)
 - A common set of assumptions on vaccination coverage, costs, and coverage of malaria preventive and curative interventions will be applied to all transmission settings based on publically available data

Outcomes and outcome metrics to be generated

Outcome metrics:

- Events averted per 100,000 vaccinated
- Events averted per dose
- Events averted per 100,000 population
 - all ages; 0-5 year olds; target age group
- Percent change in events averted
- Percent change in incidence of events averted
- Cost per event averted

Outcomes:

- Severe malaria cases averted
- Severe hospitalized malaria averted
- Malaria deaths averted
- DALYs averted

Illustrative example of outputs: events averted by malaria transmission (not based on actual estimates)

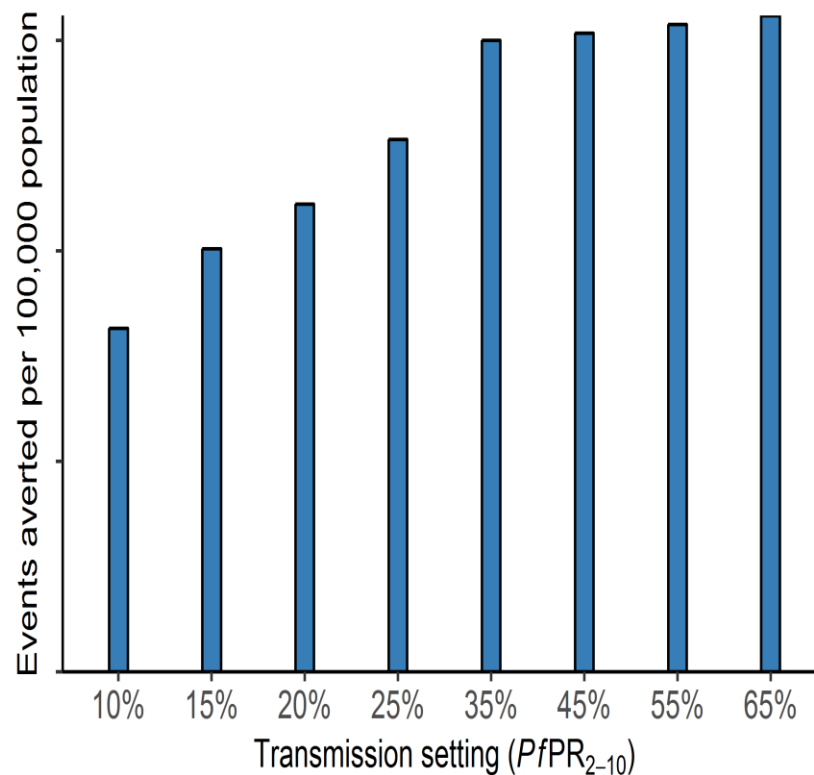


Figure 1: Events averted per 100,000 population **for a single vaccine coverage scenario**, across a range of transmission settings. This figure can be produced for specific population groups and vaccine coverage scenarios, and 95% credible intervals can be included.

Illustrative example of output: events averted by dose 4 coverage (not based on actual estimates)

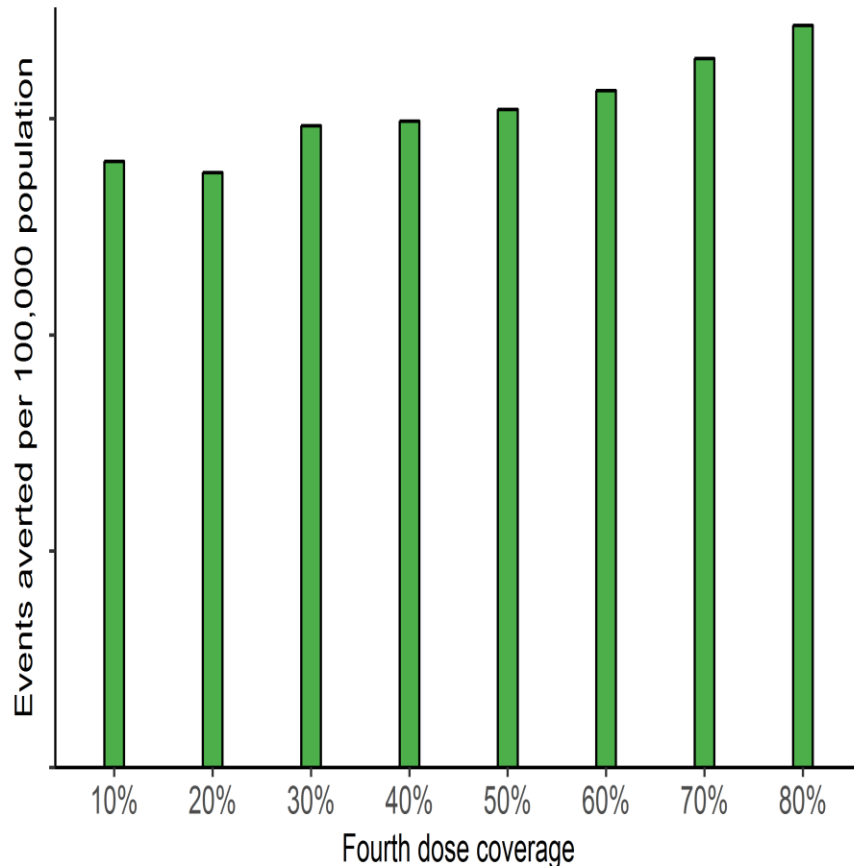


Figure 2: Events averted per 100,000 population for a single transmission setting, across a range of scenarios **for coverage of the fourth vaccine dose**. In this example, the coverage of the third dose is fixed, and the fourth dose coverage varies along the X-axis. This figure can be produced for specific population groups and transmission settings (for example in a series of plots for $PfPR_{2-10} = 10-40\%$) and different levels of coverage of the first three vaccine doses.

Illustrative examples of outputs: cost per event averted (not based on actual estimates)

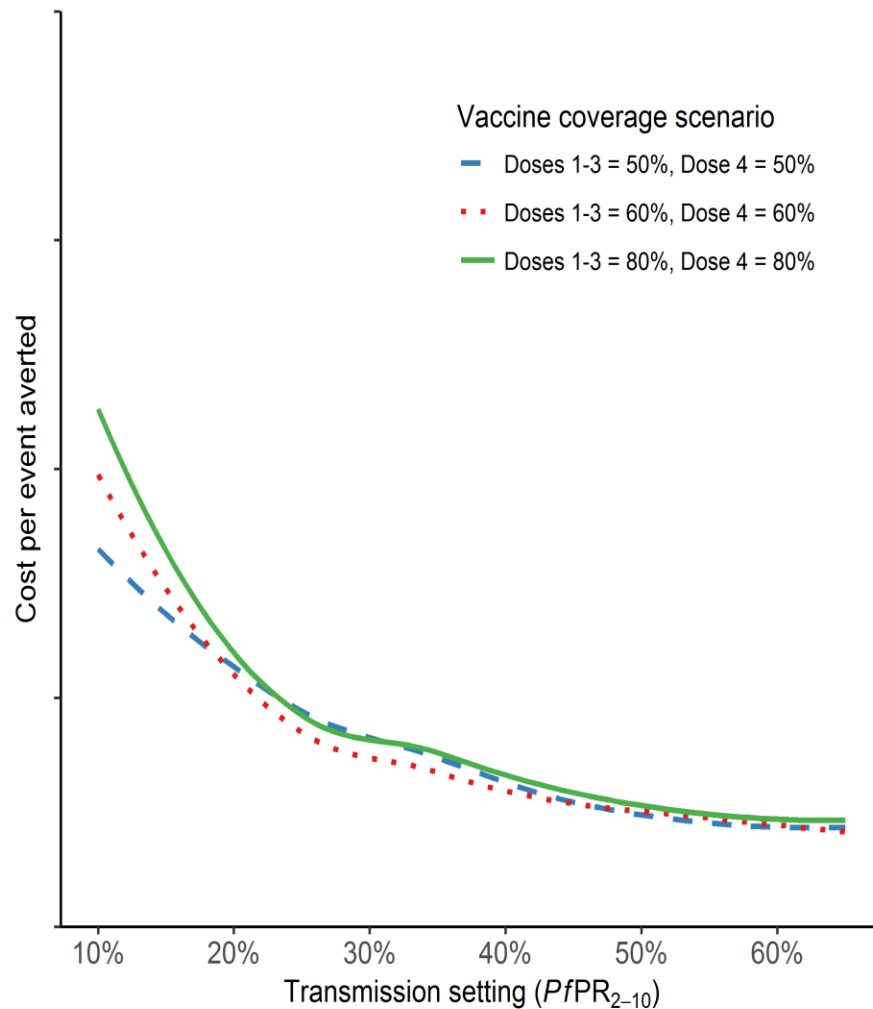


Figure 4: *Cost per event averted for a range of transmission settings, for three vaccine coverage scenarios, where coverage of doses 1–3 and dose 4 are both varied. A range of different vaccine coverage assumptions can be included.*

Timelines and activities for framework

Timeline	Activity
1Q-2Q 2018	• Seeking input on the Framework for Policy Decision, including on outcomes and associated metrics proposed for inclusion (Presented to the IVIR-AC in March 2018, PAG March 2018, SAGE/MPAC April 2018)
2Q-3Q 2018	• Modelers will generate estimates for inclusion in the Framework for Policy Decision (Presentation to IVIR-AC September 2018), modelled estimates of criteria thresholds to be incorporated into the Framework • Convene working group, including PAG and additional members from MPAC/SAGE, to deliberate on Framework Q3/4 2018 • Present the working group's report and recommendations on the Framework to SAGE and MPAC for discussion in October 2018
2Q-3Q 2019 (NOT FUNDED)	• Generate estimates using baseline household survey data from pilot areas to incorporate into the Framework (If funding allows, presentation to the PAG, SAGE, MPAC in October 2019 or April 2020)

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