World Health Organization

Background documentation for Day 1

This file contains the slides that were shown by the presenters during Day 1 of the meeting as well the background documentation shared with MPAG members ahead of the meeting.

Tuesday, 18 April 2023			
	Session 1	**Open**	
09:00 – 09:05	Opening remarks by the Director-General, World Health Organization	Dr Tedros Adhanom Ghebreyesus WHO Director-General	**For information**
09:05 – 09:10	Welcome by the Assistant Director-General for Universal Health Care/Communicable and Noncommunicable Diseases	Dr Jérôme Salomon, Assistant Director-General, UCN	
09:10 – 09:20	Welcome by the Chairperson, MPAG	Professor Dyann Wirth MPAG Chairperson	
09:20 – 10:30	Report from the Director, GMP Presentation	Dr Daniel Ngamije M. Director Global Malaria Programme	
	Session 2	**Open**	**For information**
11:00 – 11:15	Remarks and update from the US President's Malaria Initiative	Dr David Walton US Global Malaria Coordinator, US President's Malaria Initiative	
11:15- 12:00	RBM evaluation of the High burden to high impact approach Background | Presentation	Dr Melanie Renshaw RBM CRSPC Co-Chairperson	
	Session 3	**Open**	
14:00 – 15:00	Update on WHO Guidelines for malaria • Vector control and guidance on insecticide treated net prioritization • Treatment & diagnostics Presentation 1 | Presentation 2	Dr Jenny Stevenson Vector Control & Insecticide Resistance Dr Peter Olumese Diagnostics, Medicines & Resistance	**For information**
15:00 – 15:45	Revisiting comparative effectiveness in the context of the arrival of new vector control products Presentation	Dr Jan Kolaczinski Vector Control & Insecticide Resistance	**For guidance**
	Session 4	**Open**	
16:15 – 17:00	Update on certification of malaria	Dr Elkhan Gasimov	**For information**

WHO/UCN/GMP/MPAG/2023.01

	elimination and the E-2025 Global Forum Presentation	Elimination	
17:00 – 17:45	Update on RTS,S malaria vaccine implementation programme and WHO evidence review for R21 vaccine candidate Background | Presentation	Dr Mary Hamel Product & Delivery Research Ms Eliane Furrer Product & Delivery Research Dr Lindsey Wu Strategy & Agenda Setting	**For information**
17:45	*End of day*		

Report from the Global Malaria Programme

Malaria Policy Advisory Group

Geneva, Switzerland

Dr Daniel Ngamije Madandi, Director

Dr Andrea Bosman, Director a.i.

18 April 2023

Global **Malaria** Programme

World Health Organization

Welcome and thoughts from the Director, GMP

Since October …

- World malaria report 2022
- Normative guidance
- Technical meetings and publications
- Technical updates
- Country support

Outline of the *World malaria report 2022*

- Introduction
- Key events in 2021–2022
- Trends in burden of malaria
- Elimination & HBHI countries
- Surveillance
- Malaria financing
- Distribution and coverage of interventions
- Progress toward milestones of the global strategy
- Biological and other threats to malaria interventions
- PPCs and products in the R&D pipeline
- Key messages and conclusion

Four key themes in this year's report

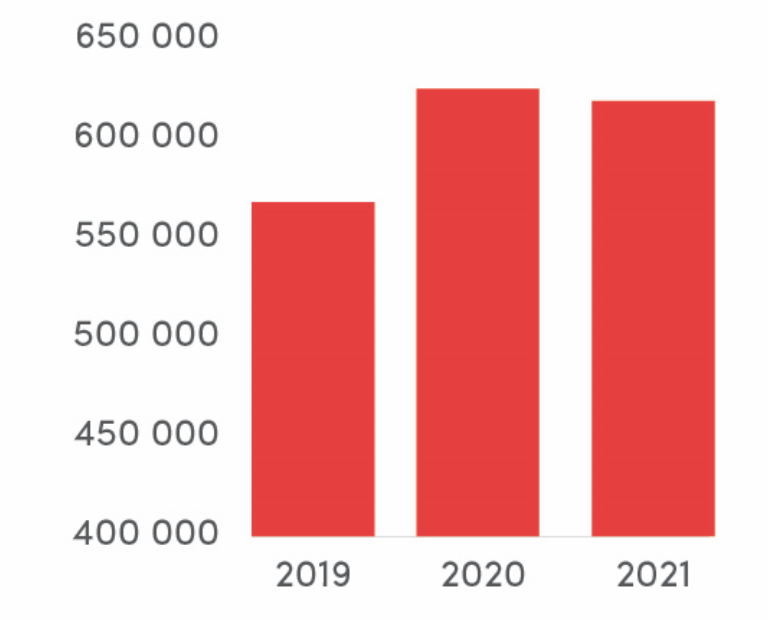
i. **Response**
ii. **Risk**
iii. **Resilience**
iv. **Research**

"By strengthening the response, understanding and mitigating the risks, building resilience and accelerating research, there is every reason to dream of a malaria-free future."

– Dr Tedros Adhanom Ghebreyesus, WHO Director-General

RESPONSE – global progress during the COVID-19 pandemic

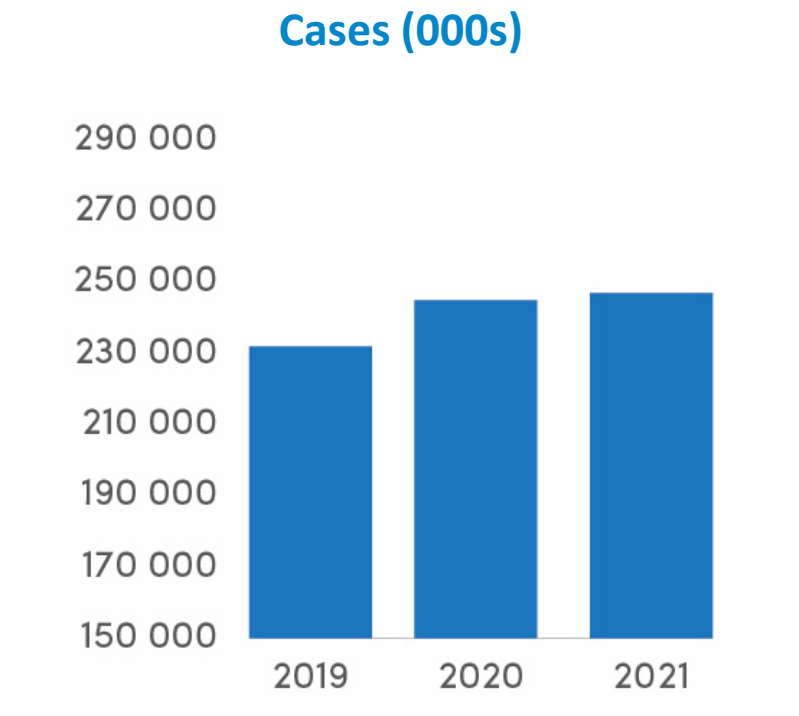
KEY MESSAGE 1: Despite COVID-related disruptions to malaria prevention, testing and treatment services, and the often-devastating impacts of the pandemic on health, social and economic systems, malaria endemic countries and their partners largely held the line against further setbacks to malaria control in 2021.



No further increase in malaria deaths in 2021:

- 568 000 in 2019
- 625 000 in 2020
- 619 000 in 2021

RESPONSE – global progress during the COVID-19 pandemic



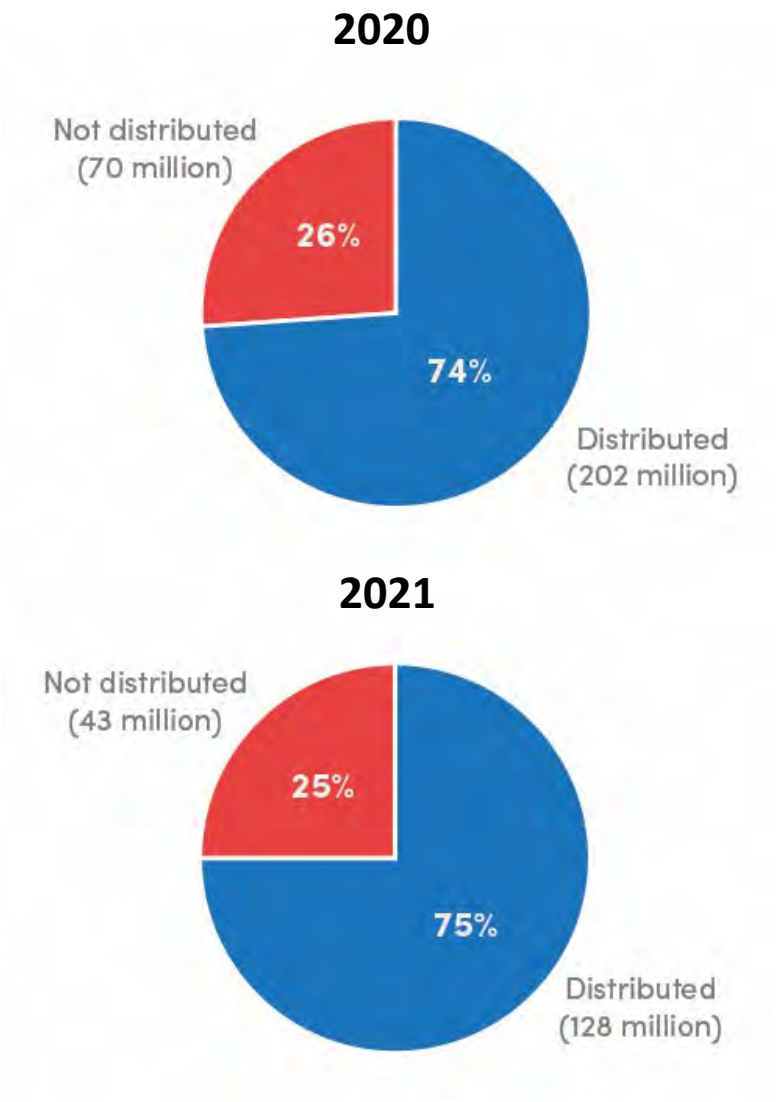
Malaria cases continued to rise between 2020 and 2021, but at a slower rate:

- **232** million cases in 2019
- **245** million cases in 2020
- **247** million cases in 2021

Two-year impact of COVID-19 pandemic:

- **63 000** more malaria deaths
- **13 million** more malaria cases

RESPONSE – distribution of ITNs remained stable

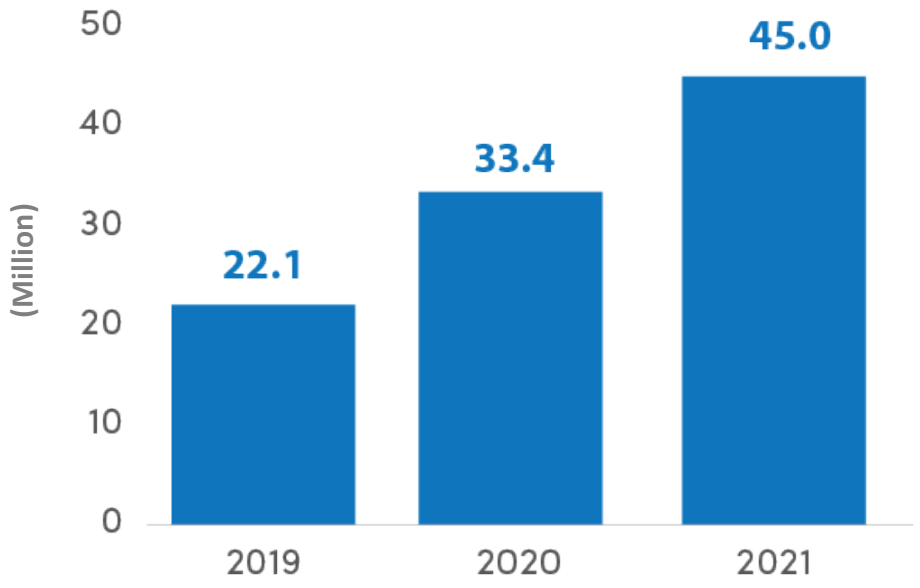


Percentage of planned insecticide-treated net (ITN) distributions that reached target communities:

- **2020: 74%** of nets (202 million)
- **2021: 75%** of nets (128 million – similar to the ITN distribution levels reported before the pandemic)

RESPONSE – expanded access to seasonal malaria chemoprevention

Average number of children treated with SMC, per cycle, by year, in 15 African countries, 2019–2021



Number of children treated with seasonal malaria chemoprevention (SMC) in 15 African countries:

- 22.1 million in 2019
- 33.4 million in 2020
- 45 million in 2021

SMC is recommended by WHO for children living in areas with highly seasonal malaria transmission in Africa

RESPONSE – roll-out of the world's first malaria vaccine, RTS,S/AS01

RTS,S/AS01 is the first vaccine recommended by WHO to prevent malaria in children living in regions with moderate-to-high *P. falciparum* malaria transmission

- In 2021, approx 364 000 children were reached with at least 1 dose of vaccine through the MVIP in Ghana, Kenya and Malawi (Nearly **1.5 million children** vaccinated to date, since 2019)
- **Gavi reports unprecedented demand for a vaccine**: At least 28 countries have expressed interest in introducing the vaccine; 14 countries have been approved for Gavi support already, and will continue or start phased introductions in early 2024
- **Increasing supply** to meet demand is a WHO priority

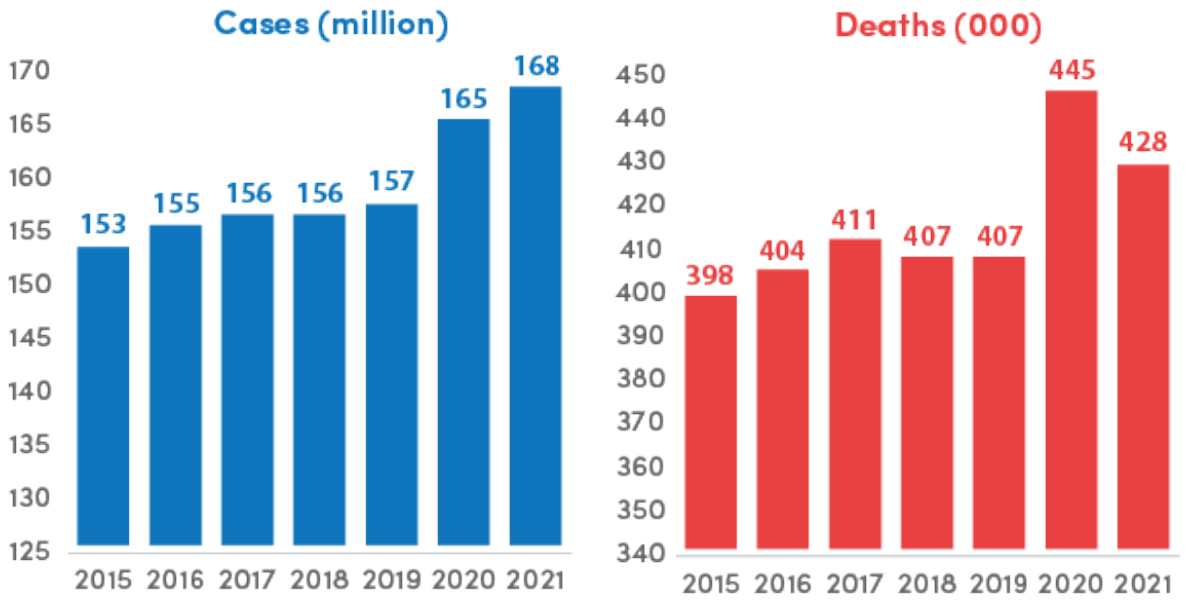
RESPONSE – distributions of ACTs and RDTs maintained

Sales and country distribution of artemisinin combination therapies (ACTs)

Despite supply chain and logistical challenges, countries maintained RDT and ACT deliveries to health facilities during the pandemic

- 262 million RDTs distributed in 2021 (similar to pre-pandemic levels) vs. 301 million RDTs in 2020 (highest on record) and 254 million RDTs in 2019.
- 242 million ACTs distributed in 2021 vs 260 million in 2020 and 239 million in 2019.

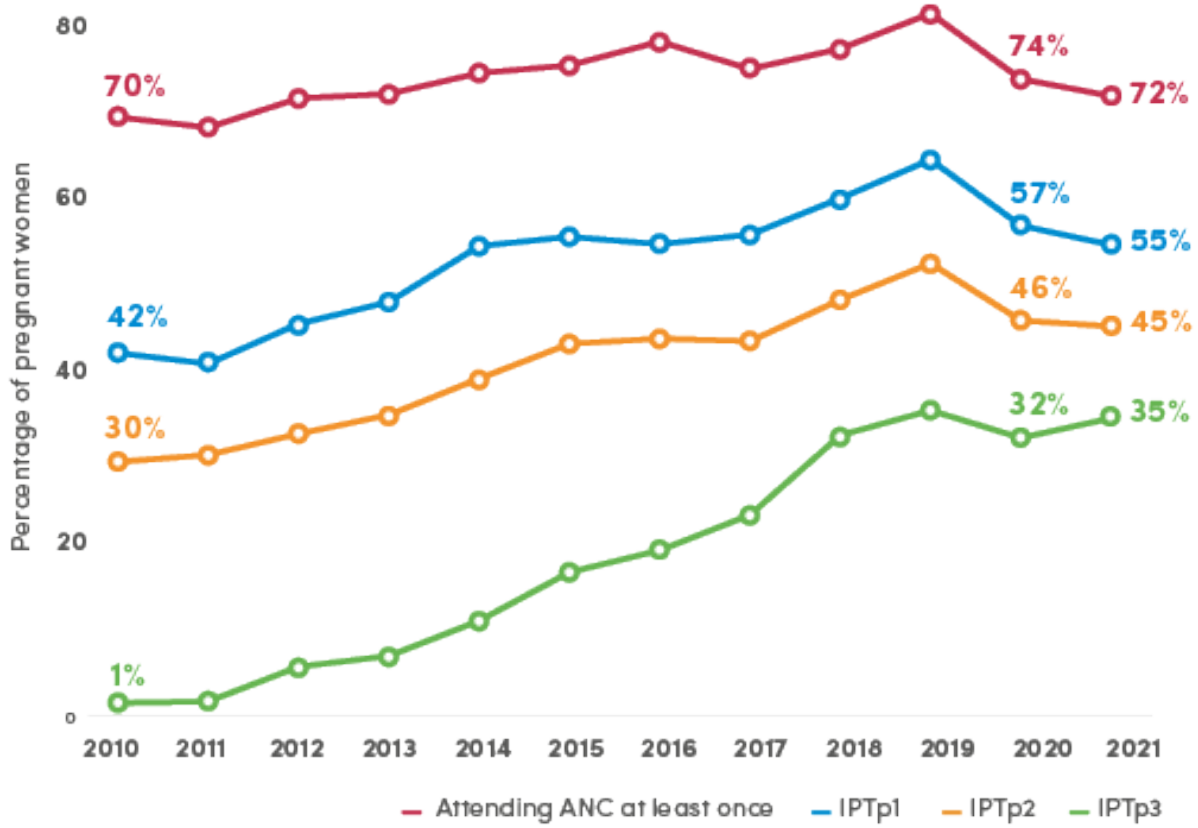
RESPONSE – cases and deaths stable in high burden countries



The 11 High Burden to High Impact (HBHI) countries largely held the line against malaria in 2021

- **2021:** 428 000 deaths and 168 million cases
- **2020:** 445 000 deaths and 165 million cases

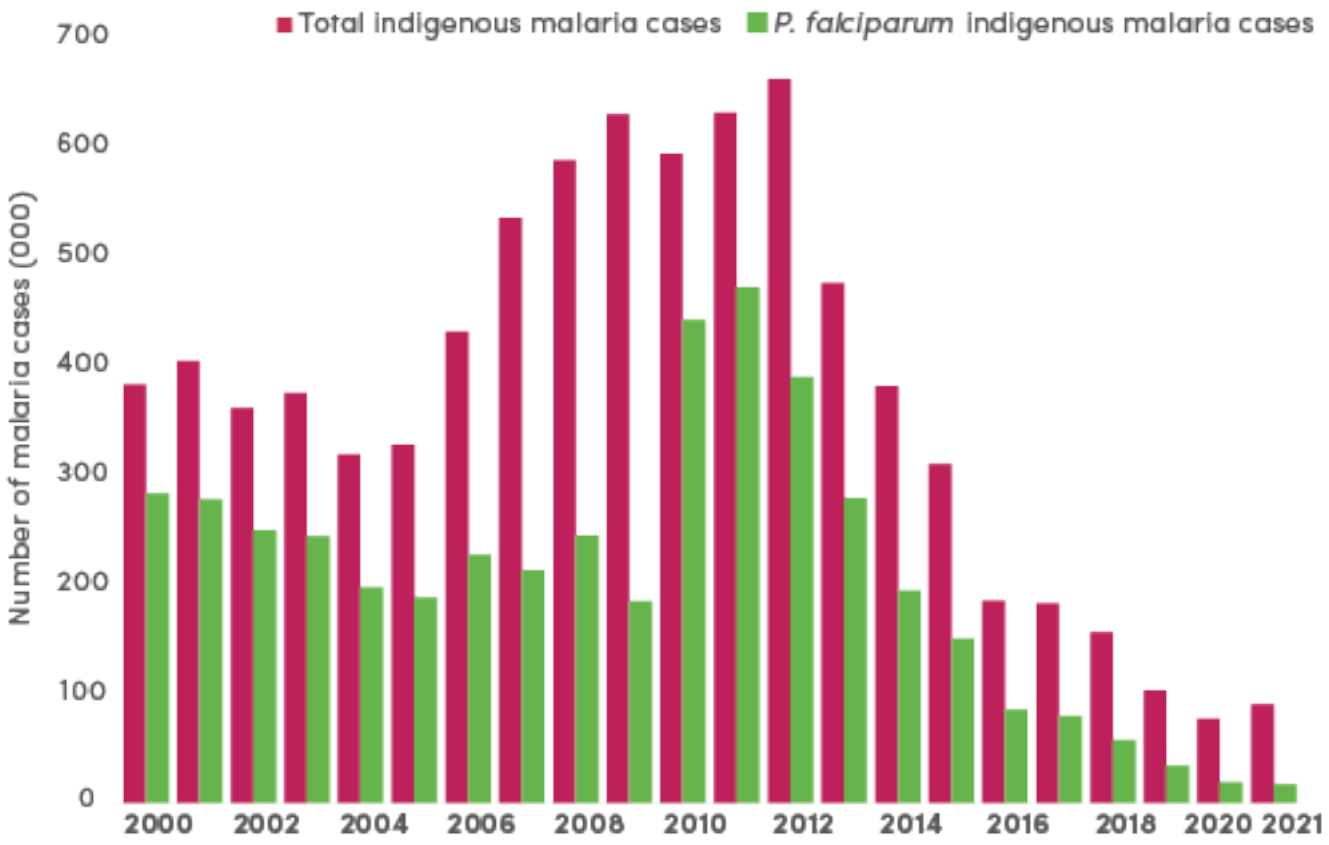
RESPONSE – stable coverage of IPTp3 for pregnant women



Overall, coverage of IPTp3 (3-dose regimen) remained stable during the pandemic – despite a reduction in antenatal care attendance:

- **2019: 35%**
- **2020: 32%**
- **2021: 35%**

RESPONSE – continued progress in the Greater Mekong subregion (GMS)

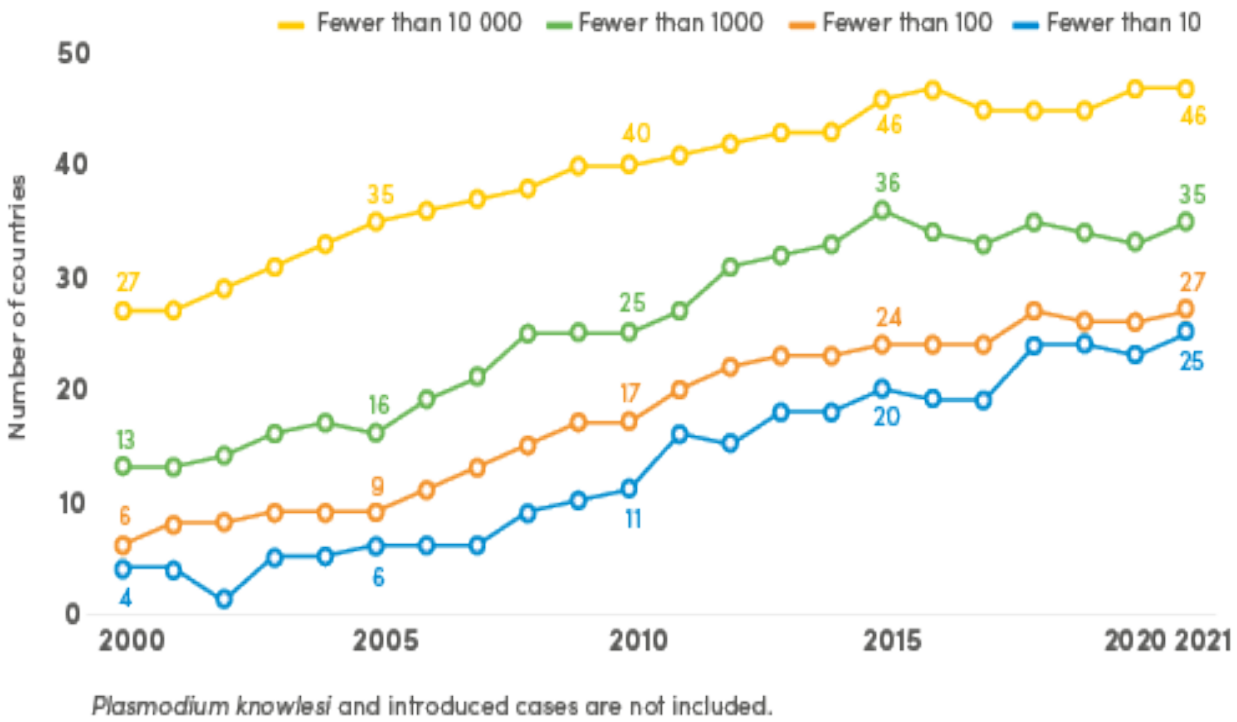


The 6 countries in the Greater Mekong subregion are Cambodia, China, the Lao People's Democratic Republic, Myanmar, Thailand and Viet Nam.

Trends in malaria cases in the 6 GMS countries between 2020 and 2021:

- 12.2% decline of *P. falciparum* cases across the subregion
  - Notable in view of ongoing threat of antimalarial drug resistance
- 17.3% increase in malaria cases overall
  - Cases of *P. vivax* malaria accounted for nearly all of this increase.

RESPONSE – progress maintained in malaria-eliminating countries

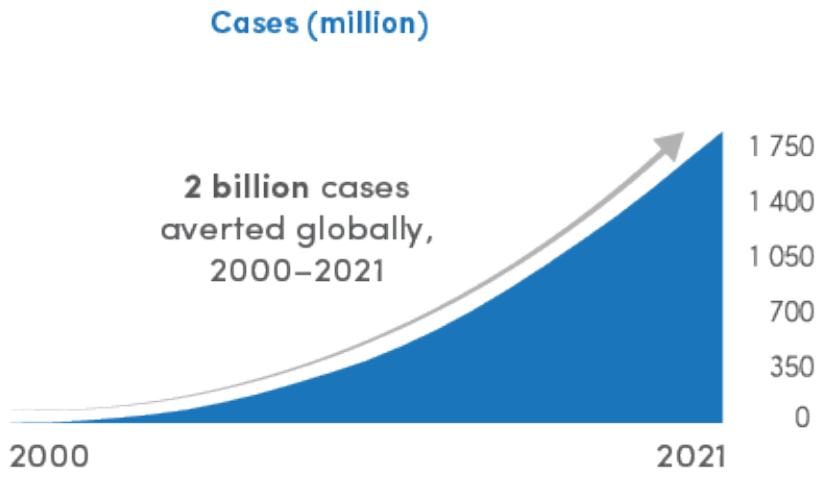


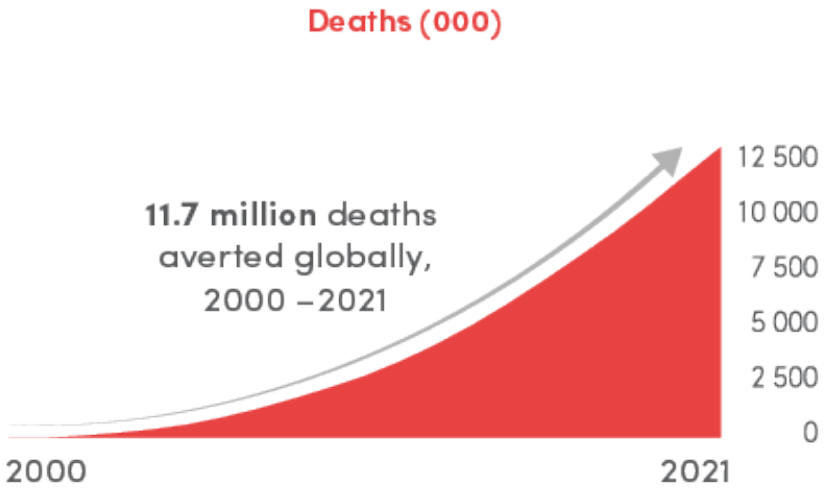
Plasmodium knowlesi and introduced cases are not included.

Many countries with a low burden of malaria maintained effective responses during the pandemic

- 35 countries with fewer than 1000 cases in 2021 vs. 33 in 2020
- 27 countries with fewer than 10 cases in 2021 vs. 26 in 2020

RESPONSE – global malaria cases and deaths averted, 2000–2021





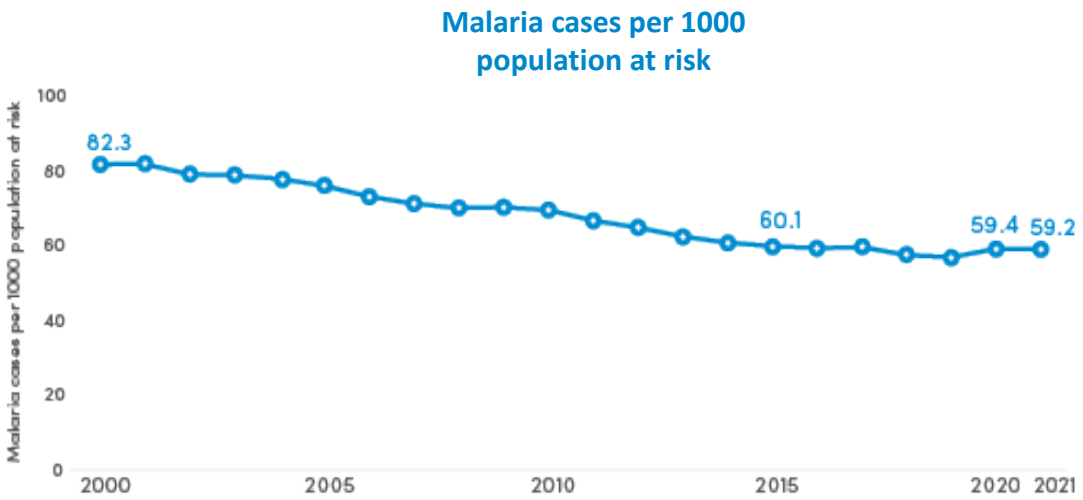
Globally, an estimated 2 billion cases and 11.7 million deaths were averted between 2000 and 2021

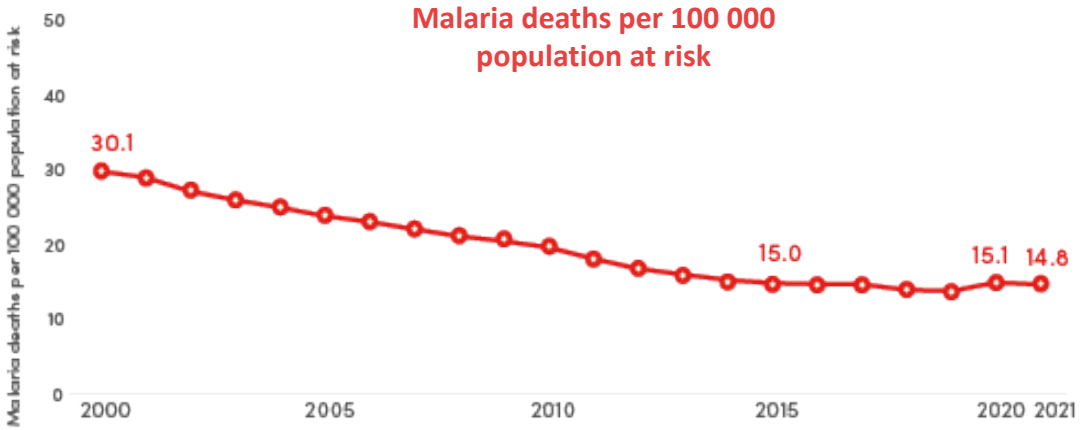
- Most of cases (82%) and deaths (95%) averted since 2000 were in the African Region

RISKS – several converging threats to process against malaria

KEY MESSAGE 2: **Efforts to curb malaria continue to face a convergence of threats, particularly in the African Region, which carries the heaviest burden of the disease. Disruptions during the pandemic together with other humanitarian crises, health system challenges, restricted funding, rising biological threats (vector insecticide resistance, 2) antimalarial drug resistance; 3) parasite pfhrp2/3 gene deletions; and 4) invasive vector species) and a decline in the effectiveness of core disease-cutting tools are undermining progress towards global malaria goals.**

RISKS – long-term trends in malaria case incidence and mortality rates



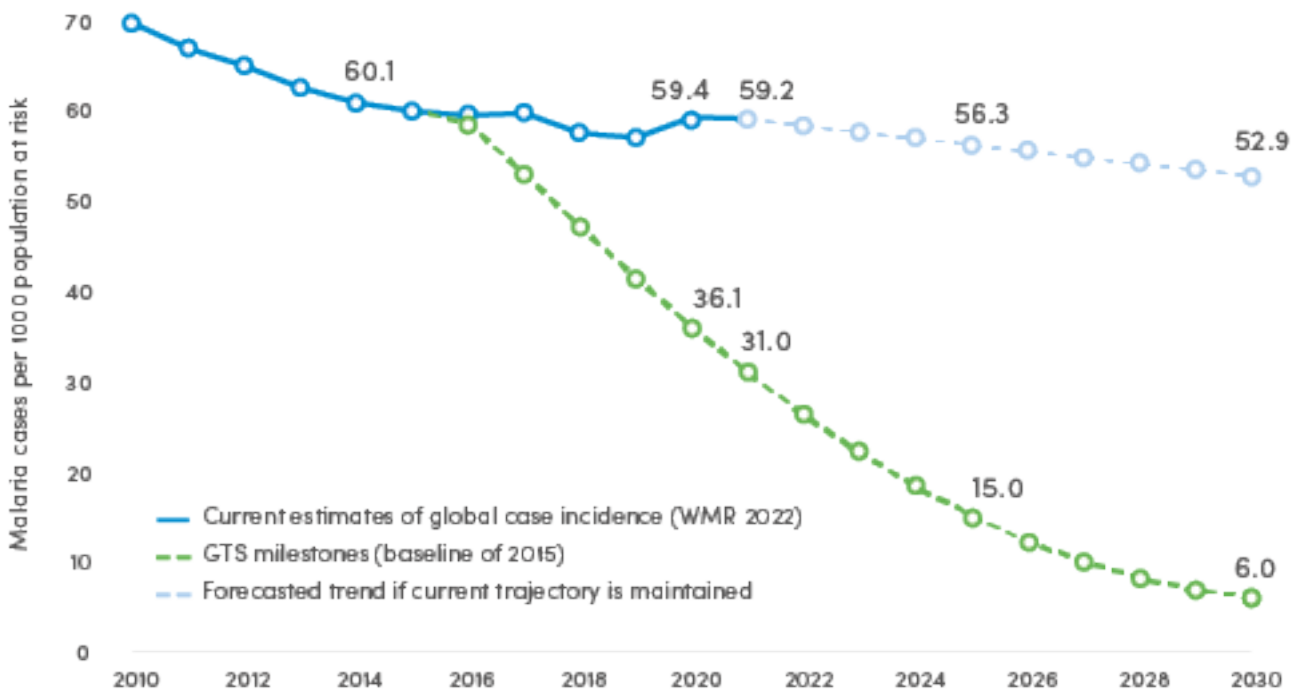


Between 2000 and 2015, a 27% reduction in global malaria case incidence and a 50% decline in mortality rates

- But by 2017 progress had stalled, particularly in high burden countries in Africa

RISKS – global progress towards GTS targets remains off track

Comparison of global progress in malaria case incidence, considering two scenarios: current trajectory maintained (blue) and GTS targets achieved (green)



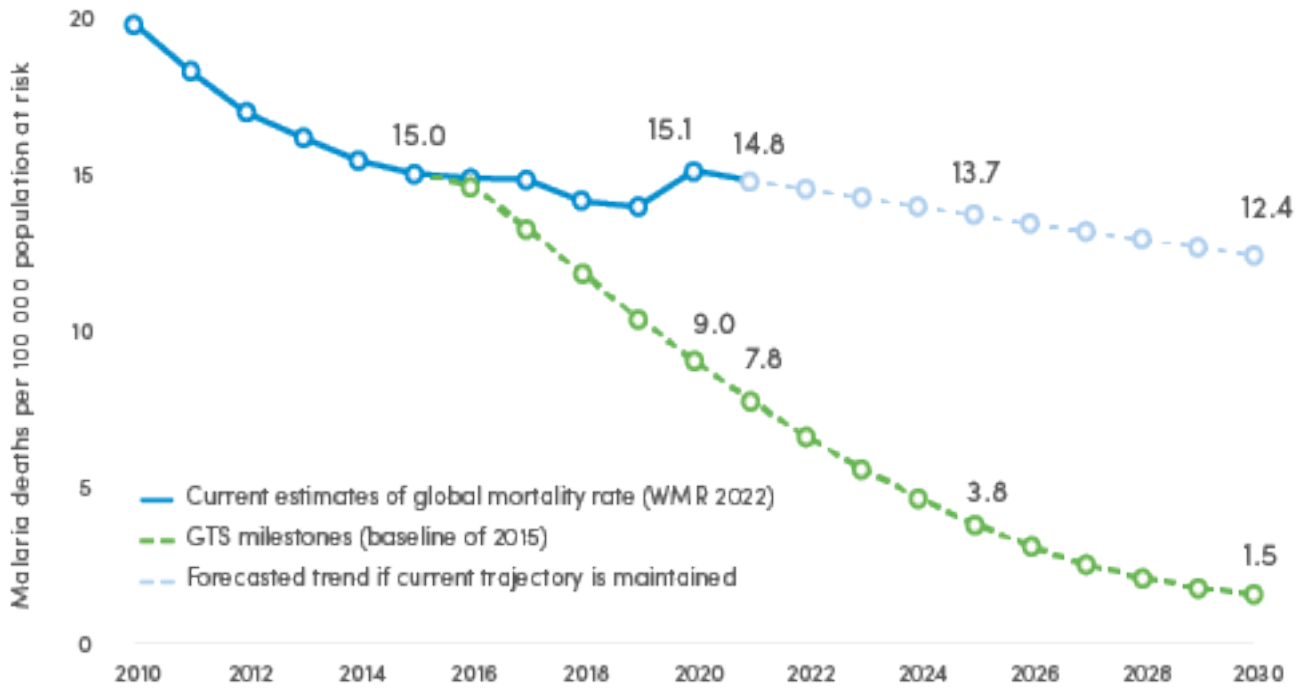
The WHO *Global technical strategy for malaria 2016-2030* (GTS) aimed to reduce malaria mortality and case incidence by at least 40% by the year 2020, at least 75% by 2025 and at least 90% by 2030.

Progress in reducing malaria case incidence remains off track:

- In 2021, global malaria case incidence was 59 cases per 1000 people at risk against a target of 31 – off track by 48%

RISKS – global progress towards GTS targets remains off track

Comparison of global progress in malaria mortality, considering two scenarios: current trajectory maintained (blue) and GTS targets achieved (green)

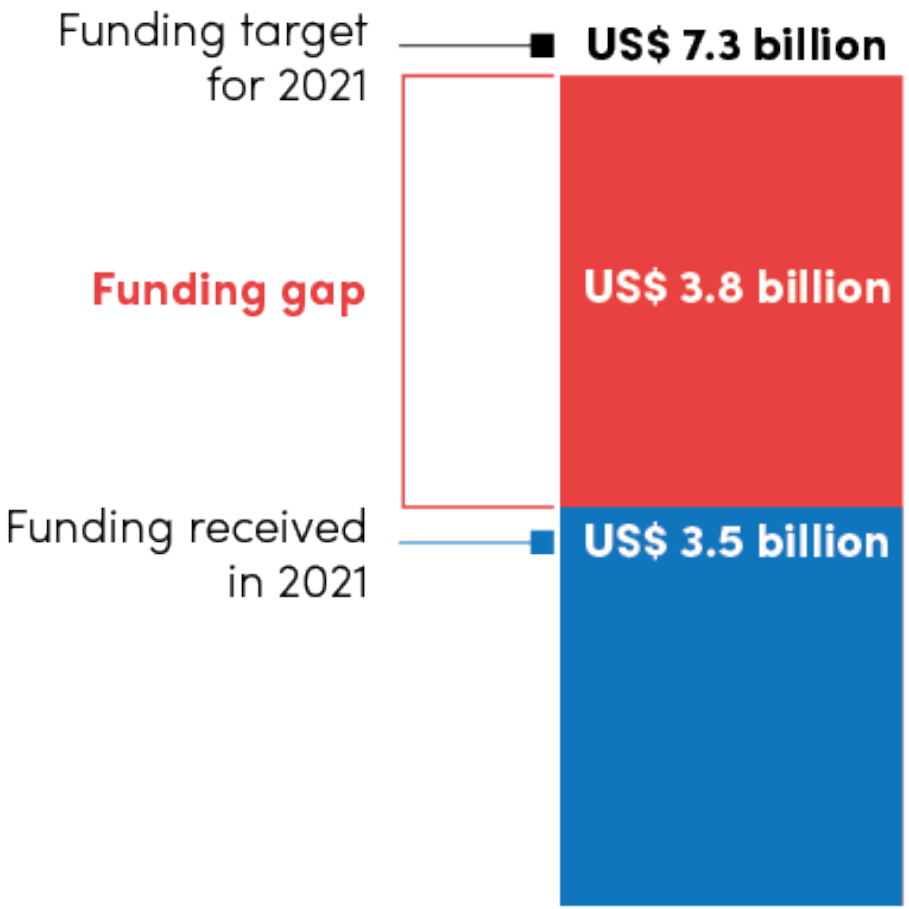


The WHO *Global technical strategy for malaria 2016-2030* (GTS) aimed to reduce malaria mortality and case incidence by at least 40% by the year 2020, at least 75% by 2025 and at least 90% by 2030.

Progress in reducing malaria mortality is also off track

- In 2021, the global mortality rate was 14.8 deaths per 100 000 people at risk against a target of 7.8 – off track by 48%

RISKS – funding far off target, and the gap continues to widen

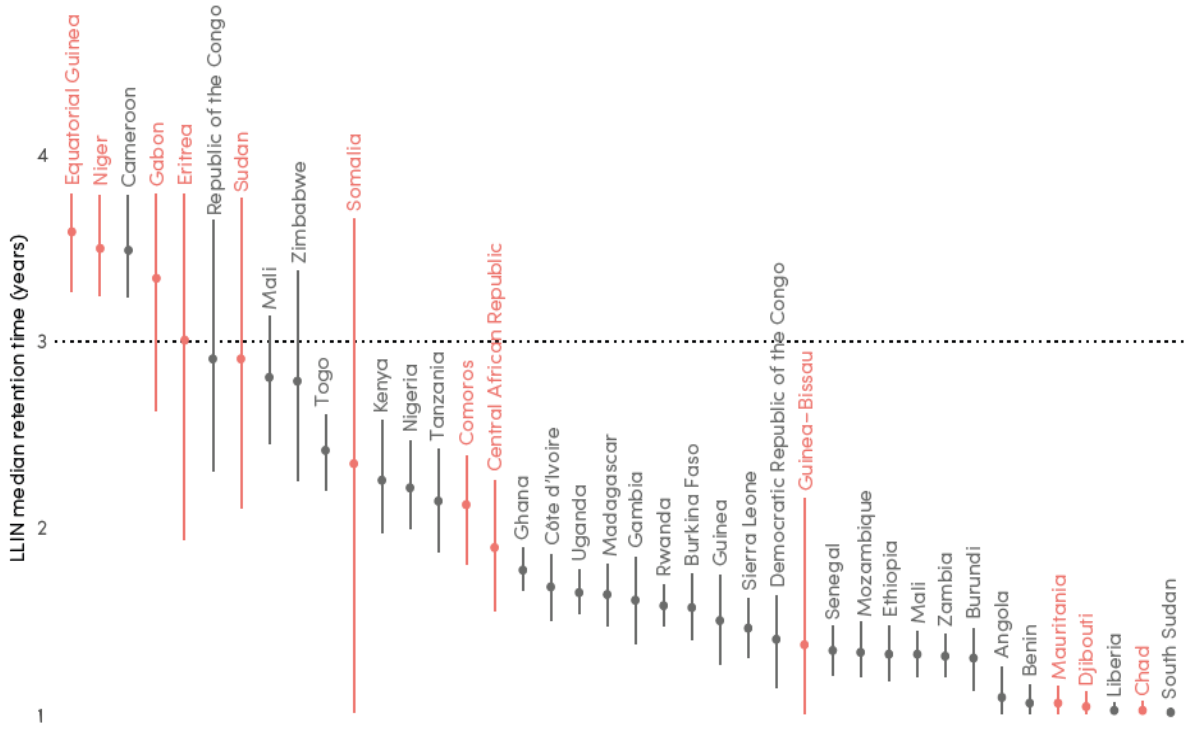


In 2021, a total of US$ 3.5 billion invested globally in malaria control and elimination against a target of US$ 7.3 billion. Funding gap has widened over the last 3 years:

- **2019:** US$ 2.6 billion
- **2020**: US$ 3.5 billion
- **2021**: US$ 3.8 billion

➢ The US$ 15.7 billion raised through the Global Fund 7th Replenishment fell short of the US$ 18 billion target

RISKS – a decline in the effectiveness of insecticide-treated nets (ITNs)

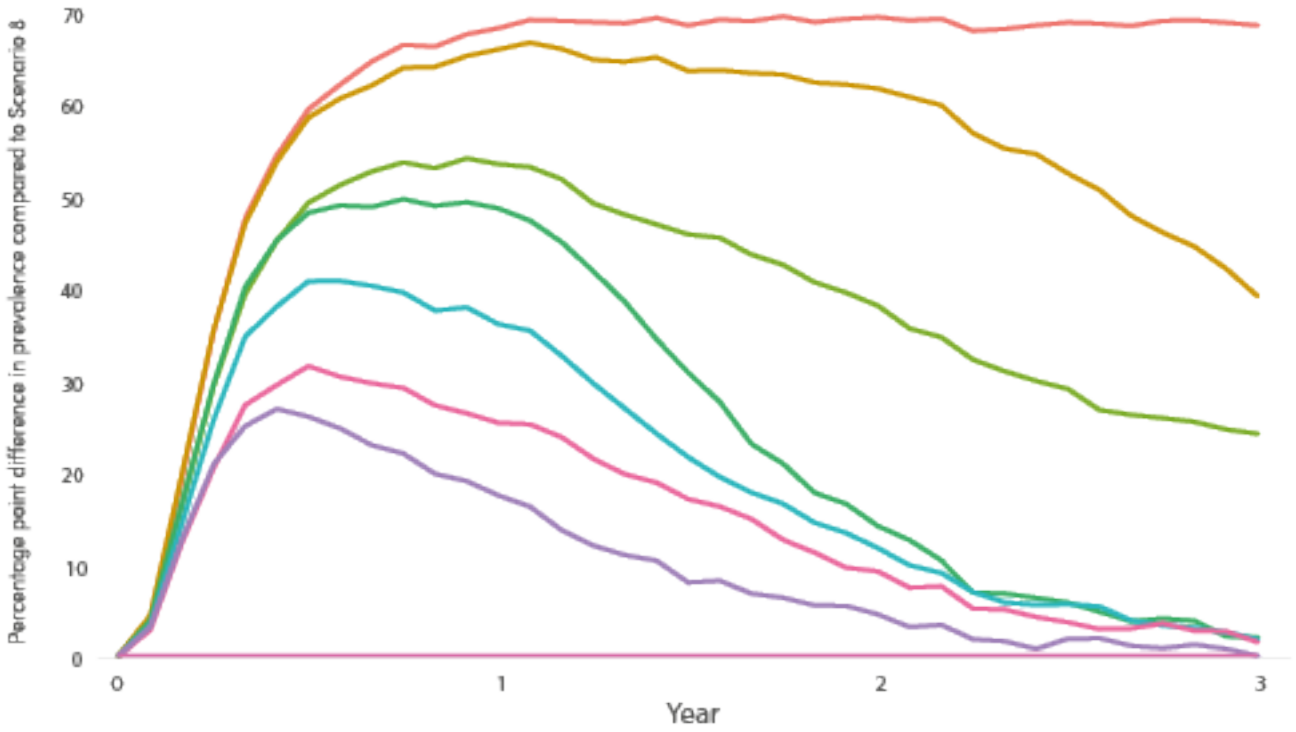


Median LLIN retention time by country, ordered from highest to lowest

From 2019–2021: about 590 million ITNs delivered in sub-Saharan Africa

- With perfect allocation and retention of ITNs, coverage should be 100%. But current coverage is only about 54%.
- **Net retention:** Households keep nets on average for **1.9 years** – but this is highly variable. Net campagins are held on average every 3 years, leaving significant gaps in protection.

RISKS – a decline in the effectiveness of insecticide-treated nets (ITNs)



- Scenario 1: "Ideal" nets, perfect campaigns, perfect net use rate, nets retained forever
- Scenario 2: "Ideal" nets except that insecticide wanes; perfect campaigns, net use rate, and net retention
- Scenario 3: "Ideal" nets except that insecticide wanes and vectors are not fully susceptible; net use rate, and net retention
- Scenario 4: "Realistic" nets: net durability wanes, insecticide wanes, and vectors are not fully susceptible; perfect campaigns, net use rate, and net retention
- Scenario 5: "Realistic" nets, realistic campaigns (87% coverage), perfect net use rate and net retention
- Scenario 6: "Realistic" nets, realistic campaigns, realistic net use rate (83%), perfect net retention
- Scenario 7: "Realistic" nets, realistic campaigns, realistic net use rate, realistic net retention (50% of nets discarded after 1.9 years)
- Scenario 8: No LLINs in use in the population

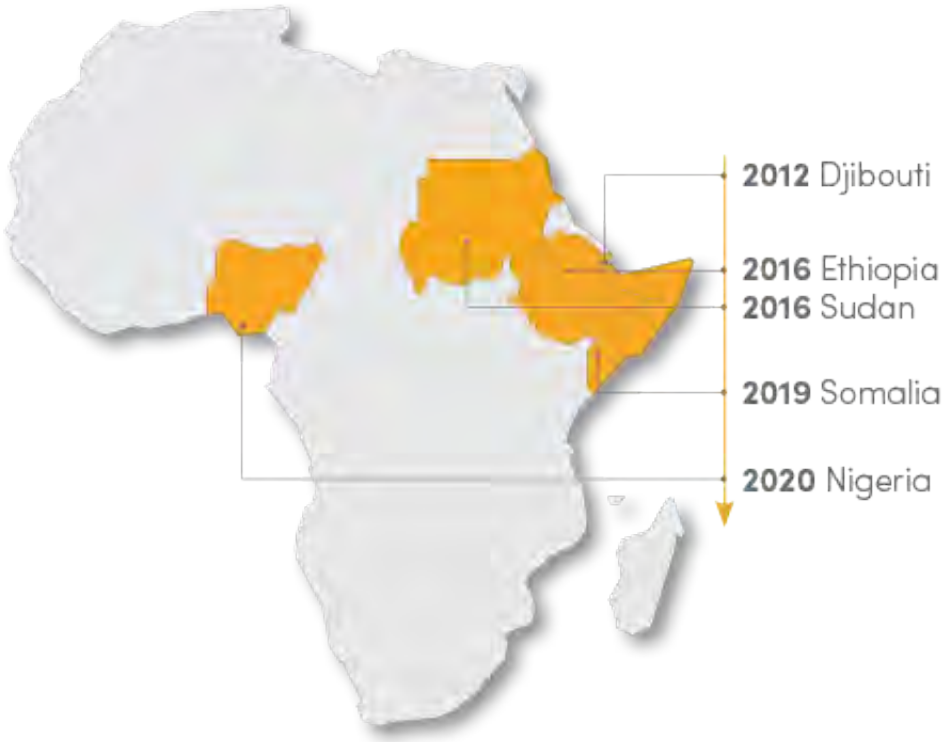
Additional challenges to the effectiveness of pyrethroid-only ITNs include insecticide resistance, insufficient access and changing behaviour of mosquitos

- Despite these challenges, WHO recommends the continued use of ITNs across malaria-endemic settings

RISKS – a decline in the effectiveness of other core malaria control tools

- **Challenges to the effectiveness of indoor residual spraying (IRS)**
  - As for ITNs, insecticide resistance is a major threat to the continued effectiveness of IRS
  - Costs of annual or more frequent IRS are high. Longer-lasting insecticides requiring fewer spray campaigns could reduce costs.
- **Decreased sensitivity of commonly used rapid diagnostic tests (RDTs)**
  - An increasing proportion of P. *falciparum* parasites no longer express the protein (HRP2) most widely used to detect malaria through rapid diagnostic tests (RDTs).
  - Such parasites can escape detection by RDTs, presenting a major threat to early diagnosis and treatment.

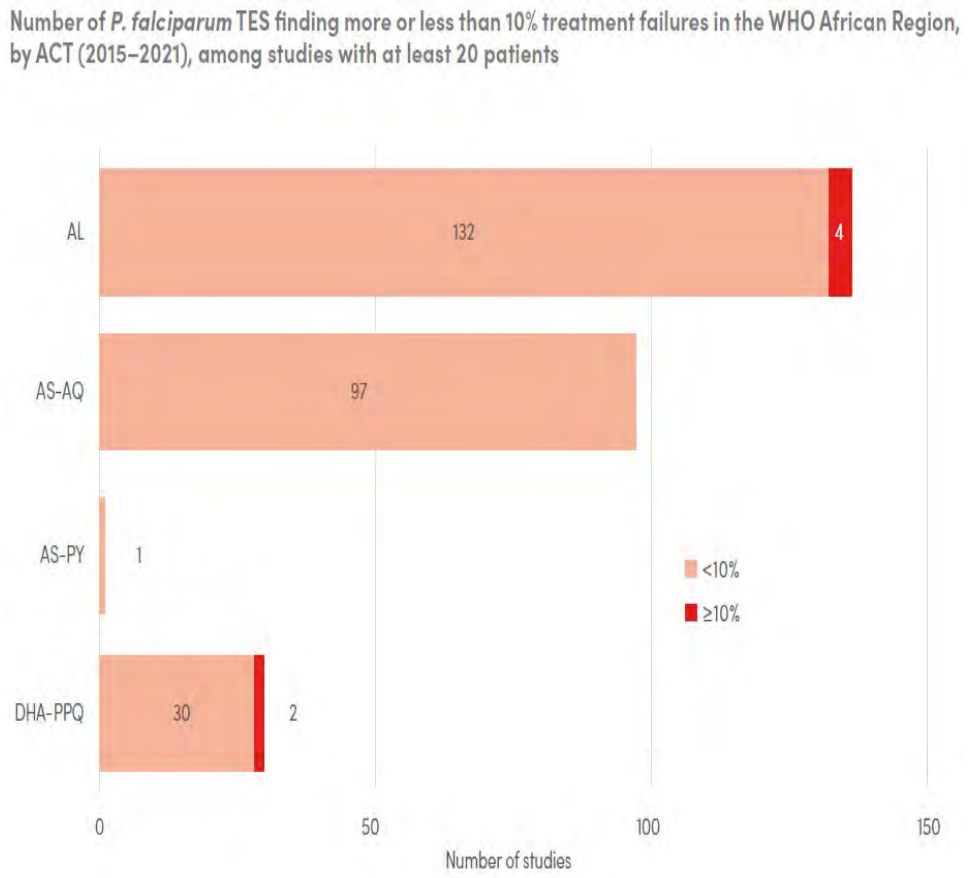
RISKS – other key threats in the global response to malaria



Invasion of Africa by the *Anopheles stephensi*

- Originally native to parts of South Asia, *An. stephensi* has been expanding its range over the last decade
- Thrives in urban environments and can transmit both *P. falciparum* and *P. vivax* malaria.
- Resistant to many of the insecticides used in public health.

RISKS – other key threats in the global response to malaria



Rising antimalarial drug resistance in Africa

- Partial resistance to artemisinin, the core compound of ACTs, confirmed in the Greater Mekong and in 3 countries in Africa: Eritrea, Rwanda and Uganda.
- Resistance to partner drugs within ACTs not confirmed to date, and the treatment remains highly efficacious. However, data are lacking for several countries, and contradictory findings need to be further assessed.
  - In view of heavy reliance on ACTs, particularly artemether-lumefantrine (AL), widespread treatment failure could have very serious consequences.

RISKS – other key threats in the global response to malaria

- **Humanitarian crises** due to conflicts, famine, flooding and other health emergencies in 37 malaria-endemic countries affected hundreds of millions of people from 2019–2021
- **Weak surveillance systems** remain a key obstacle to data-informed decision making
- **The ongoing pandemic**, the war in Ukraine, a global recession and increasing fuel and commodity costs are further undermining the global malaria response

RESILIENCE – adaptation under severe challenges, opportunities for greater resilience

KEY MESSAGE 3: **Despite these challenges, national malaria programmes have demonstrated their resilience through the worst of times. Targeted new strategies, restored funding and strengthened health systems could help countries regain lost ground and build an even more resilient response to malaria.**

RESILIENCE – mitigating impacts of the COVID-19 pandemic

- **Country leadership** – National malaria programmes showed courage in the face of adversity and a remarkable commitment to ensuring the continuity of malaria services
- **Global coordination** – WHO convened workstreams and, in collaboration with partners, developed guidance for countries and resolved bottlenecks
- **Global funding** – the COVID-19 Response Mechanism (C19RM) fund, managed by the Global Fund, and flexibilities in Global Fund and PMI core funding were critical to country responses during the pandemic

RESILIENCE – targeted strategies aim to build an even more resilient response

- **Tackling antimalarial drug resistance in Africa:** new WHO strategy to curb drug resistance in the African continent

- **Stopping the spread of *Anopheles stephensi* in Africa:** new strategy to respond to this invasive malaria vector

RESILIENCE – targeted strategies aim to build an even more resilient response

- **Responding to malaria in urban areas:** new framework from WHO and UN-Habitat provides guidance for city leaders as they work to control malaria in a rapidly urbanizing world

- **Using data for impact:** new WHO toolkit aims to help countries assess their malaria surveillance systems and identify areas for investment

RESILIENCE – increased flexibility and access to WHO malaria recommendations

Malaria Toolkit app

MAGICapp

- The consolidated *WHO guidelines for malaria* are now accessible through the MAGICapp platform in 4 languages.
- All of WHO's most up-to-date recommendations can also be found in the Malaria Toolkit mobile app
- WHO is encouraging countries to tailor the recommendations to local disease settings, using local data, for maximum impact.

RESEARCH – new tools in the pipeline

KEY MESSAGE 4: A promising R&D pipeline is poised to bring next-generation malaria control tools that could help accelerate progress towards global targets.

- Investments in R&D yielded the development of RDTs, ACTs and ITNs – the backbone of the global malaria response since 2000 – as well as the first malaria vaccine, now recommended for use and implementation ongoing or beginning in several African countries
- Looking ahead, new types of vector control technologies, diagnostics, malaria medicines and next generation vaccines hold promise.

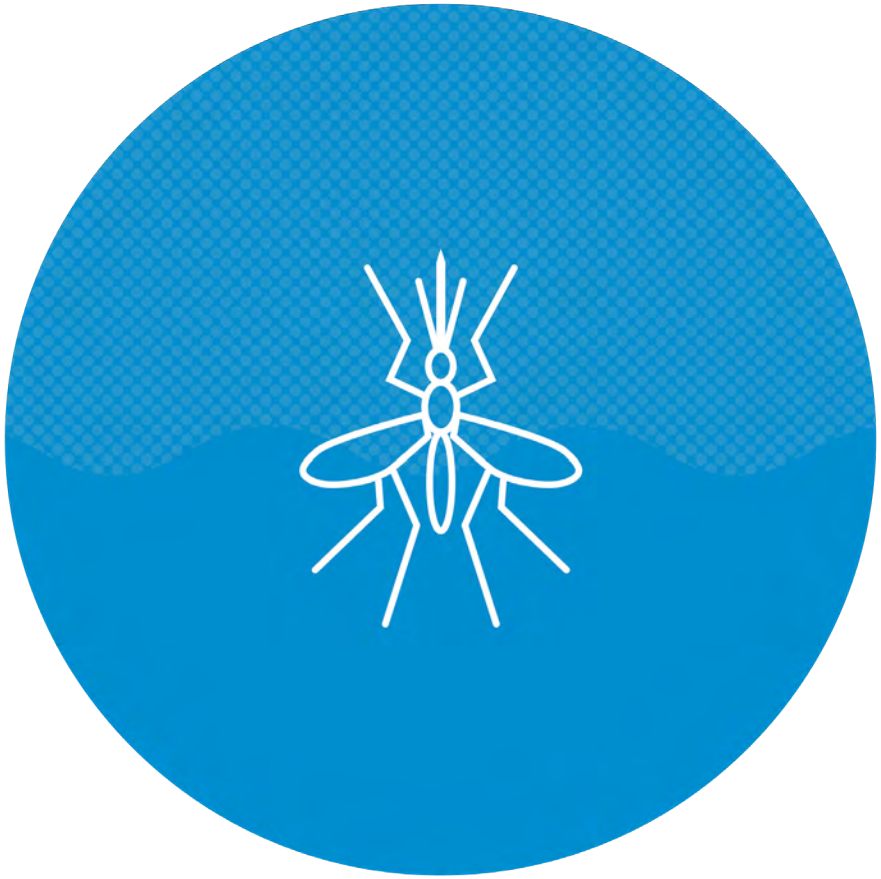
RESEARCH – WHO guidance and product development partners

Future R&D will benefit from new WHO guidance on target product profiles (TPPs) and preferred product characteristics (PPCs).

- PPCs outline the intended use, target populations and other desired attributes of malaria control products, including characteristics related to safety and efficacy.

Product development partners such as FIND, Unitaid, MMV and IVCC have also played a critical role in catalyzing malaria R&D and in bringing various products to markets.

RESEARCH – key opportunities in vector control



- **ITNs with new insecticide combinations that overcome the limitations of pyrethroid-only nets**
- **Many other vector control products in the R&D pipeline**, such as targeted sugar baits that attract mosquitoes, spatial repellents, lethal house lures and genetic engineering of mosquitoes.

RESEARCH – vaccines and monoclonal antibodies and in development

Vaccines in development

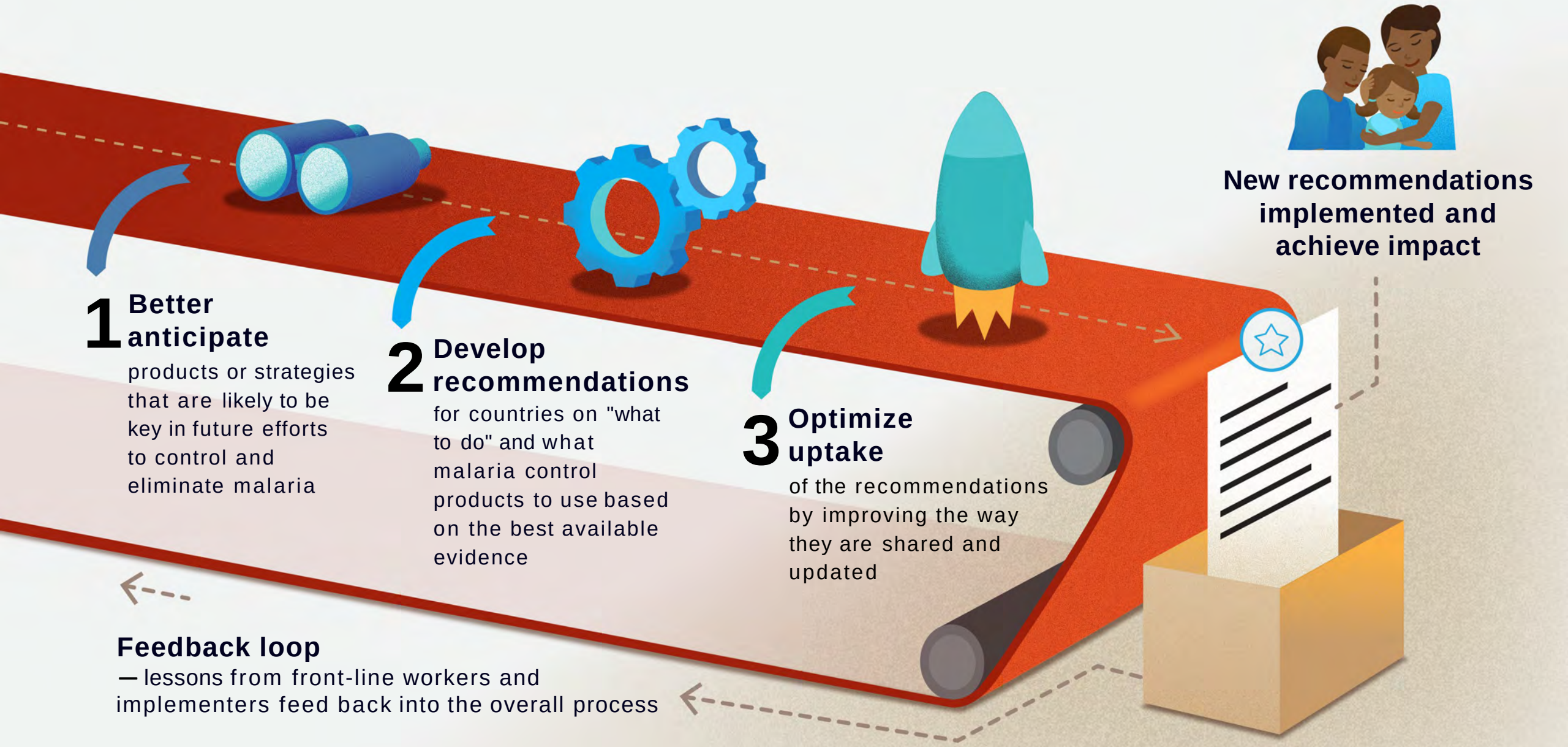
- Most advanced vaccine in clinical development is R21/MatrixM (in Phase 3), currently seeking WHO recommendation and prequalification.
    - No head-to-head comparison with RTS,S; tested in different transmission settings/context – not possible to determine if one is more efficacious than other.
- Other vaccines in the pipeline include those that target the blood-stage, aim to reduce transmission, as well as vaccines to protect against *P. vivax* malaria or malaria in pregnancy

Monoclonal antibodies (mAbs) for malaria prevention is a new area of R&D. In 2021, WHO convened a scientific development group to develop PPCs for this product area.

- Several malaria mAbs in development, including clinical trials in Kenya and Mali, which aim to reduce clinical malaria in children

Our normative work

WHO GMP normative work: 3 steps in the pathway



1 Better anticipate
products or strategies that are likely to be key in future efforts to control and eliminate malaria

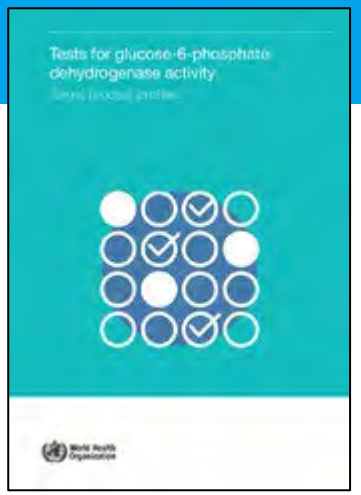
2 Develop recommendations
for countries on "what to do" and what malaria control products to use based on the best available evidence

3 Optimize uptake
of the recommendations by improving the way they are shared and updated

New recommendations implemented and achieve impact

Feedback loop
— lessons from front-line workers and implementers feed back into the overall process

Better Anticipate



Preferred product characteristics (PPCs)/ Target product profiles (TPPs) published:

- Tests for glucose-6-phosphate dehydrogenase activity
- Vector control products targeting outdoor malaria transmission Preferred product characteristics

Preferred Product Characteristics (PPCs) in development:

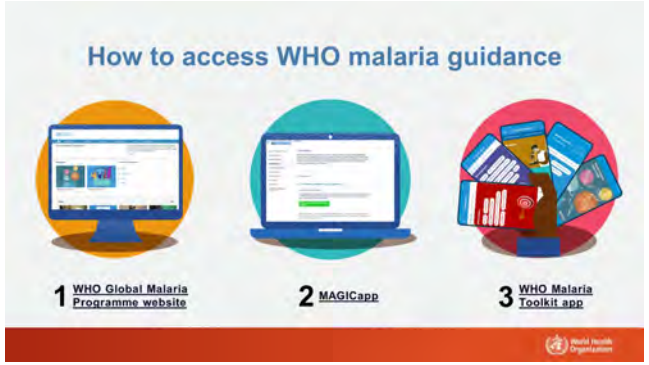
- Monoclonal antibodies
- Drugs for chemoprevention
- Tests for risk of *P. vivax* relapse (to guide radical cure and for population-based screening)

Develop recommendations: two Guideline versions released

- **25 November 2022 – updates to the case management of malaria**
  - the addition of new molecules for the treatment of uncomplicated malaria
  - optimization of the dosage regimen for anti-relapse treatment
  - updates on the use of antimalarial medicines in special risk populations including pregnant women

- **14 March 2023 – new recommendations on 2 classes of insecticide-treated nets**
  - new WHO recommendations on two classes of insecticide-treated nets that were established following the generation of evidence on the epidemiological impact of pyrethroid-chlorfenapyr and pyrethroid-pyriproxyfen ITNs
  - WHO and partners also developed separate guidance on ITN prioritization under resource constrained conditions

Optimize uptake



- **Dissemination strategy:** GMP continues to implement priorities identified in Feb 2022. Latest updates include:
  - MAGICapp: consolidated malaria guidelines available in 4 languages (Eng, Fr, Sp, Ar)
  - Mobile app: Fr and Sp language versions expected by Q3 2023
  - Animated videos: 3 new videos expected in Q2 2023 focused on (1) WHO recommendations on new types of ITNs; (2) WHO urban malaria framework; and (3) WHO initiative to stop the spread of *Anopheles stephensi*

- **Dissemination taskforce:** Informal group established in late 2021 to guide and support WHO's malaria guidance dissemination efforts. Three meetings held in 2022.
  - Members include more than 25 representatives from all regions and many partner organizations
  - Many recommendations from taskforce members have been taken on board
  - Taskforce meetings to continue on an ad hoc basis

Technical meetings and Publications

WHO Technical Meetings since October 2022

- Technical consultation to review the effectiveness of rectal artesunate used as pre-referral treatment of severe malaria in children (18-19 October; Geneva)
- 3rd Meeting of the Malaria Dissemination Taskforce (18 October; virtual)
- SAGE/MPAG Working Group on Malaria Vaccines: Review pathway and initial evidence review of R21/MatrixM (15 November and 7-8 March, virtual)
- 4th Annual Global Forum of malaria-eliminating countries (24-26 January; Cape Town, South Africa)
- Update of the WHO Response plan to PfHRP2/3 gene deletions (26 January; virtual)
- 2nd Meeting of the Technical advisory group on malaria elimination and certification (27 January; Cape Town, South Africa)

WHO Technical Meetings since October 2022 (continued)

- Technical consultation on prevention of re-establishment (21-23 February; virtual)
- SAGE/MPAG Working Group on Malaria Vaccines: Update on MVIP, Malaria Vaccine Pilot Evaluation (MVPE), case-control study, seasonal administration schedules (2 March, virtual)
- Partnership convening: a regional response to the invasion of Anopheles stephensi in Africa (8-10 March; Addis Ababa, Ethiopia)
- Preferred product characteristics: diagnostic tests for risk of P. vivax relapse (21-23 March; virtual)
- Technical consultation on prevention of re-establishment (29-30 March; Tblilisi, Georgia)

WHO publications since Oct 2022

- WHO Guidelines for malaria (25 Nov & 14 Mar)
- Guidance on the prioritization of insecticide-treated nets in situation where resources are limited (Mar)
- Vector control products targeting outdoor malaria transmission (Apr)
- Technical consultation to assess evidence on community-based delivery of intermittent preventive treatment in pregnancy for malaria – June 2022 meeting report (Mar)
- Vector alert: Anopheles stephensi invasion and spread in Africa and Sri Lanka (Jan)
- Seventeenth meeting of the WHO Vector Control Advisory Group (Jan)
- Pilot decision workshop to aid prioritization of resources for malaria control in Ghana (Jan)
- World malaria report 2022 (Dec)

WHO publications since October 2022 (continued)

- Strategy to respond to antimalarial drug resistance in Africa (Nov)
- Preparing for certification of malaria elimination, 2nd ed. (Nov)
- Tests for glucose-6 phosphate dehydrogenase activity (Nov)
- WHO technical consultation on preferred product characteristics for drugs used in malaria chemoprevention – meeting report from Dec 2020
- WHO meeting on preferred product characteristics for monoclonal antibodies for malaria prevention – meeting report from Nov 2021)
- Global framework for the response to malaria in urban areas (Oct)

Technical updates

Vector Control and Resistance

Diagnostics, Medicines and Resistance

Drug Efficacy

Strategic Information for Response

Vaccines

Vector Control and Resistance

2023 Progress to date

- Presented an update on WHO's work at VCWG meeting n Accra, Ghana; 6-8 February
- Regional meeting on *An. stephensi* held in Addis Ababa, Ethiopia; 8-10 March
- Script for educational video on *An. stephensi* developed

Priorities for the next quarter

- Review of the data on comparative effectiveness
- Draft Indoor Residual Spraying manual and initiated consultation with WHO regional offices
- Initiate case studies on integrated mosquito vector surveillance and control
- Finalize *An. stephensi* video and videos on insecticide resistance testing with translations
- Plan study tour on *An. stephensi* surveillance and control in native areas; initiate deep-dive on past and present control experience
- Update the GVCR VCNA assessment tool and data collection/collation platform
- Insecticide resistance test kit: Launch user consultation and cost of goods study

Diagnostics, Medicines and Resistance

2023 Progress to date

- Technical consultation to review effectiveness of rectal artesunate as pre-referral treatment of children with severe malaria (October 2022)
- Technical consultation to update the field implementation manual on seasonal malaria chemoprevention (November 2022)

Priorities for the next quarter

- Convene Guidelines Development Group for scoping treatment recommendations, including tafenoquine
- Convene Guidelines Development Group to review G6PD point-of-care diagnostics
- Publication of literature review on safety of antimalarials in pregnancy
- Publication of updated global pfhrp2/3 response plan and surveillance template protocols
- Technical support on pfhrp2/3 deletions to Somalia, South Sudan, Sudan, Zambia and Yemen, with networks of reference labs for molecular analysis
- Finalisation and publication of WHO field manuals on: 1) seasonal malaria chemoprevention; 2) rectal artesunate for pre-referral treatment of children with severe malaria; and 3) community delivery of IPTp

Drug Efficacy

2023 Progress to date

- Development and launch of two questionnaires for the collection of:
  - Planned and ongoing studies of drug efficacy
  - Planned and ongoing surveys of molecular markers of drug resistance
- Therapeutic Efficacy Studies (TES) planned in Djibouti, Sudan and South Sudan. Support provided for TES in Namibia and Mauritania

Priorities for the next quarter

- Protocol for TES in Djibouti, Sudan and South Sudan finalized, and implementation started
- Virtual meeting to define parameters of EQA scheme
- Collation of planned, ongoing, and finalized studies and surveys to provide information of gaps
- Development with partners and regional offices of implementation plans for the Strategy to respond to antimalarial drug resistance in Africa including plans for revitalization of African TES networks.

Strategic Information for Response

2023 Progress to date

- **Updates to the DHIS2 modules** - aggregate toolkit and finalization of documents for DSME, and training materials: launch planned in next few weeks
- **Joint modelling of routine data and *Pf*PR for risk mapping for HBHI stratification**. Nigeria and Mozambique completed, next Cameroon, Uganda and Burkina Faso
- **Strategic Information Technical Advisory Group (MSI-TAG) -** selection completed, planned meeting in June 2023
- **Finalization of response framework for malaria in urban areas -** joint launch with WHO Urban Health and UN HABITAT on 31 October 2022

Priorities for the next quarter

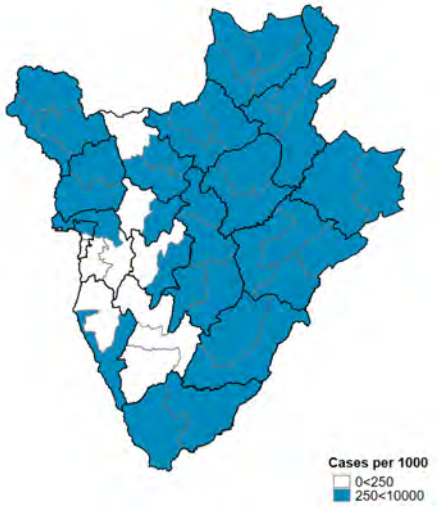
- **Guidance** –dissemination of the urban malaria framework and development, finalizing updates of Surveillance, Monitoring & Evaluation reference manual
- **Surveillance assessments** – Supporting surveillance assessment in India and other countries (TBD)
- **Digital solutions** – updating/installation/finalization of routine surveillance DHIS2 modules, including repositories
- **Training** - Training on use of data and SNT (one workshop in AFRO, 5 days, 24 countries) and development of virtual trainings materials and videos
- **Convening** – first MSI-TAG meeting in June 2023

Framework for the allocation of limited malaria vaccine supply

First priority principle of the framework: Greatest need
Allocate the vaccine to countries with areas of greatest need, where the malaria disease burden in children and the risk of death are highest

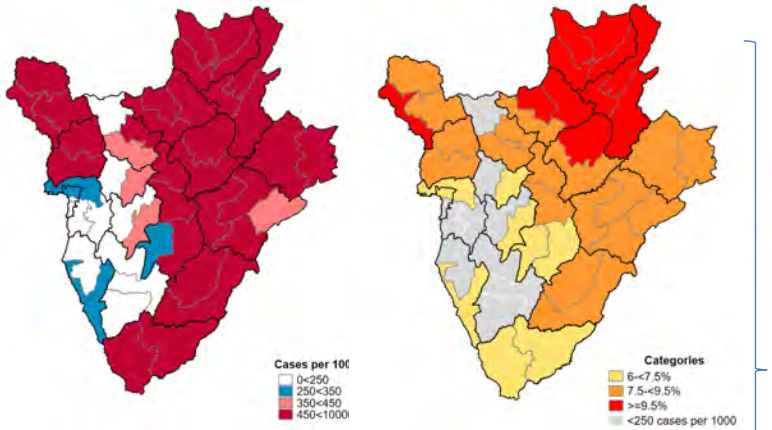
Other principles: Maximize health impact and solidarity

Step 1: Identification of areas of moderate and high transmission where the vaccine is recommended

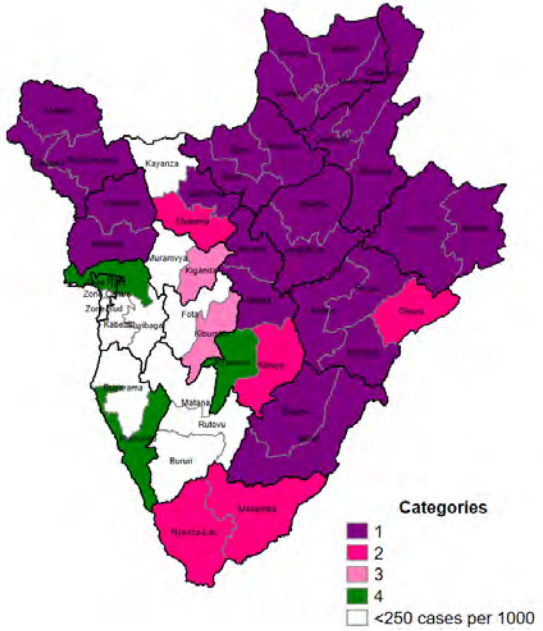


Areas with **>250 cases per 1000** (blue) identified as having moderate or high transmission intensity

Step 2: Prioritization of areas of moderate-to-high transmission into **categories of need** for the vaccine according to malaria transmission and mortality.



	Incidence (cases per 1000)	AU5MR (%)
1	350-<450	>9.5%
1	>=450	>9.5%
1	>=450	7.5%-<9.5%
2	250-350	>9.5%
2	350-450	7.5%-<9.5%
2	>=450	6.5%-7.5%
3	250-<350	7.5%-<9.5%
3	350-<450	6.5%-7.5%
3	>=450	<=6.5%
4	250-<350	6.5%-7.5%
4	350-<450	<=6.5%
5	250-<350	<=6.5%



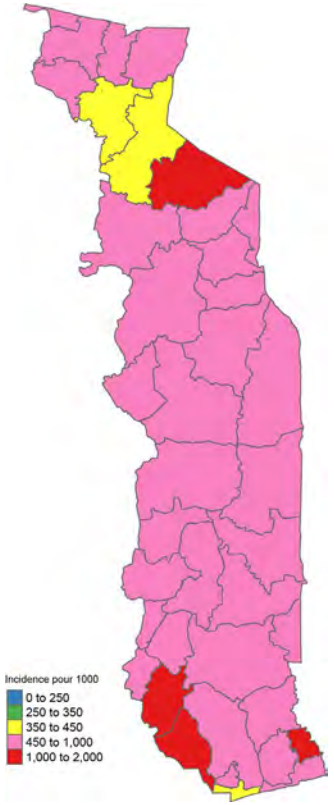
Category 1 areas (highest need) targeted for the **first phase** of vaccine introduction

Step 3: Review categorization guided by additional local data to ensure operational feasibility and coverage of districts within the maximum number of doses available per country as per the solidarity principle

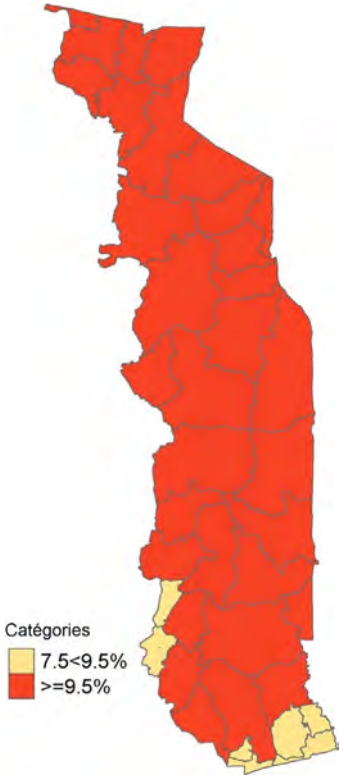
Subnational tailoring - stratification of key indicators, Togo

Epidemiological stratification

Incidence

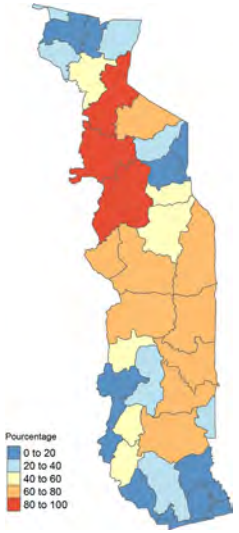


AC U5 Mortality



Contextual factor stratification

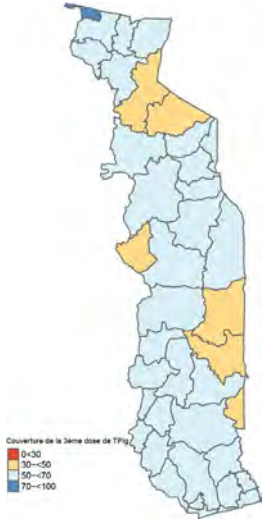
Access to care



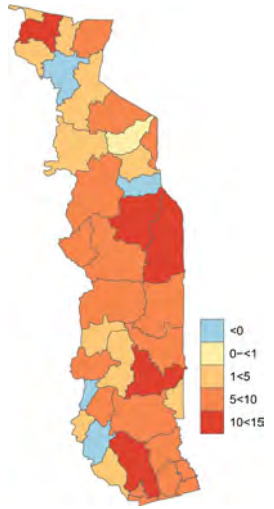
Source of care

Quality of care

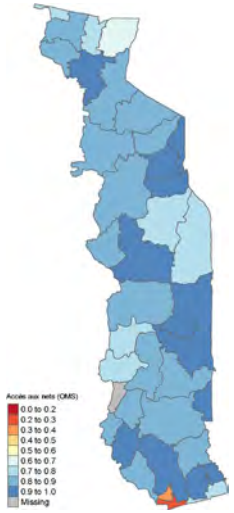
IPTp3 coverage



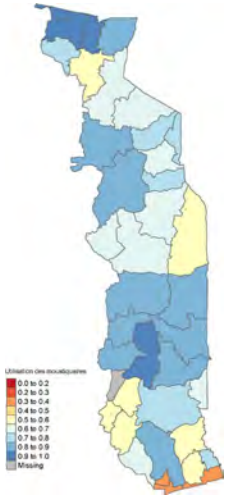
EPI coverage



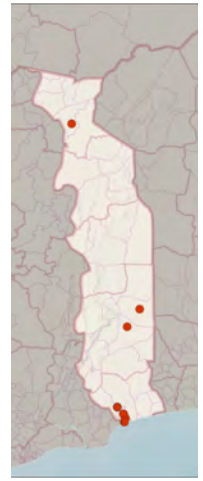
Access to ITNs



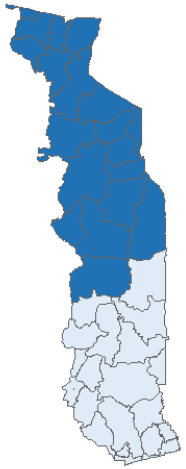
Use of ITNs



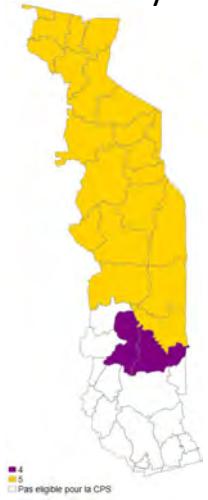
Insecticide resistance



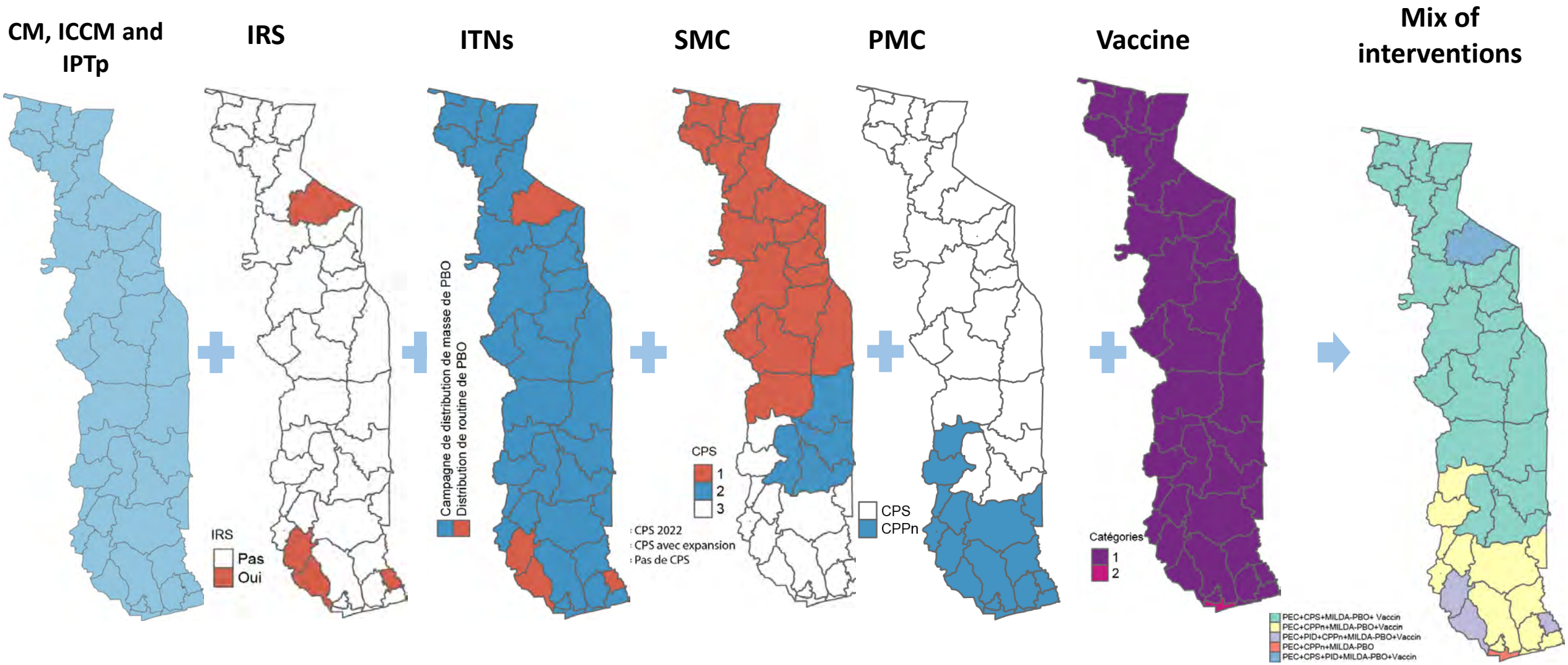
SMC coverage



Seasonality



Subnational tailoring – intervention mixes, Togo



Vaccines

2023 Progress to date

- Final year of the Malaria Vaccine Implementation Programme (MVIP) in 2023
- Gavi subteam, Malaria Vaccine Coordination Team fully functioning with participation from malaria, immunization and Gavi Alliance partners; support countries as they prepare applications and introduction of malaria vaccine
- Support provided to more than 15 African countries to prepare Gavi applications for introductions with subnational stratification support provided during face to face or virtual workshops, and to 13 countries implementing SMC to consider seasonal vaccination for highest impact
- Planning underway for WHO review of next malaria vaccine, R21/MatrixM; if approved, could increase global supply, reduce cost and optimize impact

Priorities for the next quarter

- Continue to support countries in Gavi application development and implementation plans
- Through outreach to endemic countries, develop broad research agenda on vaccine access and implementation (PMI Insights supporting), and draw Gavi learning agenda from this
- Continue market shaping activities to reduce cost and increase supply for improved sustainability (e.g., Gavi Market Shaping Roadmap; support RTS,S technology and product transfer to BBIL; and support review of 2nd malaria vaccine)

Country support

High burden to high impact

Elimination

Capacity building

High Burden to High Impact

2023 Progress to date

- Support to over 20 countries on SNT analysis (varying levels of details)
- Review of submitted funding requests vs NSP vs SNT analysis (accessing all funding requests is a challenge)
- Program reviews in DRC, India, Uganda, Mozambique, Sudan and 6 non-HBHI countries
- Technical support on GF funding request (RBM CRSPC inter-country meetings and mock TRPs)
- Technical support to control malaria in health emergencies
- Implementation of 1,7mRCTR project in 4 high burden countries (Burkina Faso, Tanzania, Senegal and Zambia

Priorities for the next quarter

- Continued SNT support to countries applying to window 2 of Global Fund applications
- Finalization of evaluation of HBHI approach
- Strengthening the HBHI approach and promoting it to other high burden countries
- Surveillance assessment (India)

Elimination

2023 Progress to date

- 4th Global forum of malaria eliminating countries was conducted on 24-26 January 2023 in Cape Town, South Africa
- Certification mission to Belize took place on 28 Feb – 08 March 2023
- Azerbaijan and Tajikistan are certified malaria free
- Translation of Malaria elimination course on OpenWHO into French and Spanish is completed. The work on posting the courses in additional languages is initiated.
- Technical consultation on PoR is launched; three of virtual meetings were conducted in February; evidence review meeting will be conducted on 29-30 March 2023 in Tbilisi, Georgia.

Priorities for the next quarter

- Continue working on development of the Global guidance on PoR
- Continue working on updating Framework for malaria elimination and Manual on certification of malaria elimination
- Certification of Cabo Verde, May 2023
- Continue working with E-2025 countries
- Organizing webinars on elimination guidelines
- MPRs in several countries

Capacity building

World Health Assembly Resolution (WHA68.2) on GTS

- Urges Member States to strengthen human resource capacity and infrastructure to improve the effectiveness, efficiency and sustainability of malaria responses, while ensuring integration and synergies with the wider health system
- Requests the Director General to strengthen the Secretariat's capacities to enable it to increase its technical support to Member States, in order to meet the global milestones and targets

Work completed

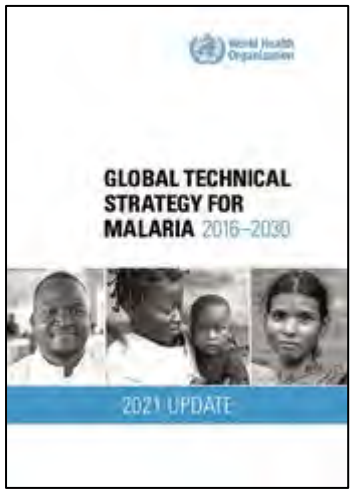
- Elimination course and Case management course (with EMRO) on OpenWHO
- Country capacity strengthening: DHIS2 HMIS modules, DHIS repositories, surveillance assessments, subnational tailoring, surveillance training and the AFRO precision public health unit support
- Surveillance for HRP2 gene deletion workshops (English completed/French is planned)

Work in progress

- Competency framework for malaria programme
- Strategy to strengthen human resource capacity for malaria programme
- Hybrid training modules on malaria programme planning and management

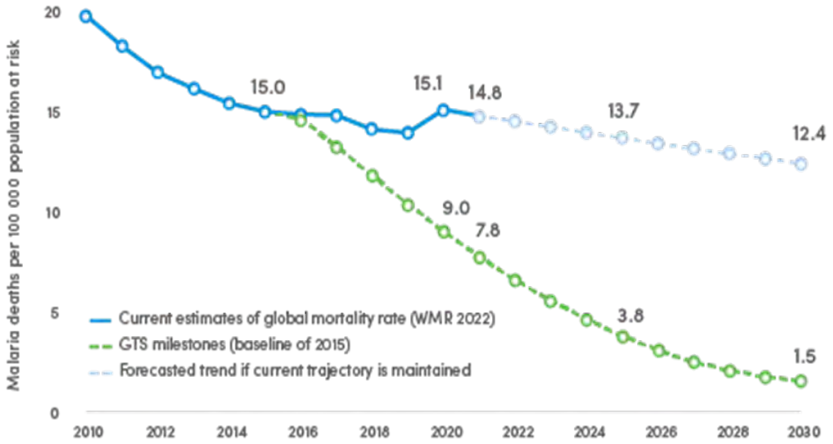
Closing thoughts and future vision from the Director, GMP

Where does that leave us?



- Mid-way between 2016 – 2030 and severely off-track on reductions in mortality and morbidity
- Key drivers of the current status:
  - Health systems, access and quality
  - Imperfect tools and biological threats
  - Limited financing and increasing costs
  - COVID and other disruptions (emergencies, climate, etc.)

- How do we get back on track?
  - Political leadership that translates into action and resources
  - Maximize the impact of available financing and interventions (subnational tailoring)
  - Identify the vulnerable and hard to reach populations that are being missed to overcome the barriers they face
  - Effective partnership at all levels
  - New tools and ability to address biological threats



Discussion

Malaria Policy Advisory Group Meeting

18—20 April 2023, Geneva, Switzerland
Background document for Session 2

RBM Partnership supported preliminary results from the evaluation of the HBHI approach

Melanie Renshaw, RBM CRSPC Co-Chair

Introduction

The High Burden to High Impact (HBHI) approach to accelerating progress against malaria was launched in 2018 by the World Health Organization (WHO) and the RBM Partnership to End Malaria, with a focus on improving the public health response in the 11 highest burden malaria endemic countries[1]. This approach categorizes the public health response in term of four elements: Political Will; Strategic Information; Better Guidance; and a Coordinated Response, and recognizes the foundational supporting role played by the overall health system and the multisectoral response.

A Steering Committee composed of RBM Partnership and WHO has been established to steer the evaluation of the HBHI. This evaluation was designed to assess how well the HBHI conceptual approach has supported countries during three years of country implementation, including over two years under the challenges of the COVID-19 pandemic. The RBM Partnership evaluation focussed on: Burkina Faso, Democratic Republic of the Congo, Mozambique, Nigeria, United Republic of Tanzania and Uganda. The WHO evaluation of the remaining countries (India, Cameroon, Mali, Ghana and Niger) is ongoing.

Evaluation objectives: The main purpose was to assess how effectively the HBHI approach has supported the highest burden malaria endemic countries, and to develop recommendations for improving the approach. The evaluation included four specific objectives:

1. Evaluating the country level outcomes of applying the HBHI approach, identifying best practices and barriers to success, and suggesting course corrections for future actions.
2. Evaluating the global level processes supporting the HBHI approach.
3. Consolidating recommendations to inform any scale up of the approach for the four response elements, effective health system, and multisectoral action in all HBHI focus countries.
4. Making further recommendations using lessons learned for expanding the HBHI approach to additional malaria endemic countries.

The evaluation employed the following approaches: i) a desk review of documents provided by the RBM Partnership, the WHO Global Malaria Programme and countries; ii) semi-structured key informant interviews (KIIs) with RBM and WHO staff, and key partner organization staff; iii) in-depth interviews with malaria programme managers from six HBHI countries; as well as country level stakeholders; iv) a survey which was electronically sent to HBHI focus country malaria programme staff and local partner organization staff. Over 100 interviews informed this evaluation.

[1] Burkina Faso, Cameroon, Democratic Republic of the Congo (DRC), Ghana, India, Mali, Mozambique, Niger, Nigeria, the United Republic of Tanzania, and Uganda

Evaluation findings

Overall impact on country performance

Findings from the first six country evaluations are presented here. Across the six countries, stakeholders agreed that while the concepts and methods outlined in the HBHI materials were already familiar to malaria programmes, they provided a well-structured tool for:

- Political engagement with national leadership;
- Encompassing and elevating the profile of existing malaria initiatives;
- Framing new national strategic plans (NSPs) and mid-term programme reviews (MPRs); and
- Providing justifications for interventions included in Global Fund grant applications.

Stakeholders across all surveyed countries reported satisfaction with the HBHI "approach" and its usefulness as a frame for communicating malaria strategies to political stakeholders. One global respondent explained: *''In almost all countries, the [HBHI] approach helped the government and partners to align their thinking. Although the ideas were not new, it helped to organize and align everyone together. One of the strongest supports was the initial political engagement. The structure and support elevated the engagement to the political class. High level officials attended and spoke on malaria, where they had not before. For developing NSPs, it strengthened the political engagement and better articulated the objectives and techniques.''*

The improved framing and articulation of countries' overall malaria strategies helped in justifying the malaria interventions to be supported through Global Fund grants. Examples include sub-national stratification and tailoring, using data at more granular levels to better define different intervention mixes for different geographical strata to maximize impact. The HBHI focus countries received a larger share of the total available funding than they had during the previous grant cycle. This meant more financial support for sub-national stratification, targeted scaling up of PBO nets, SMC scale up and other HBHI-recommended innovations and interventions.

Respondents noted that HBHI did not help with the challenge of prioritization within a fixed resource envelope. The recommendations developed through the HBHI process typically focused on the added value of additional investments such as introducing PBO and dual insecticide nets; adding new geographical areas for the application of SMC; or leveraging new resources from sectors outside of health. Respondents suggested that HBHI could better enhance support for prioritization of interventions in decreasing funding environments, especially as the approach is expanded to lower burden settings.

Countries	Overall impact on country performance
Burkina Faso	The HBHI approach informed the new NSP, which adopted a stratification analysis and a differentiated response.
Democratic Republic of Congo (DRC)	The HBHI approach supported the differentiated response in 10 high burden provinces and was integrated into the new NSP. Each pillar had a dedicated sub-committee with good partner participation and including ministries outside of health
Mozambique	The HBHI tools, orientation, and guidance were useful in changing the way people view malaria, as a disease and its socio-economic impact. The country launched their 'End Malaria Fund'
Nigeria	HBHI helped to "sharpen and focus" the new NSP and also provided a new approach to the malaria programme review and Global Fund proposal. The Nigeria End Malaria Council was launched by the President of Nigeria
United Republic of Tanzania	HBHI helped to further institutionalise the granular malaria stratification of malaria transmission up to the ward level, allowing for the tailoring of interventions to the local transmission patterns
Uganda	It was recognized that the HBHI approach was aligned with the country's existing Mass Action Against Malaria (MAAM) advocacy campaign and supported its political and technical objectives. The Malaria Free Uganda (End Malaria Council) was launched

Political will

The "Political Will" pillar of the HBHI approach which is intended to enhance country ownership and commitment was widely accepted by country stakeholders as a necessary component for building and maintaining progress against malaria. Multiple country respondents recounted that the HBHI approach facilitated operational political objectives in the fight against malaria, including examples such as:

- Increased financing for malaria at national and sub-national levels;
- Greater availability of human capital, and financial resources for malaria activities from all sectors;
- Commitments from political leaders for policies and actions to fight malaria;
- Accountability and results for malaria commitments;
- Engagement and participation of new malaria champions; and
- Elevation in status and visibility of malaria programmes and financing efforts.

Across all of the surveyed countries, increased financing from the Global Fund to HBHI countries constituted a clear political gain. However, the extent to which internal political will increased directly through HBHI engagement was mixed. In some instances, the timing and engagement of the HBHI approach directly influenced country-level political stakeholders and raised the profile of malaria. In Nigeria, for example, respondents attributed the increased engagement of the President's office to HBHI. In other countries, HBHI reinforced existing Presidential engagement, as in Mozambique and Uganda, where presidential-led political movements for malaria had already been launched, or parliamentarian engagement in Tanzania. In Burkina Faso and the DRC, respondents emphasized ongoing challenges in the area of political will and indicated that the HBHI approach has yet to fulfil its potential under this pillar.

The COVID-19 pandemic proved an incredibly difficult challenge to raising the political will for malaria. In addition to the competing political attention and financing directed to addressing COVID-19, malaria programme managers and staff were often re-assigned to COVID-19 response, delaying a number of planned malaria activities, such as Zero Malaria Starts with Me (ZMSWM) campaigns, End Malaria

Council and Fund (EMC/EMF) work plans, and even HBHI preparations themselves. Although often delayed, malaria-focused political engagement did resume. Despite the COVID-19 pandemic that affected the overall health system, SMC, IRS and LLIN campaigns in all HBHI countries were prioritized. More children than ever before were reached through SMC, and more nets than ever before were delivered in 2022. This commitment to the continuity of malaria programming during the COVID-19 pandemic, demonstrates the political commitment to continue delivering essential malaria services where many other campaigns were halted, such as NTD Mass drug administration, vaccination campaigns etc.

In Nigeria, respondents were overall convinced that the implementation of the HBHI approach led to greater funding commitments to malaria from the government at all levels. At the federal level sufficient financing was provided to increase counterpart financing for Global Fund supported activities. Of particular political significance, state-level funding also increased.

In Uganda, the launch of the MAAM movement and the Uganda Parliamentary Forum for Malaria (UPFM) both presaged the broader Zero Malaria movement and the HBHI approach. Of particular note, the national malaria programme was elevated to a "Division" within the Ministry of Health and the Manager promoted to an Assistant Commissioner, both of which gave greater voice to malaria concerns within the ministry's senior management structure. Also, the establishment of the Uganda Malaria Multisectoral Forum, chaired by the Prime Minister, supported the engagement with and leveraging of other sectors' human, capital, and financial resources in the fight against malaria.

In Mozambique, the HBHI approach dovetailed well with existing political engagements, such as Zero Malaria and aligned with the country's progress towards operationalizing an EMC/EMF.

As a global stakeholder put it: *"The HBHI plan that countries produced helped to mainstream other efforts already being done and gave them broader political recognition, such as the formation of End Malaria Councils and Funds, use of malaria scorecards, a more thoughtful multisectoral strategy, and Zero Malaria Starts with Me campaigns."*

Overall, the HBHI political will pillar encapsulated the approach that national malaria programmes and global stakeholders viewed as essential, if challenging. All countries received some additional funding through the Global Fund (and a greater share of the available funds than in the previous grant cycle). In addition, some countries also realized practical political gains and increased local funding, despite the challenges of the COVID-19 pandemic. In others, the promise of the approach has yet to realize its full potential for increased domestic resource mobilization or high-level political engagement.

Key achievements under the Pillar "Political Will" are summarized below:

Countries	Achievements under "Political will"
Burkina Faso	• Initiation of the End Malaria Council/End Malaria Fund process (development of concept note and a political engagement/declaration, meetings with stakeholders) • Advocacy meetings with regions and municipalities and development of regional and municipal development plans • Launching of Zero Malaria Starts with Me campaign and the Zero business initiative • Increased accountability with the support of civil society organizations led to the capacity building of community health workers for sensitization and services delivery for malaria, diarrhoea and pneumonia to remote communities • Increased awareness through the celebration of World Malaria day, ZMSWM campaign • Increased political commitment and High priority given to malaria through the Head of State declaration during WMD • Engagement and participation of new champions in the fight against malaria • Increased financing for malaria through Global Funds, private sector, domestic funding, including the creation of budget line for malaria • US$79.5 million committed in malaria co-financing
Democratic Republic of Congo (DRC)	• Participation of political leaders (governors and provincial health ministers, President's health advisors) in the HBHI launching meeting • Commitment for the establishment of a national committee for malaria elimination • Governors' commitment to support universal health coverage (UHC). • US$76.7 million committed in malaria co-financing
Mozambique	• Empowered political structures that ensure political support for malaria (increased leadership of NMCP, updating of the organigram at a sub-national level) • Creation of 'End Malaria Fund' • US$13.2 million committed in malaria co-financing
Nigeria	• HBHI helped malaria stakeholders to capitalize on the often-stated commitment of governments at all levels to malaria control and elimination • HBHI helps to keep malaria on the global agenda: malaria became a front-burner issue in the Office of the President • National EMC/EMF launched in August 2022 by HE President Buhari • HBHI approach supported the focus on accountability with the introduction of the scorecard • US$350.2 million committed in malaria co-financing
United Republic of Tanzania	• The HBHI approach supported development of the framework for the EMC • Tanzania Parliamentarians Against Malaria (TAPAMA) raised awareness within parliament and overall country leadership. • The launching of the "Zero Malaria Starts with Me" campaign contributed to helping foster an environment of accountability and action among the community and country leadership. • The Malaria Scorecard increased the advocacy role of the leadership, but also visibility of malaria control efforts beyond the health sector
Uganda	• The HBHI approach helped maintain political commitment and support from the President • The HBHI approach led to the development and rollout of district taskforce and multi-sectoral malaria oversight committees • The NMCP was elevated from a program to a Division with the Program Manager promoted to the position of an Assistant Commissioner • Increased accountability with the creation of Parliamentary Malaria Scorecard • Increased domestic funding through the Malaria Free Uganda fund (MFU)

Strategic Information

From the earliest conceptual stages of developing the HBHI approach, the WHO and the RBM partnership recognized that countries had the potential to use more granular epidemiological and programmatic data to better target interventions for maximum impact and, in some cases, to reduce funding for some interventions or geographies to potentially expand others. For example, reducing LLIN coverage in urban areas to reallocate funding for prevention to other geographies or with other tools. Country stakeholders and partners agreed that more detailed and geographically specific information was desirable and that a clear methodology for identifying the appropriate mix and prioritization of tools would improve the malaria response. Across the surveyed countries, the HBHI approach, tools, and technical assistance to drive impact through strategic information have been well received by stakeholders. Areas of effective implementation have included:

- Development of national malaria databases;
- Digitization of malaria campaign tools;
- Stratification analysis of malaria at more granular levels;
- Development of different intervention mixes for different geographic strata; and
- Regular review of DHIS2 data and malaria scorecards.

Country stakeholders are largely positive about donor and partner engagement in this HBHI pillar. However, funding for analysis and for implementing new mixtures of interventions remains a challenge.

In Nigeria, a stakeholder remarked: *"The HBHI process and tool enabled the country to sit around the table to make a critical and honest diagnosis of the malaria situation and reach a consensus on prioritizing and moving forward."* Respondents concurred that stratification analysis marked an important development in Nigeria's strategy which supported the Global Fund grant proposal and provided the evidence for expanding Seasonal Malaria Chemoprevention (SMC) from 227 to 383 Local Government Areas.

In Burkina Faso, application of the HBHI approach to strategic information included progress in the development of a national malaria database, digitization of campaign tools, use of a national stratification analysis, monthly review of DHIS2 data, and electronic distribution of quarterly community health newsletters to partners. External funding and technical assistance helped support these efforts and stakeholders all acknowledged the effectiveness of their implementation. Nonetheless, insufficient funding for the NMDW still needs to be addressed.

In the DRC, microstratification and remote surveillance have been supported under HBHI with technical assistance from the WHO. In Uganda, development of a data repository was initiated. However, a structured malaria database does exist, is integrated into the DHIS2, and includes entomological surveillance indicators.

In Mozambique, the implementation of malaria scorecards has produced the biggest impact on performance, and also helped to maintain malaria on the political agenda. Using provincial and district level indicators from the scorecards, governors, provincial and district directors, chief medical officers and heads of health facilities have become more conversant about performance against malaria and taken direct action to address poorly performing indicators.

Tanzania developed a malaria data repository and used subnational tailoring and stratification to prioritize interventions to maximize impact. Malaria Scorecards and dashboards that provide simple visual outputs that can be understood by non-experts have enhanced access to data beyond health staff to include leadership at various levels as a tool for decision making and enhancement of accountability.

Key achievements under the **Pillar "Strategic information"** are summarized below:

Countries	Achievements under "Strategic information"
Burkina Faso	• Progress in the development of a national malaria data warehouse (NMDW) • Digitization of campaign tools • Use of a national stratification analysis, monthly review of DHIS2 data, and electronic distribution of quarterly community health newsletters to partners. • Decentralisation of the malaria scorecard
Democratic Republic of Congo (DRC)	• Microstratification and remote surveillance through the analysis of epidemiological data at the health zone level • Decentralisation of the malaria scorecard
Mozambique	• Functioning national malaria data repositories with programme tracking dashboards • Data analysis for stratification, optimal intervention mixes and prioritization for NSP development and implementation • Implementation of malaria scorecards to monitor performance • Sub-national operational plans linked to sub-national health plans • Ongoing sub-national monitoring and evaluation of programmatic activities
Nigeria	• Establishment of the National Malaria Data Repository (NMDR) • More effective use of information for programming • Stratification towards a prioritized mix of interventions at the state level. • Generation of evidence for expanding SMC under the Global Fund grants
United Republic of Tanzania	• Establishment of the National Malaria Data Repository • Stratification and subnational tailoring to maximise impact with the available resources • The malaria scorecard enhanced engagement of non-health actors including Parliamentarians
Uganda	• Initiation of the development of a malaria data repository • Malaria risk stratification conducted and national malaria database updated • Use of HBHI approach to guide strategic planning and implementation

Better guidance, policies, and strategies

In its role in providing global guidance on malaria surveillance, prevention, diagnosis, and treatment, the WHO has supported implementation of this HBHI pillar with a commitment to provide more tailored and context-flexible guidance for countries, including routinely updating policies and strategies as new information is collected and new tools are developed. In this area of continuous improvement and updating of guidance, policies, and strategies, country stakeholders noted improvements in:

- Development and updating of new policies, Standards of Practice (SOP), job aids, and tools for data collection and analysis;
- Capacity building at lower levels for service delivery and reporting; and
- Formulation of new national strategic plans (NSPs) in line with the HBHI approach.

Across the countries, there was satisfaction with progress in this pillar and recognition that its conceptual formulation in HBHI was appropriate. In particular, countries employed the HBHI conceptual organization in their Global Fund applications and those developing new NSPs also applied the framing.

Key achievements under the **Pillar "Better Guidance, Policies, and Strategies"** are summarized below:

Countries	Achievements under "Better guidance, policies & strategies"
Burkina Faso	• Continue update of guidelines: Malaria case management and malaria surveillance, use of insecticide and vector control • Better guidance for the deployment of new generation nets and selection of insecticide for IRS • Effective deployment of national policies • Reinforced monitoring of the national policies/guideline implementation
Democratic Republic of Congo (DRC)	• Development of annual work plans (POA) integrating the HBHI approach • Development and deployment of guidelines and policies: guidelines and SOPs for entomological surveillance; malaria case management policy; surveillance, monitoring-evaluation guidelines for malaria control activities • Establishment of working groups for updating/harmonizing malaria guidelines/policies and monitoring progress: Multisectoral Technical Group for Malaria Vector Control (GTLAV), Malaria Case Management Working Group and the Sentinel Sites Technical Group.
Mozambique	• Better guidance for country level implementation**:** Strategies update and dissemination
Nigeria	• Continuous review of policies and guidelines as necessary to incorporate new guidance from WHO and best practices from the global community.
Uganda	• Continuous update of malaria control guidelines: management of insecticide resistance, epidemic preparedness and response, malaria diagnosis and case management and integrated vector management

Programme coordination

Malaria programmes have effectively coordinated external partners in several countries, while challenges remain in others. Engagement and coordination of other government ministries, departments and agencies outside of the health sector requires different political and organisational assets than those required for coordinating external partners, though both forms of coordination are necessary. While there was agreement on the importance of programme coordination as a pillar for HBHI, assessments about the current state of programme management varied. Some noted that the malaria programme so effectively managed partners that there was little additional room for improvement under the HBHI process. Others noted challenges in programme management and explicitly used the roll-out of HBHI itself as an example, observing that there was incomplete understanding among country partners about the meaning and purpose of HBHI and that there was insufficient information sharing and engagement between global and country-level partners. Other challenges in programme coordination included the difficulty in engaging with the private sector and inadequate coordination at sub-national levels.

In Nigeria, the malaria coordination framework explicitly incorporated the HBHI approach, with roles, responsibilities, and structures for internal and external coordination specified. Stakeholders noted that meetings are being held more regularly and with appropriate representation, and that debates are more substantive than before. To address insufficient private sector involvement, a new public-private partnership framework has been set up with a committee to oversee its operation and staff from the malaria programme to support it. Uganda has also attempted to address private sector engagement and appointed a lead in this area within the malaria programme. Uganda's private sector strategy emphasizes resource mobilization, targeting service quality in the private for-profit health sector and supporting further decentralization in the management of facility-level funds. In Burkina Faso, HBHI has impacted the approach to malaria programme coordination, clearly defining roles and

responsibilities in the NSP and in the malaria programme's engagement with the Global Fund Country Coordinating Mechanism.

In Mozambique, coordination structures are clearly defined and harmonized across the health sector. Partner support and funding are in line with costed national strategies and large institutional donors and non-traditional donors are harmonized.

Key achievements under the **Pillar "Coordination"** are summarized below:

Countries	Achievements under "Coordination"
Burkina Faso	• Enabled malaria coordination mechanisms: working groups, steering committees • Alignment of Partners with the country priorities defined in the PSNs
Democratic Republic of Congo (DRC)	• Ongoing revitalization of RBM Task Force and quarterly thematic group meetings
Mozambique	• Ongoing harmonization of partner support including non-traditional donors • Ongoing establish/strengthen coordination mechanisms at subnational level, ensuring alignment to NMCP priorities • Continuous engagement and collaboration with partners for effective implementation of Mozambique Relief Fund
Nigeria	• Strengthening the malaria coordination structures in the country • Development of a Public-Private Partnership (PPP) framework to articulate the private sector response to malaria elimination and control, and help to mobilize additional resources
Tanzania	• Revitalization of the Technical Working Groups (TWGs) including the Integrated Malaria Vector Control (IMVC-TWG) and the Diagnosis, Treatment and Preventive Therapies (DT&PT-TWG).
Uganda	• Strengthening of consultation/coordination meetings despite de COVID (weekly virtual programmatic/technical update meetings, • Engagement of Private sector in the coordination framework

Multisectoral Action for Malaria

The multisectoral response and effective health system are foundations for the HBHI approach. Because malaria contributes to and is exacerbated by poverty and the conditions which either perpetuate or prevent malaria are responsive to environmental variables affected by multiple sectors, the HBHI approach emphasizes the need to engage and leverage the broader multisectoral development response.

Across the surveyed countries, there was broad recognition that multisectoral engagement and action was an important component of the HBHI approach. A combination of political barriers, limited funding, and lack of a comprehensive multisectoral strategy continue to pose challenges for some countries.

In Nigeria, the malaria programme reaches out to ministries, departments, and agencies (MDAs) outside of health to report on the fight against malaria and highlight potential areas of collaboration. Respondents noted that most malaria prevention campaigns succeed because of multisectoral collaboration at the state level, particularly from the involvement of the security forces and the Ministry of Information.

In Burkina Faso, multisectoral action is also specified in the national strategic plan for malaria, including examples such as: inclusion of sessions on malaria in annual teacher training; inclusion of sessions on insecticide resistance and misuse of pesticides in Ministry of Agriculture training; Entomological surveillance involves sectors including agriculture, environment, defense, territorial administration, and finance. However, insufficient funding and a lack of monitoring & evaluation for

multisectoral plans has limited the scope of potential actions. Stakeholders also reported that the HBHI process has had little impact on the country's objectives for multisectoral action. In the DRC, multisectoral needs have been identified by the malaria programme, but engagement outside of the health sector has been limited.

In Uganda, the Malaria Free Uganda Fund was set up to advocate, mobilize resources, action, and accountability from the private sector towards supporting malaria reduction and elimination. Together with multisectoral End Malaria Councils, End Malaria Funds such as Uganda's have proven to be effective mechanisms for engaging sectors outside of health, and mainstreaming malaria needs into the budgets and work plans of MDAs outside of health. Mozambique has established and launched the Malaria Fund Association to support the NMCP's ZMSWM campaign. Although the private sector environment in the country is challenging, some engagement with the private sector to support the malaria response, particularly in the area of malaria commodity logistics, has proved fruitful. Nigeria launched their End Malaria Council, chaired by Aliko Dangote.

Health system integration

Like multisectoral action, an effective health system is also recognized as an essential foundation of the malaria response. More specifically, stakeholders recognize the importance of an integrated malaria response within the health system. This area needs further elaboration and direction from the HBHI conceptual framework and faces fundamental challenges from entrenched governance structures. In Burkina Faso, stakeholders responded positively that HBHI has had an impact on the country's objectives for health system integration. They pointed to examples such as systematic malaria screening in nutritional recovery centres as well as awareness-raising on essential family practices including the proper use of mosquito nets, hygiene, etc.; integration of malaria with sexual and reproductive health (SRH) services, the response to internally displaced persons (IDP), and with Antenatal care (ANC), the capacity building of community health workers for services delivery for malaria, diarrhoea and pneumonia (IMCI) to remote communities, continuous review of DHIS2 data.

Global implementation processes

Country satisfaction with the global processes supporting the introduction and rollout of the HBHI approach varied, although there was overall approval of the final product and appreciation for the conceptual framework. Global stakeholders noted that communication about the nature of HBHI as an "approach" rather than as a "project" could have been more clearly articulated at the outset, and recommended that this point be more explicitly explained as new countries adopt the approach.

In Nigeria, all respondents rated the quality of technical assistance in support of HBHI very highly. This included support for development of the national malaria data warehouse, a stratification analysis, setting up the End Malaria Council, improved data use of the Health Management Information System (HMIS) and Malaria Indicator Survey (MIS), and an organizational capacity assessment of the national malaria programme, among others.

Best practices and recommendations

Across the countries surveyed in this evaluation, overall satisfaction with the HBHI conceptual framework was high. Country stakeholders recommended continued implementation of the approach and the supportive interventions rolled out in conjunction with HBHI, providing additional examples of best practices from their experience and other suggestions for expansion into other countries. As a Nigeria stakeholder enthusiastically asserted: *"The HBHI approach is a fantastic idea. WHO and the RBM Partnership empower countries to critically look at how their programmes are running and then look for home-grown solutions."* Global stakeholders were likewise supportive of the conceptual framework.

In Nigeria, the HBHI process produced a number of good practices, including improved relationships with the political leadership in support of malaria elimination at the national and sub-national levels; improved generation and use of strategic information to guide programmatic decision making; establishment of a national malaria data warehouse; appropriation of existing community staff for local monitoring and accountability; the use of national and sub-national scorecards for tracking performance and promoting friendly competition; strengthening of coordination structures and leadership of the national malaria programme; and fostering collaboration both within and outside of the health sector to address malaria. The advocacy efforts of in-country partners together with the state-level data from the stratification analysis helped to leverage the additional budgetary and logistical support from the national and state level governments in the malaria response.

In Burkina Faso, some of the best practice examples include use of geographic stratification to deploy next-generation LLINs and insecticides for Indoor Residual Spraying (IRS); creation of new larviciding units in particular districts; integration of malaria into regional and municipal development plans; and monitoring of malaria indicators under the president's national development plan. From these experiences, stakeholders in Burkina Faso recommended involving local authorities and sectors outside of health at the earliest stages of planning and sensitization about the HBHI approach. Stakeholders also recommended accelerating the establishment of an EMC/EMF.

In the DRC, involvement of the provincial malaria coordinators at the outset of HBHI and conducting the malaria stratification exercise down to the district level were among the recommendations from respondents. Stakeholders also advised that countries try to mobilize new resources before rolling out HBHI and to engage ministries outside of the health sector to get a more robust response. Here the respondents were particularly concerned that new financing was essential for HBHI's success, not only to implement new approaches, but to gain domestic political traction as well.

In Mozambique, the use of the malaria scorecard has been the most effective advocacy tool for both national and provincial government engagement during the period of adopting the HBHI approach. According to respondents, since the launch of the scorecard in 2018, "*governors, provincial and district directors, chief medical officers and heads of health facilities can speak about malaria and discuss performance of their districts with more confidence*." On the broader strategic generation and use of information, the malaria stratification analysis and piloting of different interventions mixes was also well supported under the banner of HBHI and included interventions such as SMC expansion from two districts to an entire province; three different next generation LLINs piloted across different districts; and the piloting of Intermittent Preventive Therapy for Infants (IPTi) in a single province. Development of a national data repository was identified as a valuable tool for monitoring the results of these pilots.

In Uganda, stakeholders emphasized the importance of communicating about HBHI effectively at the start, ensuring that country governments and partners do not view it as a stand-alone initiative.

Global stakeholders also provided recommendations on the importance of communication and setting appropriate expectations when introducing the HBHI approach. They were particularly concerned with the issue of prioritization, and the need to develop models and guidelines for effective use of limited financial resources, especially when applying the approach to lower burden countries, which will receive reduced external funding as progress against the disease accelerates.

Recognizing the value of the stratification exercises, one stakeholder argued that significantly greater numbers of epidemiological modellers need to be engaged in the global malaria response. Also, the area of resource mobilisation has far too few experts focusing on malaria. Finally, national malaria programmes themselves need to engage more explicitly in the integrated health sector responses in their countries and prioritize those areas of the overall health system that need to be strengthened in order to continue making progress against malaria. This would mean better integration of malaria programmes with other health sector interventions as well as better multisectoral engagement.

Conclusion

The “High Burden to High Impact” approach was born from the concern that the priorities of global malaria partners had strayed away from the highest disease burden, poorest countries (predominantly in sub-Saharan Africa) in favour of investing in malaria elimination countries and settings. While initially and incorrectly perceived by some as a new project or intervention to reduce malaria deaths in the highest burden countries, the HBHI approach attempted to encapsulate the complicated mixture of socio-economic, political, technical, and practical aspects of ending malaria in an organized conceptual framework that countries could adapt to their context. The primary added value of this approach and its conceptual framing was rhetorical. That is, it gave a common language for national malaria programmes to use for internal advocacy with government officials at all levels and for external advocacy with bilateral and multilateral financing organizations to increase funding for different aspects of the national malaria response. The extent to which it continues to be useful will depend on its ability to incorporate and adapt to changing programme needs and to provide guidance on how to allocate financial resources to the impactful interventions at the right places and at the right times, including when funding falls short

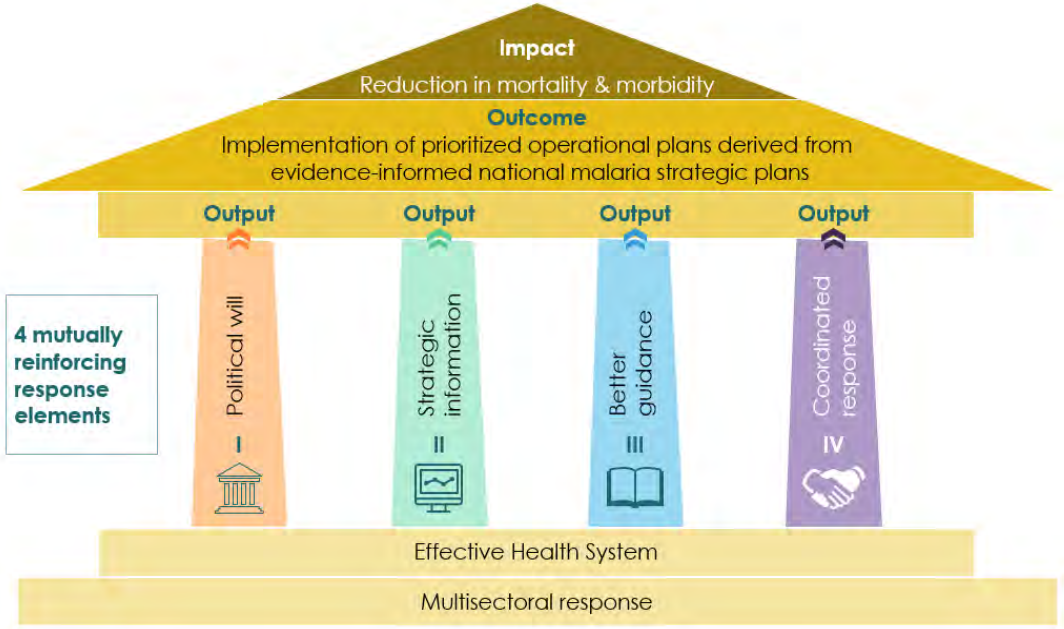
High Burden High Impact (HBHI)

RBM Partnership supported Preliminary Results from the Evaluation of the HBHI approach

RBM Partnership
To End Malaria

HBHI : Background

- HBHI approach **accelerating progress against malaria** was launched in 2018 by WHO and the RBM Partnership to End Malaria
- In 2022, a Steering Committee of RBM and WHO was established to steer the evaluation, designed to assess how well the HBHI conceptual approach has supported countries since the launch
- The RBM Partnership evaluation focussed on: Burkina Faso, Democratic Republic of the Congo, Mozambique, Nigeria, Tanzania and Uganda. The WHO evaluation of the remaining countries (India, Cameroon, Mali, Ghana and Niger) is ongoing.



Evaluation Objectives

To assess how effectively the HBHI approach has supported the highest burden malaria endemic countries, and to develop recommendations for improving the approach. The evaluation included four specific objectives:

1. Evaluating country level outcomes of applying the HBHI approach, identifying best practices and barriers to success, and suggesting course corrections for future actions
2. Evaluating the global level processes supporting the HBHI approach
3. Consolidating recommendations to inform any scale up of the approach for the 4 response elements, effective health system, and multisectoral action in all HBHI focus countries
4. Making further recommendations using lessons learned for expanding the HBHI approach to additional malaria endemic countries

The evaluation has **not** been an evaluation of country performance but focuses on the **process and value of the HBHI approach**.

Research Methods and Processes for the Evaluation

Study design

Qualitative research methods

- Desk review of HBHI documents
- HBHI Country consultations
- Questionnaire design for different interview formats

Interviews

Interview methods

- Key Informant Interviews (KII), global and country level
- Electronic survey (English, French, and Portuguese)
- In-depth interviews with malaria programme managers

Evaluation Findings: Overall Impact on Country Performance

Evaluation participants noted that whilst the concepts in the HBHI approach were not new, they **provided a well-structured tool** for:

- Political engagement with national leadership
- Encompassing and elevating the profile of existing malaria initiatives
- Framing the development of new NSPs and MPRs
- Providing justifications for interventions in Global Fund grant applications

The improved framing and articulation of countries' overall strategies helped in justifying the malaria interventions to be supported through Global Fund grants including the use of more granular data through sub-national tailoring to better define different intervention mixes for different geographical strata to maximize impact.

However, country respondents noted that whilst subnational tailoring has helped to prioritize interventions, there remain significant difficulties in prioritization when resources are insufficient.

Political Will: Evaluation Findings (1/2)

"Political Will" is widely accepted as a necessity for countries to build and maintain progress against malaria.

Some positive examples have included:

- Increased financing for malaria at national and subnational levels
- Greater availability of human, capital, and financial resources for malaria activities from all sectors
- Commitments from political leaders for policies and actions to fight malaria
- Accountability and results for malaria commitments
- Engagement and participation of new champions in the fight against malaria
- Elevation in status and visibility of malaria programmes and financing efforts

The COVID-19 pandemic proved an incredibly difficult challenge to raising the political will for malaria. However, despite the COVID-19 pandemic that affected the overall health system, SMC, IRS and LLIN campaigns in all HBHI countries were prioritized. More children than ever before were reached through SMC, and more nets than ever before were delivered in 2022.

Respondents noted that this commitment to the continuity of malaria programming during the COVID-19 pandemic, demonstrates the political commitment to continue delivering essential malaria services where many other campaigns were halted, such as NTD Mass drug administration, vaccination campaigns etc.

Political Will: Evaluation Findings (2/2)

The elevation of the Malaria Programme to a Division and the promotion of the Manager to an Assistant Commissioner provided the ability "to be more visible, exert influence, and be heard at the senior management meetings."

– Uganda stakeholder

The HBHI plan that countries produced helped to mainstream other efforts already being done and gave them broader political recognition, such as the formation of End Malaria Councils and Funds, use of malaria scorecards, a more thoughtful multisectoral strategy, and Zero Malaria Starts with Me campaigns.

– Global Stakeholder

Political Will: Examples of Success (1/2)

Burkina Faso

- Advocacy meetings with regions and municipalities and development of regional and municipal development plans
- Launching of Zero Malaria Starts with Me campaign and the Zero business initiative
- Increased accountability with the support of CSOs led to capacity building of CHWs for iCCM service delivery
- Engagement and participation of new champions in the fight against malaria
- Increased financing for malaria through Global Funds, private sector, domestic funding, including the creation of budget line for malaria including US$79.5 million committed in malaria domestic financing

DRC

- Participation of political leaders (governors and provincial health ministers, President's health advisors) in the HBHI launch meeting
- Commitment for the establishment of a national committee for malaria elimination
- Governors' commitment to support universal health coverage (UHC).
- US$76.7 million committed in malaria co-financing

Mozambique

- Empowered political structures that ensure political support for malaria (increased leadership of NMCP, updating of the organigram at a sub-national level)
- Creation of 'End Malaria Fund'
- US$13.2 million committed in malaria co-financing

Political Will: Examples of Success (2/2)

Nigeria

- HBHI helped malaria stakeholders to capitalize on the often-stated commitment of governments at all levels to malaria control
- HBHI helps to keep malaria on the global agenda: malaria became a front-burner issue in the Office of the President
- National EMC/EMF launched in August 2022 by HE President Buhari
- HBHI approach supported the focus on accountability with the introduction of the scorecard
- US$350.2 million committed in malaria co-financing

Tanzania

- The HBHI approach supported development of the framework for the EMC
- Tanzania Parliamentarians Against Malaria (TAPAMA) raised awareness within parliament and overall country leadership.
- Launching of "Zero Malaria Starts with Me" helped to foster an environment of accountability and action among the community and country leadership.
- The Malaria Scorecard increased the advocacy role of the leadership and visibility of malaria control efforts beyond the health sector

Uganda

- HBHI helped maintain political commitment and support from the President
- HBHI led to the rollout of district taskforce and multi-sectoral malaria oversight committees
- The NMCP was elevated from a program to a Division with the Manager promoted to the position of Assistant Commissioner
- Increased accountability with the creation of Parliamentary Malaria Scorecard
- Increased domestic funding through the Malaria Free Uganda fund (MFU)

Strategic Information: Evaluation Findings

The HBHI approach, tools, and technical assistance to drive impact through Strategic Information have been well received by stakeholders

Areas of effective implementation have included:

- Development of National Malaria Data Warehouses
- Digitalization of malaria campaign tools
- Stratification analysis of malaria at more granular levels
- Development of different intervention mixes for different geographical strata
- Regular review of DHIS2 data and malaria scorecards

The [HBHI] process and tool enables the country to sit around the table and make a critical and honest diagnosis of the malaria situation and reach a consensus on prioritizing and moving forward.

– Nigeria Stakeholder

Strategic Information: Examples of Success (1/2)

Burkina Faso

- Progress in the development of a national malaria data warehouse (NMDW)
- Digitization of campaign tools
- Use of a national stratification analysis, monthly review of DHIS2 data, and electronic distribution of quarterly community health newsletters to partners.
- Decentralisation of the malaria scorecard

DRC

- Microstratification and remote surveillance through the analysis of epidemiological data at the health zone level
- Decentralisation of the malaria scorecard

Mozambique

- Functioning national malaria data repositories with programme tracking dashboards
- Data analysis for stratification, optimal intervention mixes and prioritization for NSP development and implementation
- Implementation of malaria scorecards to monitor performance
- Sub-national operational plans linked to sub-national health plans
- Ongoing sub-national monitoring and evaluation of programmatic activities

Strategic Information: Examples of Success (2/2)

Nigeria

- Establishment of the National Malaria Data Repository (NMDR)
- More effective use of information for programming
- Stratification towards a prioritized mix of interventions at the state level.
- Generation of evidence for expanding SMC under the Global Fund grants

Tanzania

- Establishment of the National Malaria Data Repository (NMDR)
- Stratification and subnational tailoring to maximise impact with the available resources
- The malaria scorecard enhanced engagement of non-health actors including Parliamentarians

Uganda

- Initiation of the development of a malaria data repository
- Malaria risk stratification conducted and national malaria database updated
- Use of HBHI approach to guide strategic planning and implementation

Better Guidance, Policies, and Strategies: Evaluation Findings

Continuous improvement and updating of guidance, policies, and strategies is recognized by all stakeholders as important to maintaining progress

Countries noted improvements in areas such as:

- Development and updating of new policies, SOPs, job aids, and tools for data collection and analysis
- Building capacity at lower levels for service delivery and reporting
- Formulating new NSPs in line with the HBHI approach

The HBHI approach has had a "significant impact" on the country's objectives for better policies and strategies.

– Burkina Faso Stakeholder

Better Guidance, Policies, and Strategies: Examples of Success

Burkina Faso	• Continue update of guidelines: Malaria case management and malaria surveillance, use of insecticide and vector control • Better guidance for the deployment of new generation nets and selection of insecticide for IRS • Effective deployment of national policies • Reinforced monitoring of the national policies/guideline implementation
DRC	• Development of annual work plans (POA) integrating the HBHI approach • Development and deployment of guidelines and policies: guidelines and SOPs for entomological surveillance; malaria case management policy; surveillance, monitoring-evaluation guidelines for malaria control activities • Establishment of working groups for updating/harmonizing malaria guidelines/policies and monitoring progress: Multisectoral Technical Group for Malaria Vector Control (GTLAV), Malaria Case Management Working Group and the Sentinel Sites Technical Group.
Mozambique	• Better guidance for country level implementation: Strategies update and dissemination
Nigeria	• Continuous review of policies and guidelines as necessary to incorporate new guidance from WHO and best practices from the global community.
Uganda	• Continuous update of malaria control guidelines: management of insecticide resistance, epidemic preparedness and response, malaria diagnosis and case management and integrated vector management

Coordination: Evaluation Findings

Malaria programmes have effectively coordinated external partners in a number of countries, while challenges remain in others. Engagement and coordination of other government ministries, departments and agencies outside of the health sector **requires different political and organizational assets than coordination with external partners**, though both are widely acknowledged to be necessary

Some stakeholders claimed that programme coordination **was already working very well** and so little new work needed to be done.

However, others noted some challenges with the HBHI approach in supporting programme coordination including:

- Incomplete understanding among country partners about the meaning and purpose of HBHI
- Insufficient information sharing and engagement among global and country partners
- Inadequate private sector involvement in programme coordination
- A lack of coordination efforts at the sub-national levels

Coordination: Examples of Success

Burkina Faso	• Enabled malaria coordination mechanisms: working groups, steering committees • Alignment of Partners with the country priorities defined in the PSNs
DRC	• Ongoing revitalization of RBM Task Force and quarterly thematic group meetings
Mozambique	• Ongoing harmonization of partner support including non-traditional donors • Ongoing establish/strengthen coordination mechanisms at subnational level, ensuring alignment to NMCP priorities • Continuous engagement and collaboration with partners for effective implementation of Mozambique Relief Fund
Nigeria	• Strengthening the malaria coordination structures in the country • Development of a Public-Private Partnership (PPP) framework to articulate the private sector response to malaria elimination and control, and help to mobilize additional resources
Uganda	• Strengthening of consultation/coordination meetings despite de COVID (weekly virtual programmatic/technical update meetings, • Engagement of Private sector in the coordination framework

Multisectoral Action for Malaria: Evaluation Findings

National End Malaria Councils and Funds have been identified as effective mechanisms for engaging sectors outside of health, and mainstreaming malaria needs into the budgets and work plans of ministries, departments, and agencies across sectors. **However, the HBHI approach not been seen as providing a roadmap for improvement in this area.**

Barriers to this work include:

- Incentives to joint collaboration for other sectors
- Non-existent platforms for multisectoral dialogue on malaria
- Funding for multisectoral plans, and M&E

Some non-health sector interventions in the malaria NSP include annual teacher training on malaria; training on insecticide use, disuse, and resistance; and development of a multisector entomological surveillance and national resistance management plan.

– Burkina Faso Stakeholder

Health System Integration: Evaluation Findings

Although stakeholders widely recognize that success against malaria requires effective integration with other health services, most malaria programmes are structured and financial incentivized to perform as vertical programmes.

Some proposals for improving on the status quo include:

- Joint development of funding proposals in malaria and health systems from the outset
- Including the concept of integrated programming in the curriculum of medical training institutions
- Changing the organizational structure of disease programmes away from their current silos

Even efforts such as the integration of malaria and RSSH Global Fund grants do not seem to have realized the desired effect of integration in strategic planning and implementation.

Satisfaction with the HBHI Approach

Country stakeholders were **largely satisfied with the conceptual framing of the HBHI approach** and claimed that it encompasses the necessary components of a successful malaria program.

Many argued that the approach was **equally valuable for countries with low malaria burdens** as well.

Stakeholders were also satisfied that the HBHI approach **effectively encompassed activities and initiatives that were already in progress**. HBHI provided a framing and a justification after the fact that could be useful for communication with national leaders as well as with international funders.

It was especially noteworthy that all HBHI countries got comparative increases in their Global Fund malaria allocations, and that the HBHI approach informed the funding requests and proposed intervention mixes.

Satisfaction with the HBHI Approach

The HBHI approach is a fantastic idea. WHO and the RBM Partnership empower countries to critically look at how their programs are running and then look for home-grown solutions.

– Nigeria Stakeholder

Areas of Concern with the HBHI Approach

Many country stakeholders anticipated that the launch of the HBHI approach **would be accompanied by a separate stream of dedicated financial resources**, in line with the presumption that this was a type of malaria project.

While the framing of HBHI was seen as appropriately broad and holistic, **technical and financial support were concentrated primarily in certain areas** (such as in strategic information) with less support for others (such as coordination or health system integration).

> ***Countries asked for additional resources to implement new approaches, but funds were often not available.***
>
> – Global stakeholder

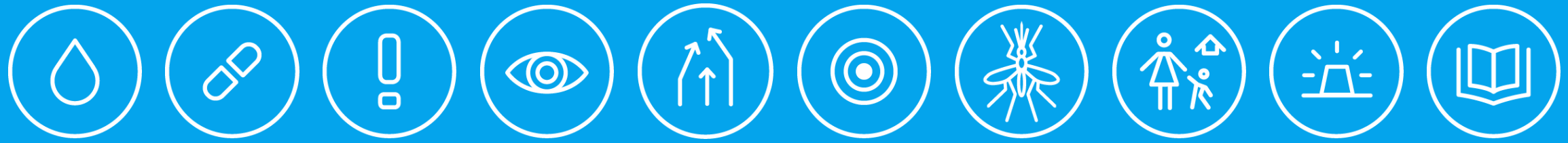
Conclusions

While initially and incorrectly perceived by some as a new project or intervention to reduce malaria deaths in the highest burden countries, the HBHI approach **attempted to encapsulate the complicated mixture of socio-economic, political, technical, and practical aspects of ending malaria in an organized conceptual framework** that countries could adapt to their context.

The primary added value of this approach is that its conceptual framing gave **a common language for national malaria programmes to use for internal advocacy with government officials at all levels and for external advocacy with bilateral and multilateral financing organizations** to increase funding for different aspects of the national malaria response.

The extent to which it continues to be useful **will depend on its ability to incorporate and adapt to changing programme needs and to provide guidance on how to allocate financial resources** to the impactful interventions at the right places and at the right times, including when funding falls short

Malaria Vector Control: Guideline updates



Dr Jennifer Stevenson
Vector Control and Insecticide Resistance Unit
vcguidelines@who.int

Global **Malaria** Programme

World Health Organization

Malaria vector control interventions recommended for *large-scale deployment*

Intervention	Strength & evidence	Unchanged/ revised/new
Pyrethroid-only nets	**Strong for, high certainty evidence**	Unchanged
Pyrethroid-PBO nets	**Conditional for, moderate certainty evidence**	Revised 2021
Pyrethroid-chlorfenapyr *vs* pyrethroid-only nets	**Strong for, moderate certainty evidence**	New 2023
Pyrethroid-chlorfenapyr *vs* pyrethroid-PBO nets	**Conditional for, Moderate certainty evidence**	New 2023
Pyrethroid-pyriproxyfen *vs* pyrethroid-only nets	**Conditional, for Moderate certainty evidence**	New 2023
Pyrethroid-pyriproxyfen *vs* pyrethroid-PBO nets	**Conditional against, Moderate certainty evidence**	New 2023
Indoor residual spraying	**Strong for, low certainty evidence**	Unchanged
Co-deploying IRS & ITNs	**Conditional against, Moderate certainty evidence**	Unchanged

Malaria vector control interventions recommended for *humanitarian emergencies*

Intervention	Strength & evidence	Unchanged/ revised/new
ITNs	**Strong for, high certainty evidence**	New 2022
Indoor residual spraying	**Conditional for, very low certainty evidence**	New 2022

When considering deployment of ITNs in humanitarian emergencies, the infrastructure, access, logistical capacity and resources available must be taken into account, as these may influence the feasibility and cost of procuring and deploying nets.

When deciding whether IRS may be appropriate for prevention and control of malaria in humanitarian emergency settings, programmes should consider:

- whether the structures are suitable for spraying. Some shelters provided in emergency settings may not be suitable for application of insecticides, such as open-sided structures and those built from materials that affect the residual nature of the insecticides;
- whether the target coverage of IRS can be feasibly achieved in the setting;
- whether there are sufficient resources to cover the relatively high costs associated with an IRS programme. In such settings, transport of commodities to hard-to-reach areas, coupled with the need to quickly procure items and establish human capacity to deliver the intervention, is likely to incur higher costs than when deploying IRS in more stable settings.

Malaria vector control recommendations *supplementary interventions*

Intervention	Strength & evidence	Unchanged/ revised/new
Larviciding	**Conditional for, low certainty evidence**	Unchanged
Topical repellents*	**Conditional against, low certainty evidence**	Unchanged
Insecticide-treated clothing*	**Conditional against, low certainty evidence**	Unchanged
Space spraying	**Conditional against, very low certainty evidence**	Unchanged
House screening	**Conditional for, low certainty evidence**	New 2021

The GDG determined that a conditional recommendation should be given for house screening because of the low- to moderate-certainty evidence of an impact against malaria. Furthermore, programmes would need to consider a number of local contextual factors when considering screening of residential houses as a public health strategy, such as:

- how the intervention will be delivered and maintained;
- whether the structure and condition of the residential houses in the community allow for the installation of screening;
- the feasibility and resources needed for implementation, especially if deployed on a large scale.

*If the aim is to reduce malaria at the community level

Progress of planned update of guidelines 2021 -2023

- Areas planned for update
  - Background information on 'how nets work': Personal protec
  - Larval habitat management and manipulation
  - Housing modifications

Evidence reviewed by GDG Nov 2020, revised recommendations published July 2021

  - New evidence on use of pyrethroid-PBO nets
  - Vector control in complex emergencies

Evidence reviewed by GDG June 2021, revised recommendations published March 2022

  - Use of dual active-ingredient nets: chlorfenapyr & pyrethroic

Evidence reviewed by GDG Nov 2022, published March 2023

  - Latest evidence for use of IRS
  - Use of topical repellents for both personal and community-le

Reviewed by GDG Nov 2022, publication expected Q2 2023

  - Cost and cost-effectiveness of vector control and resource co

Resources, cost & cost effectiveness included in 2021, 2022, 2023 publications.
To be included in Q2 2023 publication

Vector Control process updates and timeline (3rd set of revisions)

7-10 Nov 2022

GDG meeting: review evidence, formulation of recommendations

Systematic reviews on
- **residual surface treatments**
- **dual a.i. nets**
- **topical repellents**

Nov - Dec 2022

Recommendations drafted and approved by GDG

Dec 2022 – Jan 2023

External review group provide peer review

Jan – Feb 2023 2023

Editing, GRC internal review

March 2023

Publication of recommendations for dual ai nets in MAGICApp and as pdf

May 2023

Publication of recommendations on IRS and topical repellents in MAGICApp and as pdf

https://www.who.int/publications/i/item/guidelines-for-malaria

Dual active ingredient nets:
Pyrethroid-chlorfenapyr nets

Public health value assessed by VCAG in October 2022

Strong recommendation for, Moderate certainty evidence

Pyrethroid-chlorfenapyr ITNs vs pyrethroid-only LLINs (2023)

Pyrethroid-chlorfenapyr ITNs should be deployed instead of pyrethroid-only LLINs for prevention of malaria in adults and children in areas with pyrethroid resistance.

Conditional recommendation for, Moderate certainty evidence

Pyrethroid-chlorfenapyr ITNs vs pyrethroid-PBO ITNs (2023)

Pyrethroid-chlorfenapyr ITNs can be deployed instead of pyrethroid-PBO ITNs for prevention of malaria in adults and children in areas with pyrethroid resistance.

The conditionality of the recommendation to deploy pyrethroid-chlorfenapyr ITNs instead of pyrethroid-PBO ITNs is based on the GDG's judgement that the balance of desirable and undesirable effects probably favours pyrethroid-chlorfenapyr ITNs over pyrethroid-PBO ITNs. However, the evidence for this recommendation is from only one trial in Africa.

In deciding whether to deploy pyrethroid-chlorfenapyr ITNs instead of pyrethroid-only LLINs or pyrethroid-PBO ITNs, malaria programmes should:

- determine whether resources are adequate to cover the extra costs compared to pyrethroid-only LLINs or pyrethroid-PBO ITNs, while ensuring optimal coverage of populations at risk of malaria;
- generate additional information or conduct analyses with the aim of maximizing impact through targeted deployment (e.g. stratification of malaria risk, assessment of the characteristics of local vectors, such as pyrethroid resistance mechanisms). ITNs for prevention of malaria in adults and children in areas with pyrethroid resistance; and
- note that WHO recommends that ITNs prequalified by WHO be selected for deployment.

Conditional recommendation for, Moderate certainty evidence

Pyrethroid-pyriproxyfen ITNs vs pyrethroid-only LLINs (2023)

Pyrethroid-pyriproxyfen ITNs can be deployed instead of pyrethroid-only LLINs for prevention of malaria in adults and children in areas with pyrethroid resistance.

The conditionality of the recommendation to deploy pyrethroid-pyriproxyfen ITNs instead of pyrethroid-only LLINs is based on the GDG's concerns that the available evidence indicates poor cost-effectiveness of pyrethroid-pyriproxyfen ITNs compared to pyrethroid-only LLINs and that the extra resources currently required to purchase these ITNs may negatively impact on coverage and equity.

In deciding whether pyrethroid-pyriproxyfen ITNs should be deployed instead of pyrethroid-only LLINs, malaria programmes should:

- determine whether resources are adequate to cover the extra cost compared to pyrethroid-only LLINs, while ensuring optimal coverage of populations at risk of malaria;
- generate additional information or conduct analyses with the aim of maximizing impact through targeted deployment (e.g. stratification of malaria risk, assessment of the characteristics of local vectors, such as pyrethroid resistance mechanisms); and
- note that WHO recommends that ITNs prequalified by WHO be selected for deployment.

Conditional recommendation against, Moderate certainty evidence

Pyrethroid-pyriproxyfen ITNs vs pyrethroid-PBO ITNs (2023)

Pyrethroid-pyriproxyfen ITNs are not recommended for deployment over pyrethroid-PBO ITNs for prevention of malaria in adults and children in areas with pyrethroid resistance.

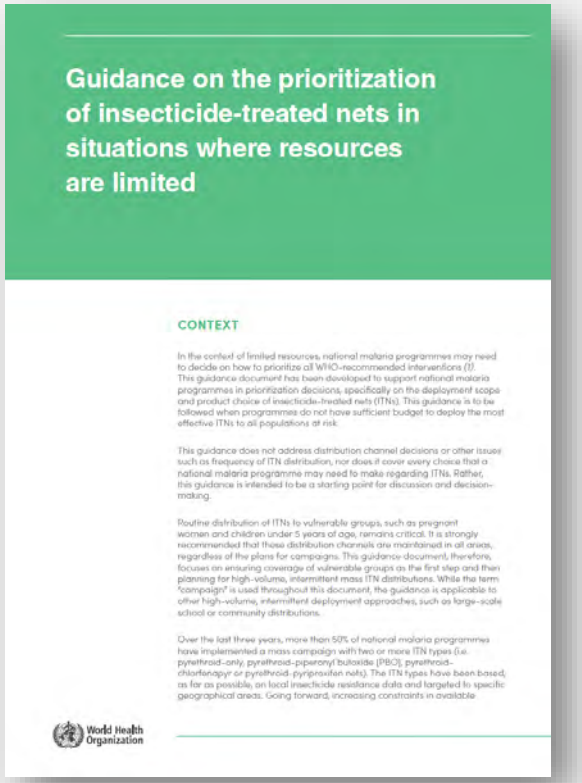
The conditionality of the recommendation against the deployment of pyrethroid-pyriproxyfen ITNs instead of pyrethroid-PBO ITNs is based on the GDG's judgement that the balance of effects favours pyrethroid-PBO ITNs over pyrethroid-pyriproxyfen ITNs and that, based on current cost and efficacy data, pyrethroid-PBO ITNs are more cost-effective. The GDG acknowledged that evidence to support this recommendation is derived from only a single trial in Africa.

Dual active ingredient nets: **Pyrethroid-pyriproxyfen nets**

Public health value assessed by VCAG in October 2022

Guidance on the prioritization of insecticide-treated nets in situations where resources are limited

In 2023, guidance developed to support national malaria programs prioritize ITN distribution and product choice in resource-limited settings



https://www.who.int/publications/i/item/9789240069428

Currently being translated into French and Spanish

Breakthrough ACTION and VectorWorks ITN access and use report to aid prioritization
https://breakthroughactionandresearch.org/resources/itn-use-and-access-report/

ITN deployment prioritization steps

Step 1: Ensure access for vulnerable groups

Commit funding for routine ITN distribution to vulnerable groups in all areas with risk of malaria

Step 2: Define ITN deployment scope

Identify and exclude areas with very low current and historical malaria risk (will it remain so in the absence of ITNs?)

List and rank the areas targeted for ITN campaigns according to malaria risk.

Step 3: Maximize coverage

Calculate the funding needed to ensure full coverage of these at-risk areas with pyrethroid-only nets

Step 4: Maximize effectiveness

4a. Replace pyrethroid-PBO or pyrethroid-chlorfenapyr nets in areas that already have them

If resources remain, go to 4b. If not, Step 5

4b. Substitute pyrethroid-only ITNs with more effective ITNs in additional areas in decreasing order of malaria risk

Step 5: Identify funding gaps

Identify financial needs to increase coverage and make information available to potential financers

Step 6: Ensure adequate funding for surveillance

Allocate sufficient funding to strengthen surveillance and system maintenance

A robust surveillance system is needed to ensure timely detection of potential resurgence of malaria in areas no longer receiving ITNs,

Next steps

May/June 2023: Publication of revised recommendations on IRS and topical repellents

Systematic review/stakeholders interviews to be commissioned on contextual factors, particularly acceptability and feasibility across a range of vector control interventions

No other updates planned for 2023

Interventions on the horizon, being evaluated under VCAG that may trigger establishing a systematic review of the evidence

- Spatial repellents
- ATSBs
- Ivermectin

VCAG: https://www.who.int/groups/vector-control-advisory-group

WHO process on how new interventions are evaluated
https://www.who.int/multi-media/details/vector-control-the-who-evaluation-process-for-new-interventions

Malaria Diagnostics and Treatment: Guideline updates

Malaria Policy Advisory Group (MPAG) Meeting

Geneva, 18-20 April 2022

Dr Peter Olumese
Diagnostics, Medicines and Resistance Team

Global **Malaria** Programme

World Health Organization

Diagnosis

Diagnosis updates and timeline

- General Scope
  - The general scope of this guideline is make recommendations on use of near patient G6PD tests based on their accuracy around thresholds important to support safe treatment of individuals with 8-aminoquinoline drugs for P. vivax malaria.
- PICO Question
  - In patients undergoing G6PD activity testing, how accurate are near-patient tests for G6PD deficiency compared to quantitative spectrophotometric G6PD testing at thresholds *(30% and 70% of normal activity)* critical to informing administration of 8-aminoquinolines to prevent relapses of P.vivax and P.ovale?
- Cochrane systematic review of diagnostic test accuracy of near- patient G6PD tests in people undergoing treatment or prophylaxis with primaquine or tafenoquine or in people susceptible to malaria *(currently underway)*

Diagnosis updates and timeline

Task	Start date	Completion date	Comments
Define the general scope of the guideline	November 2022	January 2023	
Prepare the planning proposal and define the key questions	December 2022	January 2023	
Submit the planning proposal to the GRC		January 2022	Reviewed - March 2022
GDG scoping meeting		March 2023	
Identify and perform or update systematic reviews	March 2023	May 2023	Assuming update to ongoing review can be accommodated
Guideline Development Group meeting to formulate recommendations		June 2023	
Draft the guideline document		July 2023	
Peer review of the guideline document		August-September 2023	
Submit the guideline to the GRC		September 2023	
Electronic publication		November 2023	

Treatment

Treatment recommendations – published in November 2022

Strong recommendation for, low certainty evidence

Artesunate -pyronaridine for uncomplicated malaria (2022)

Artesunate-pyronaridine (ASPY) is recommended as an ACT option for the treatment of uncomplicated *Plasmodium falciparum* malaria.

Strong recommendation for, low certainty evidence

Treatment in the first trimester of pregnancy (2022)

Treat pregnant women with uncomplicated P. falciparum malaria during the first trimester with artemether-lumefantrine.

Treatment recommendations – published November 2022

Strong recommendation for, very low certainty evidence

Short course standard dose primaquine treatment (2022)

To prevent relapse, an additional treatment option of using primaquine 0.5mg/kg /day for 7 days is recommended to treat *P. vivax* or *P. ovale* malaria in children and adults (except pregnant women, infants aged < 6 months, women breastfeeding infants aged < 6 months, women breastfeeding older infants unless they are known not to be G6PD deficient, and people with G6PD deficiency).

Conditional recommendation against, Very low certainty evidence

Short course standard high dose primaquine treatment (2022)

To prevent relapse, WHO recommends against an additional treatment option of using primaquine 1.0 mg/kg /day for 7 days to treat *P. vivax* or *P. ovale* malaria.

Treatment updates and timeline

Task	Start date	Completion date	Comments
GDG scoping meeting		May 2023	GDG Scoping meeting
Prepare the planning proposal and define the key questions	May 2023	June 2023	
Submit the planning proposal to the GRC		June 2023	
Commission or update systematic reviews	June 2023	September 2023	
Guideline Development Group meeting to formulate recommendations		October 2023	GDG Meeting
Peer review of the draft guideline document		October-November 2023	
Submit the guideline to the GRC		November 2023	
Electronic publication		December 2023	

Revisiting comparative effectiveness in the context of the arrival of new vector control products

Malaria Policy Advisory Group Meeting, 18 April 2023

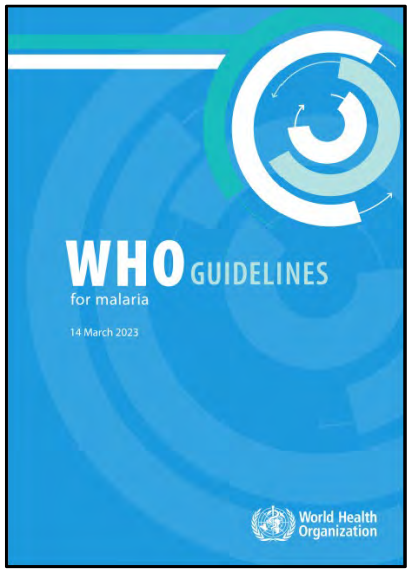
Jan Kolaczinski

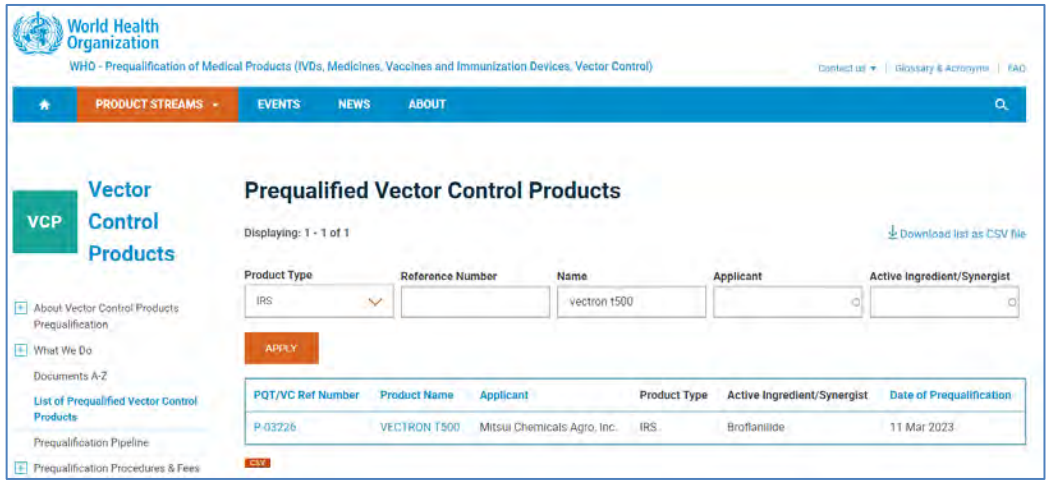
Head, Vector Control & Insecticide Resistance Unit

Global **Malaria** Programme

World Health Organization

Developments since MPAG October 2022 Meeting





- New ITN recommendations released based on data from RCTs on pyrethroid-chlorfenapyr and pyrethroid-pyriproxyfen nets
- New IRS product from a new insecticide class (broflanilides) prequalified
- Second ITN containing pyrethroid + chlorfenapyr prequalified

Products of collaboration across a broad range of stakeholders united in the fight against malaria

WHO GMP requirements for VC guidance development

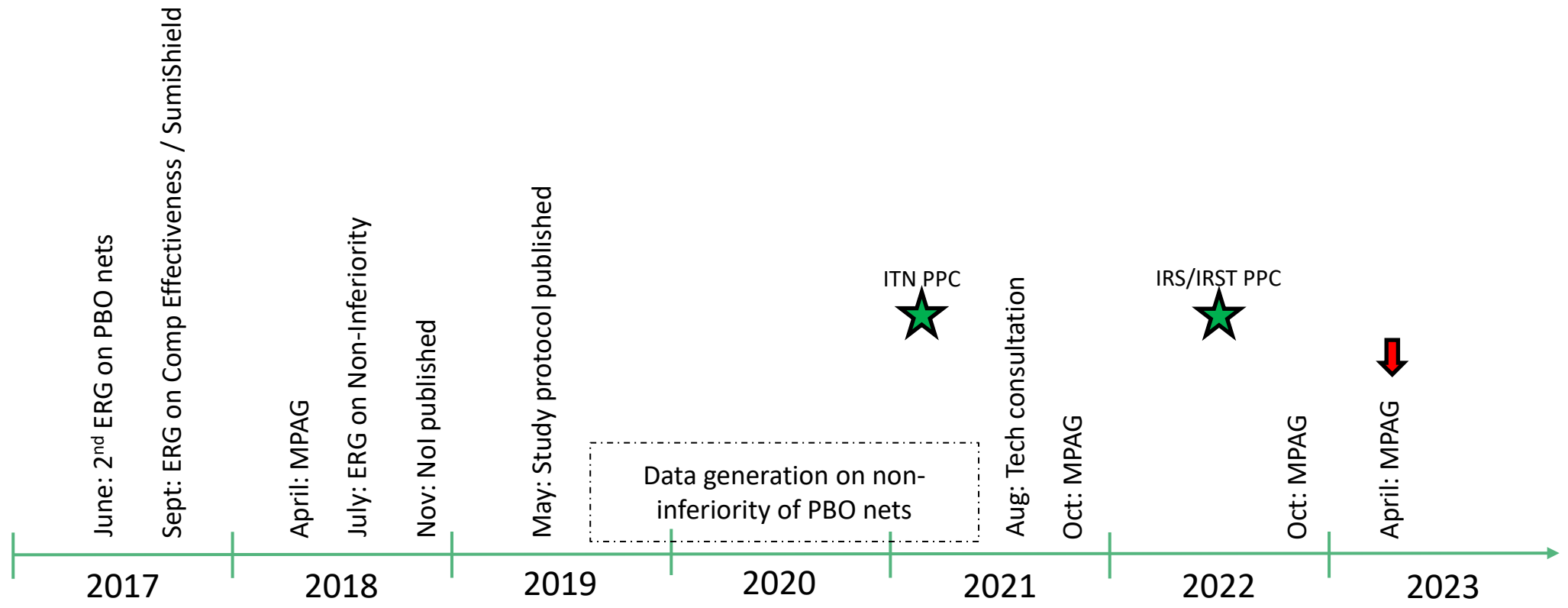
Recommendation Development

- Explicit demonstration of an intervention's epidemiological impact (= public health value) is essential. In most cases data are generated by conducting at least two randomized controlled trials (RCTs) that assess new interventions against one or more current standards of care.
- RCTs are costly and lengthy
- To minimize required investment and speed up market access, WHO has broadened vector control intervention classes, meaning that:
  - overall, fewer trials with epidemiological endpoints may be needed to develop a recommendation (≥2 / class)
  - products within a broadened class (and hence covered by a WHO recommendation) are increasingly diverse

Recommendation Validation / Extension

- Since 2017, WHO advisory groups have identified the need for assurance that similar impact will be achieved by the increasingly diverse products grouped within an intervention class.
- Entomological data are considered as a potential surrogate measure. As for epidemiological data, comparison against the standard of care is considered best practice for assessment of entomological data.

History of comparative effectiveness discussions & investigations in malaria vector control



Publication of Preferred Product Characteristics (PPC), including evaluation criteria / data needs

PPCs in the context of comparative effectiveness

Parameter	Preferred product characteristic
Entomological efficacy	
	• Based on the entomological effect of current fast-acting IRS, IRST products are expected to demonstrate high kill (≥ 80%) of insecticide-resistant mosquito vector(s) within 24 hours of exposure, as measured using WHO cone bioassays *(5)*, to be considered under the fast-acting IRST intervention class. For products that cause at least 80% mortality in the period up to 10 days after insecticide exposure and/or that have an entomological effect other than direct mortality (e.g. reduced blood-feeding, reduced fecundity), data on epidemiological efficacy will be required for WHO to assess their public health value and thereby confirm the provisional slow-acting IRST class *(9)*. • Rapid knockdown of *Anopheles* mosquitoes would be preferable, as would be bite prevention by other means. • For each round of IRS/IRST, the entomological effect(s) should be achieved for a minimum of three months, with a desired duration of residual efficacy being one year or longer (see section on *residual effect/continued efficacy*).
Epidemiological efficacy	
	• Protective efficacy to reduce and/or prevent malaria infection and/or disease in humans in areas where the primary vector(s) is/are resistant to insecticides o A systematic review on IRS updated in 2019 was unable to quantify the effect size for this intervention due to a lack of data and due to low-certainty evidence of protective efficacy compared to no IRS *(3)*. In the absence of such estimate, the preferred epidemiological efficacy targets for IRST should be considered those set by ITNs when deployed in areas of pyrethroid susceptibility *(7)*. ITNs compared to no nets achieved a 17% reduction in all-cause mortality in children, a 45% reduction in the incidence of uncomplicated episodes of *P. falciparum* malaria, and a 17% reduction in *P. falciparum* malaria prevalence *(7)*. o For fast-acting IRST, an extension of the class to new products will be informed by data demonstrating non-inferiority compared to products currently covered by the WHO recommendation for IRS, as was done for neonicotinoids in 2017 *(8)*.

- Preferred Product Characteristics (PPCs) were introduced as part of GMP's revised process for development of WHO recommendations
- Information from technical consultations and MPAG guidance regarding data requirements for comparative assessments has been incorporated in the PPC on IRS/IRST
- Other PPCs will need to be updated to incorporate information on comparative effectiveness

(Re-)emerging technical /policy questions

- What is the variability of products within a class / covered by one WHO recommendation?
- To what extent does this variability matter to malaria control efforts?
- Where does a WHO recommendation ‘stop’? or When does extrapolation based on the epidemiological impact data generated for one type of product(s) cease?
- How can assurance of similar disease impact across an increasingly diverse product range within a class be provided?


Global Malaria Programme

Data requirements and methods to support the evaluation of new vector control products

DECEMBER 2017 RECOMMENDATIONS

BACKGROUND

WHO's process for the evaluation of vector control tools, technologies and approaches has been revised to better meet the needs of countries endemic for, or at risk of, vector-borne diseases. Under the revised process, the evaluation pathway to be followed is determined by whether or not a product is part of a product class with an existing WHO policy recommendation for its use.[1]

Products covered by an existing WHO policy recommendation will follow the *Prequalification Pathway*, while all new tools, technologies and approaches will follow the *New Intervention Pathway*, supported by the Vector Control Advisory Group (VCAG). VCAG will validate whether the intervention under assessment has public health value.[2] Once public health value has been demonstrated, WHO will issue a policy recommendation.

Following a request from the Malaria Policy Advisory Committee (MPAC) in March 2017, WHO is reviewing the data requirement associated with the evaluation of new vector control interventions to ensure that these can be deployed as soon as possible, while also ensuring that policy recommendations to guide deployment remain evidence-based.

With the move to a revised evaluation system and the arrival of new vector control products, WHO must also guide assessment of products that clearly fall within an established intervention class, but that differ in product specification and/or design (e.g. location of insecticide or synergists on panels of mosquito nets) from the first-in-class product that established the class and for which epidemiological data are available. For such new products, WHO requires reassurance of similar performance (for disease or vector control) to provide normative guidance to vector control programmes faced with the challenge of selecting a reliable product. Examples of such

World Health Organization

(Re-)emerging technical /policy questions

Following a request from the Malaria Policy Advisory Committee (MPAC) in March 2017, WHO is reviewing the data requirement associated with the evaluation of new vector control interventions to ensure that these can be deployed as soon as possible, while also ensuring that policy recommendations to guide deployment remain evidence-based.

With the move to a revised evaluation system and the arrival of new vector control products, WHO must also guide assessment of products that clearly fall within an established intervention class, but that differ in product specification and/or design (e.g. location of insecticide or synergists on panels of mosquito nets) from the first-in-class product that established the class and for which epidemiological data are available. For such new products, WHO requires reassurance of similar performance (for disease or vector control) to provide normative guidance to vector control programmes faced with the challenge of selecting a reliable product. Examples of such

From: Evidence review group report on *Data requirements and methods to support the evaluation of new vector control products.* WHO 2017. Available from: http://apps.who.int/iris/handle/10665/259536

(Re-)emerging operational questions

- Who is asking for comparative data and why?
- How are these data going to be used?
- How are any findings of comparative assessments going to be communicated?
- Where does assessment of comparative effectiveness sit within the vector control evaluation process and more generally within WHO?

Questions & Answers

Who is asking for comparative data and why?

- WHO GMP and its advisory groups have since 2017 consistently identified the need for comparative data within with established classes. GMP has now issued a specific data call.
- Anecdotal (rather than systematically collected) evidence also indicated the value of these data to WHO Member States in contributing to prioritization decisions, and to their procurement partners.

How are these data going to be used by WHO?

- To date, WHO used comparative effectiveness data to inform discussions by evidence review groups / technical consultations and to formulate advice to WHO for consultation with MPAG. The aim of these meetings was to:
  - Assess the evidence-base to support extension of WHO's IRS recommendation to neonicotinoid insecticides
  - Develop a methodology for data generation to allow comparative assessments
  - Review available data on pyrethroid-PBO nets to assess whether these types of nets are of comparative entomological performance, and to use the data set to inform evolution of the methods and overall approach
  - Based on this precedence, another technical consultation is planned for 2023 to review comparative effectiveness of pyrethroid-PBO nets not included in the 2021 review, other new types of nets, and to assess the applicability of WHO's IRS recommendation to new insecticide classes (broflanilides, pyrroles, etc.)

Questions & Answers

How are any findings of comparative assessments going to be communicated?

- To date, WHO has communicated all findings in summary form through meeting reports
- As comparative assessments start to become routine, alternatives for the dissemination of findings need to be explored (e.g. dedicated website to bring together the outcomes of different technical meetings)

Where does assessment of comparative effectiveness sit within the vector control evaluation process and more generally within WHO?

- At present comparative assessments are an emerging area of evaluation within GMP focused on vector control and linked to validating applicability of WHO recommendations in this area. Up to now this area has been overseen by the GMP VCR unit.
- VCR links to other departments across WHO with the aim of: i) evolving the process, and ii) the organizational position on comparative assessments as part of WHO's broader mandate to provide evidence-based guidance to WHO member states

Questions to MPAC

- Is there a need to further validate the value of comparative assessments in the context of WHO's work of providing evidence-based guidance?
- Is the process for data generation, data submission and analysis, as well as for communication of findings, in need of further clarification/evolution?
- What next steps does MPAG recommend to GMP and to WHO more generally?

Questions to WHO GMP? vc-noninferiority@who.int

Update on the E-2025 Global Forum and certification of malaria elimination

Malaria Policy Advisory Group meeting, 18-20 April 2023

Dr Elkhan Gasimov, Head of Elimination Unit

Global Malaria Programme

Global **Malaria** Programme

World Health Organization

4th Global Forum of malaria eliminating countries
24-26 January 2023, Cape Town, South Africa

Global **Malaria** Programme

World Health Organization

Global Forum agenda

Day 1

Progress and challenges

Four working groups

- ***Presentation by each country representative***
- ***Feedback from each group***

Day 2

Accelerate elimination

Update on WHO guidelines for malaria and Monitoring of surveillance systems

Country experiences

- ***MDA in Sao Tome and Principe***
- ***Subnational verification in Thailand***
- ***Acceleration of malaria elimination in Cambodia***
- ***Maintaining surveillance among other health crisis in Malaysia***
- ***Verification of the absence or under-reporting of indigenous malaria transmission, PAHO/El Salvador***

Panel discussions

Building and sustaining capacity to accelerate malaria elimination and prevent re-establishment of transmission.

Day 3

Technical consultation on PoR

Country experiences

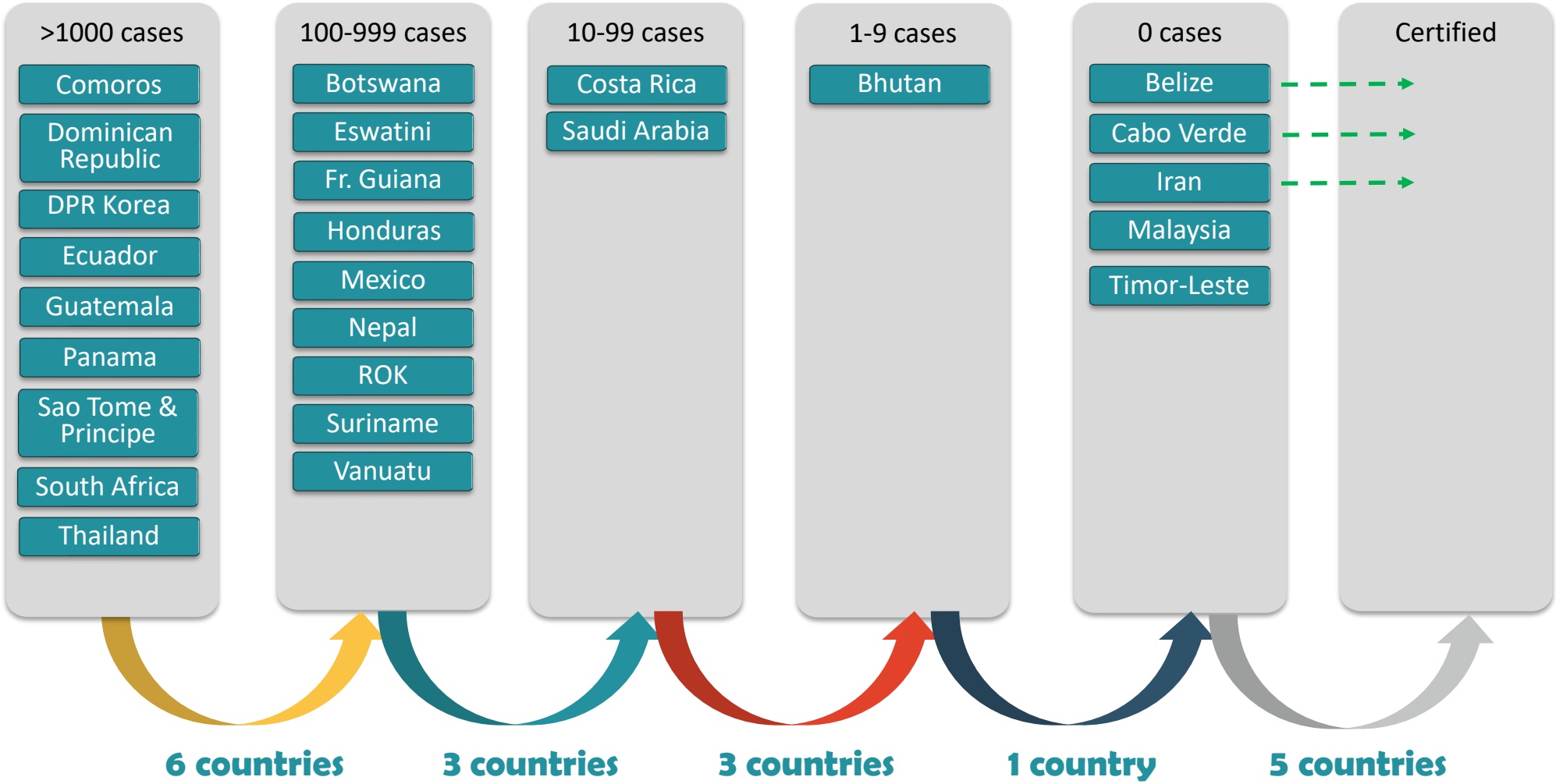
- ***China and El Salvador***

Panel discussion

- ***Entomological surveillance and integrated vector control***
- ***Maintain case surveillance***
- ***Human and financial resources***
- ***Outbreak preparedness and response***

E-2025 Initiative: expected outcomes by 2023

Where we are in 2021



Country	2015	2016	2017	2018	2019	2020	2021
Belize	9	4	7	3	0	0	0
Bhutan	34	15	11	6	2	22	9
Botswana	284	659	1,847	534	169	884	703
Cabo Verde	7	49	423	2	0	0	0
Comoros	1,884	1,467	3,896	15,613	17,599	4,546	10,537
Costa Rica	0	4	12	70	95	90	189
Democratic People's Republic of Korea	7,022	5,033	4,603	3,698	1,869	1,819	2,357
Dominican Republic	631	690	341	433	1,291	826	284
Ecuador	618	1,191	1,275	1,653	1,803	1,934	2,175
Eswatini	318	250	440	686	235	233	505
French Guinana	374	217	554	546	212	140	143
Guatemala	5,538	5,000	4,121	3,018	2,069	1,058	1,273
Honduras	3,555	4,094	1,273	632	330	815	1,550
Iran (Islamic Republic of)	167	81	57	0	0	0	0
Malaysia	242	266	85	0	0	0	0
Mexico	517	551	736	803	618	356	242
Nepal	591	507	623	493	127	73	32
Panama	546	769	649	684	1,756	1,946	4,354
Republic of Korea	627	602	436	501	485	356	274
Sao Tome and Principe	2,056	2,238	2,239	2,937	2,732	1,933	2,719
Saudi Arabia	83	272	177	61	38	83	0
South Africa	4,959	4,323	23,381	9,540	3,096	4,463	2,958
Suriname	81	78	137	37	104	156	22
Thailand	14,265	12,076	7,416	5,110	4,065	3,123	2,426
Timor-Leste	80	81	16	0	0	3	0
Vanuatu	571	2,243	1,227	632	567	493	312

Key challenges specified by countries

- Political Commitment, awareness and urgency of malaria elimination among local authorities and key stakeholders
- Shortage of human resources for malaria elimination (quantity and quality) and financial resources
- Resilience of the health system
- Inadequate multisectoral collaboration
- Cross border collaborative activities
- Population movement (within country and between countries)
- Reduced risk perception among communities and delayed health seeking behaviors

Global Forum conclusions / recommendations

- Country leadership and political will is vital in elimination of malaria. WHO has an important role in advocating for elimination.
- Acceleration towards elimination is important and needed to get countries back on track. It is important to better document where acceleration has been successful and how this was facilitated.
- Strengthening capacity of WHO staff at the regional and country level is equally important as capacity building of the national malaria programme.
- Sustained funding of elimination programmes has to be ensured.
- Regional/subregional perspective is important, particularly in situations when malaria situation in neighboring countries greatly affect those in elimination.
- Additional efforts are needed to disseminate / clearly communicate new WHO guidelines on elimination and provide clear guidance on implementation of the guidelines.

Certification of malaria elimination: progress


CERTIFICATION OF MALARIA ELIMINATION

Republic of Azerbaijan

The World Health Organization certifies that the Republic of Azerbaijan has eliminated indigenous transmission of all human malaria parasites within the nation's borders.

23 March 2023

World Health Organization

Dr Tedros Adhanom Ghebreyesus
Director-General


СЕРТИФИКАЦИЯ ЭЛИМИНАЦИИ МАЛЯРИИ

Республика Таджикистан

Всемирная организация здравоохранения настоящим сертифицирует элиминацию в Республике Таджикистан местной передачи в пределах границ страны всех малярийных паразитов, вызывающих малярию у человека.

23 марта 2023 г.

Всемирная организация здравоохранения

Д-р Тедрос Адханом Гебрейесус
Генеральный директор

23 March 2023: Azerbaijan and Tajikistan are certified

Certification of malaria elimination

11 COUNTRIES	15 COUNTRIES and 1 TERRITORY	0	7 COUNTRIES	8 COUNTRIES
1955–1969	1970–1987	1988–2006	2007–2017	2018–2023
• Bulgaria • Cyprus • Dominica • Grenada • Hungary • Jamaica • Poland • Romania • Saint Lucia • Spain • Trinidad and Tobago	• Australia • Bosnia-Herzegovina • Brunei Darussalam • Croatia • Cuba • Italy • La Réunion (France) • Mauritius • Montenegro • Netherlands • North Macedonia, • Portugal • Serbia • Singapore • Slovenia • United States of America		• Armenia • Kyrgyzstan • Maldives • Morocco • Sri Lanka • Turkmenistan • United Arab Emirates	• Algeria • Argentina • Azerbaijan • China • El Salvador • Paraguay • Tajikistan • Uzbekistan

- 41 countries and 1 territory have been certified malaria-free.
- 61 countries listed in supplementary list.

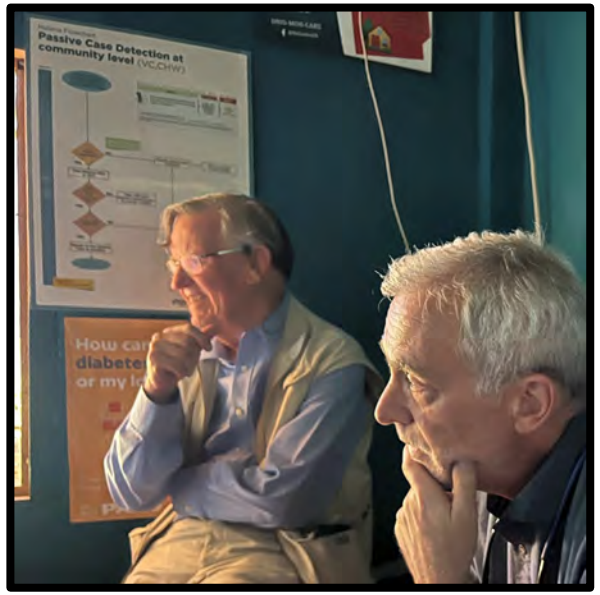
Certification status in the WHO European region

Georgia: the process is initiated

Turkey:

Certification plans

Belize



Brian Greenwood
Larry Slutsker
Feb 28th – March 8th 2023

Cabo Verde

- 1st WHO-led mission: **June-July 2022**
- 2nd WHO-led mission: **May-June 2023**
- Final mission: **Q4 2023**

Georgia

- January 2023: initiated process for preparing for certification
- Certification is planned in **2024**

Timor-Leste

- February 2023: meeting with the Minister of Health
- Official request is expected in September 2023
- Certification is planned in **2024**

Prevention of re-establishment of malaria transmission

Technical consultation on prevention of re-establishment of malaria transmission to *review and update current WHO guidance on prevention of re-establishment to support countries' efforts at maintaining malaria-free status at national and sub-national levels*.

Technical consultation on PoR: Workplan

	EVENT	OBJECTIVE	TIMELINE
1	Officially launch the technical consultation on prevention of re-establishment during the fourth Global Forum of malaria-eliminating countries	• Launch the technical consultation • Review and discuss two case studies: China and El Salvador • Discuss challenges to prevention of re-establishment	24-26 Jan 2023
2	Virtual meetings to review case studies and updates on WHO policies and recommendations on health systems	Greece and Paraguay Sri Lanka, Oman, Mauritius Tajikistan, Uzbekistan, Georgia	21-23 Feb 2023
3	Evidence review in Tbilisi, Georgia	Evidence review meeting	29-30 Mar 2023
4	Publish the product of the technical consultation		Dec 2023

Technical consultation on PoR: Workplan

	EVENT	OBJECTIVE	TIMELINE
1	Officially launch the technical consultation on prevention of re-establishment during the fourth Global Forum of malaria-eliminating countries	• Launch the technical consultation • Review and discuss two case studies: China and El Salvador • Discuss challenges to prevention of re-establishment	26 Jan 2023

Technical consultation on PoR: Workplan

	EVENT	OBJECTIVE	TIMELINE
2	Virtual meetings to review case studies and updates on WHO policies and recommendations on health systems	Greece and Paraguay Sri Lanka, Oman, Mauritius Tajikistan, Uzbekistan, Georgia	21-23 Feb 2023

Prevention of re-establishment of malaria transmission

Evidence to be reviewed

1. Literature and grey literature review on prevention of re-establishment, including on:
   - factors that contribute to the resurgence of malaria after elimination is achieved
   - factors that might contribute to the stability of malaria elimination in malaria-free countries
2. Review on the refractoriness to Plasmodium infections in Anopheles species/strains and biological factors that could result in refractoriness.

Technical consultation on PoR: Workplan

	EVENT	OBJECTIVE	TIMELINE
3	Evidence review in Tbilisi, Georgia	Evidence review meeting	29-30 Mar 2023

Technical consultation on PoR: Workplan

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4	Publish the product of the technical consultation		Dec 2023

Thank you!

Malaria Policy Advisory Group Meeting
18—20 April 2023, Geneva, Switzerland
Background document for Session 4

Update on the RTS,S/AS01 malaria vaccine implementation programme and WHO evidence review of R21/MatrixM

April 2023

1. Background

In October 2021, the World Health Organization (WHO) recommended the first malaria vaccine (RTS,S/AS01) to be used for the prevention of *Plasmodium falciparum* malaria in children living in regions with moderate to high malaria transmission *(1)*. The WHO recommendation was informed by data and insights generated by the pilot implementation of the malaria vaccine in routine immunization programmes in selected areas of Ghana, Kenya and Malawi, and other available RTS,S clinical evidence *(2)*. Subsequently, the Gavi Board approved a malaria vaccine programme to support roll-out in Gavi-eligible countries. In July 2022, the vaccine was prequalified by WHO.

The malaria vaccine implementation programme (MVIP) will continue in the three pilot countries through December 2023, with continued monitoring of data on safety, impact, coverage achieved and the added benefit of a fourth dose. An embedded case-control study, led by Kintampo Health Research Centre, is measuring the added value of a four-dose schedule over a three-dose schedule. Results are expected in 2024. WHO and partners are facilitating the scale-up of the malaria vaccine, coordinating efforts through the Malaria Vaccine Coordination Team. Efforts include the dissemination of pilot experience and evidence to inform country decision-making on vaccine adoption as part of national malaria control strategies. Gavi has reported unprecedented demand for a vaccine, with the three pilot countries and 12 additional countries submitting applications to introduce the malaria vaccine during the first available Gavi application rounds.

Since the recommendation of RTS,S/AS01, the research and development pipeline for malaria vaccines has continued to advance. R21/MatrixM, developed by the University of Oxford and manufactured by Serum Institute India, will be the second malaria vaccine to be reviewed by WHO for a potential recommendation for use. A WHO policy recommendation for malaria vaccines is already in place. Therefore, if R21/MatrixM is considered sufficiently similar to the currently recommended malaria vaccine and safety and efficacy are determined to be adequate, this second vaccine could be included under the existing WHO policy recommendation for malaria vaccines.

2. The MVIP

Vaccine uptake and coverage in the three MVIP countries continues to be good. Community and health worker acceptance of the vaccine is high. As of March 2023, over 4.2 million doses of the malaria vaccine had been administered across the three countries, and more than 1.4 million children had received at least one dose of the RTS,S vaccine. Based on administrative data for 2022, coverage for the first dose was 77% in Ghana (third dose: 74%; fourth dose: 53%), 83% in Kenya (third dose: 72%; fourth dose: 36%) and 89% in Malawi (third dose: 76%; fourth dose:50%; data until September 2022) These coverage levels continue to demonstrate strong demand among caregivers and communities, good acceptance and understanding of the vaccine among health workers and feasibility of implementation via the routine immunization programme. The lower coverage for the fourth dose follows a similar trend for other vaccines administered in the second year of a child's life, pointing to

generic (rather than vaccine-specific) challenges of reaching children at an older age. The vaccine has been shown to be safe, with no safety signals seen after more than 4 million doses delivered. Impact is high, with a significant 25–30% reduction in child hospitalizations for severe malaria since the vaccine was introduced in the pilot areas, and a reduction in all-cause child mortality in children who are age-eligible for the vaccine. Priority actions to maintain and further improve immunization performance, particularly with respect to the uptake of the fourth dose, continue to be taken by the national immunization programmes, supported by partners.

The Ministries of Health of Ghana, Kenya and Malawi have all expanded vaccine delivery to comparator areas of the pilot and have been successful in their applications to Gavi to continue vaccine delivery after the MVIP ends. Malawi expanded vaccine delivery to the pilot areas that had not yet begun providing the malaria vaccine (i.e. comparator areas) in Q4 2022, while Ghana and Kenya expanded in Q1 2023, supported by the vaccine doses donated by GSK for the MVIP and additional funding provided through a grant from Open Philanthropy to PATH.

3. High demand for malaria vaccine roll-out

In December 2021, soon after the WHO recommendation for the malaria vaccine, the Gavi Board approved support to facilitate roll-out of the malaria vaccine in Gavi-eligible countries *(4)*. Gavi has reported unprecedented demand for the malaria vaccine, with at least 28 countries expressing interest in introducing it. Of these, 15 countries already submitted an application to Gavi for support, and more than 15 additional applications are expected later this year. The three MVIP countries have already been approved by Gavi to receive vaccine support to maintain malaria vaccination services in pilot areas once the MVIP ends. Anticipating the initial gap between high demand and available supply, WHO coordinated the development of a Framework for allocation of limited malaria vaccine supply, to guide in a transparent and fair manner where initial limited vaccine doses should be allocated *(5)*. It was developed with guidance from expert advisers, most of whom are from malaria-affected countries in Africa, and inputs from stakeholders during a broad consultation process. The priority principle of the Framework is to allocate the malaria vaccine to areas of greatest need across countries, that is, to areas where the malaria disease burden in children and the risk of death are highest. A primary implication is that all countries will have to consider a phased approach to vaccine implementation, starting at subnational level in the areas of greatest need, with expansion as supply increases. Given the severity of supply constraints, it is likely that not all countries that apply for Gavi support may get malaria vaccine doses in the initial years.

4. WHO evidence review of R21/MatrixM for potential recommendation for use

Similar to RTS,S/AS01, R21/MatrixM is a pre-erythrocytic stage vaccine indicated for the reduction of clinical malaria due to *P. falciparum* in infants and young children. R21/MatrixM targets the circumsporozoite protein (the same target as RTS,S/AS01) and is formulated with the adjuvant MatrixM, which is bulk manufactured by Novavax AB and provided to Serum Institute India. A Phase 2 trial conducted in areas of highly seasonal transmission (where transmission is largely limited to four or five months of the year) showed high efficacy when the vaccine was provided to children from 5 months of age just prior to the high transmission season *(6)*. Although direct comparison is problematic for a number of reasons, the level of efficacy appears to be similar to that of RTS,S/AS01 when given in similar highly seasonal transmission settings just prior to the high transmission season *(7).*

A Phase 3 multi-centre randomized controlled trial began in January 2021 to evaluate the efficacy of 5 µg R21/50 µg MatrixM against clinical malaria in African children. The trial is evaluating two vaccine administration strategies:

- age-based administration in children aged 5–36 months in Dandé, Burkina Faso; Kilifi, Kenya; and Bagamoyo, United Republic of Tanzania (total of 2400 participants, all in low or low/moderate perennial transmission areas), with a three-dose primary series followed by a fourth dose given 12 months after the third vaccination;
- seasonal administration in children aged 5–36 months in Nanoro, Burkina Faso, and Bougouni, Mali (total of 2400 participants in areas of highly seasonal transmission), with a three-dose primary series given from April/May to June/July prior to the malaria transmission season, followed by a fourth dose given annually in June/July the following year.

WHO policy and evidence review process

There are several groups involved in the WHO review of R21/MatrixM. The Strategic Advisory Group of Experts on Immunization (SAGE) Steering Group on Vaccination Policy Guidance (SG) is an internal WHO group that assesses whether a new product can be accommodated under an existing WHO recommendation or position. For malaria, the SG will include experts from the WHO Department for Immunization, Vaccines and Biologicals and the Global Malaria Programme. In addition, the SAGE/Malaria Policy Advisory Group Working Group on Malaria Vaccines (SAGE/MPAG WG) has been asked to review the evidence and provide recommendations to the SG.

A WHO policy recommendation for malaria vaccines is already in place. Therefore, if R21/MatrixM is considered sufficiently similar to the currently recommended vaccine and the safety and efficacy data are considered adequate, it could potentially be included under the existing WHO recommendation for malaria vaccines, allowing for a more efficient recommendation pathway without the need for a separate review by SAGE. If R21/MatrixM is not considered sufficiently similar to the currently recommended malaria vaccine, a full review by SAGE and MPAG would be conducted to develop a new WHO policy. This would result in a longer timeline to potential recommendation; however, this does not seem to be the likely pathway based on the initial data.

In March 2023, the SAGE/MPAG WG conducted an initial evidence review based on the data available (approximately 90% of participants had completed the 12-month follow-up post dose three in standard administration sites and 90% had completed the 18-month follow-up in seasonal sites). Key topics discussed included study design, transmission intensity and patterns, seasonal versus standard age-based vaccine administration schedules, vaccine efficacy against clinical malaria and severe malaria, duration of protection, waning vaccine efficacy and safety.

The R21/MatrixM Phase 3 trial is currently ongoing, and the next review by the SAGE/MPAG WG and the SG will occur when the 18-month follow-up is complete for seasonal administration and the 12-month follow-up is complete for age-based administration. The timeline for review is very dependent on the timely submission of data and analyses from the developers.

Should a second malaria vaccine be recommended, it could be highly beneficial to malaria control by increasing the supply to meet the unprecedented high demand, resulting in greater access and more lives saved.

References

1. Malaria vaccine: WHO position paper – March 2022. Geneva: World Health Organization; 2022 (https://apps.who.int/iris/handle/10665/352337, accessed 4 April 2023).
2. Malaria vaccine implementation programme [website]. Geneva: World Health Organization (https://www.who.int/initiatives/malaria-vaccine-implementation-programme, accessed 4 April 2023).
3. Mosquirix product overview [website]. In: WHO – Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control). Geneva: World Health Organization (https://extranet.who.int/pqweb/content/mosquirix, accessed 4 April 2023).
4. Gavi Board approves funding to support malaria vaccine roll-out in sub-Saharan Africa [website]. Geneva: Gavi, the Vaccine Alliance; 2021 (https://www.gavi.org/news/media-room/gavi-board-approves-funding-support-malaria-vaccine-roll-out-sub-saharan-africa, accessed 4 April 2023).
5. Framework for the allocation of limited malaria vaccine supply. Geneva: World Health Organization; 2022 (https://www.who.int/publications/m/item/framework-for-allocation-of-limited-malaria-vaccine-supply, accessed 4 April 2023).
6. Datoo MS, Natama HM, Somé A, Bellamy D, Traoré O, Rouamba T, et al. Efficacy and immunogenicity of R21/Matrix-M vaccine against clinical malaria after 2 years' follow-up in children in Burkina Faso: a phase 1/2b randomised controlled trial. Lancet Infect Dis. 2022. doi:10.1016/S1473-3099(22)00442-X.
7. Chandramohan D, Zongo I, Sagara I, Cairns M, Yerbanga RS, Diarra M, et al. Seasonal malaria vaccination with or without seasonal malaria chemoprevention. N Engl J Med. 2021. doi:10.1056/NEJMoa2026330.

Contact

For more information, please contact:

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Update on RTS,S/AS01 malaria vaccine implementation programme and WHO evidence review for R21/Matrix-M malaria vaccine

Mary Hamel, Lindsey Wu, Eliane Furrer (WHO)

Credit: WHO/Fanjan Combrink.

MPAG April 2023 meeting

Session 4: Malaria Vaccines – FOR INFORMATION

- Update on the Malaria Vaccine Implementation Programme (MVIP) and RTS,S/AS01 malaria vaccine roll-out
- Update on WHO evidence review for R21/MatrixM malaria vaccine

Malaria Vaccine Implementation Programme (MVIP) and RTS,S/AS01 roll out

Mary Hamel and Eliane Furrer, WHO

Credit: WHO/Neil Thomas.

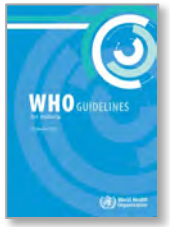
WHO recommendation on use of the first malaria vaccine: Oct 2021

WHO recommends the RTS,S/AS01 malaria vaccine be used for the prevention of *P. falciparum* malaria in children living in regions with moderate to high transmission as defined by WHO

- RTS,S/AS01 malaria vaccine should be provided in a schedule of 4 doses in children from 5 months of age for the reduction of malaria disease and burden.
- Countries may consider providing the RTS,S/AS01 vaccine seasonally, with a 5-dose strategy in areas with highly seasonal malaria or areas with perennial malaria transmission with seasonal peaks.

Useful links

WHO malaria vaccine position paper
https://www.who.int/publications/i/item/who-wer9709-61%E2%80%9380



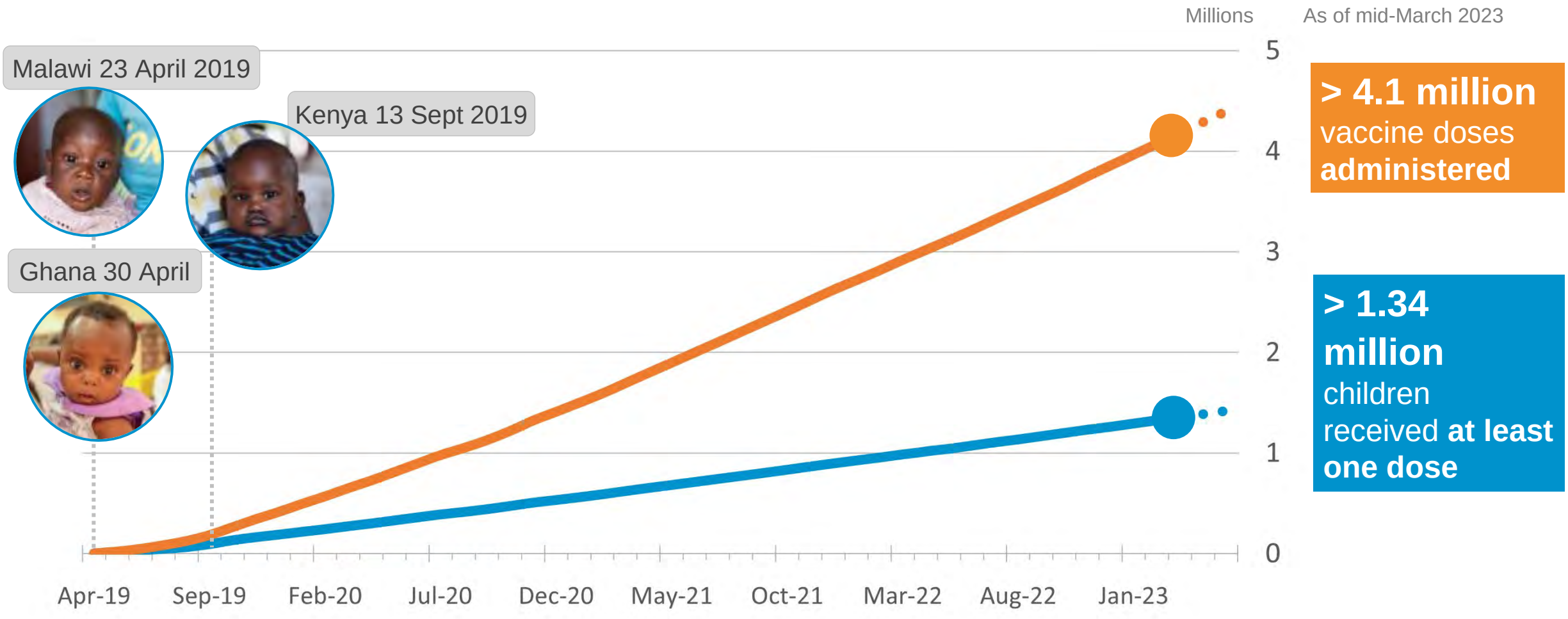
WHO Guidelines for malaria
PDF version:
https://www.who.int/publications/i/item/guidelines-for-malaria
MAGICapp Online platform:
https://app.magicapp.org/#/guideline/5701

Malaria Vaccine Implementation Programme
https://www.who.int/initiatives/malaria-vaccine-implementation-programme

NITAG Resource center
https://www.nitag-resource.org/

Malaria Vaccine Implementation Programme progressing well

World Health Organization



> 4.1 million
vaccine doses **administered**

> 1.34 million
children received **at least one dose**

Estimates as of mid-March 2023 - based on monthly MOH/EPI administrative data reports until January 2023 (for Kenya and Ghana) and September 2022 (for Malawi) and MVIP team projections for subsequent months

Expansion of vaccination to MVIP comparator areas

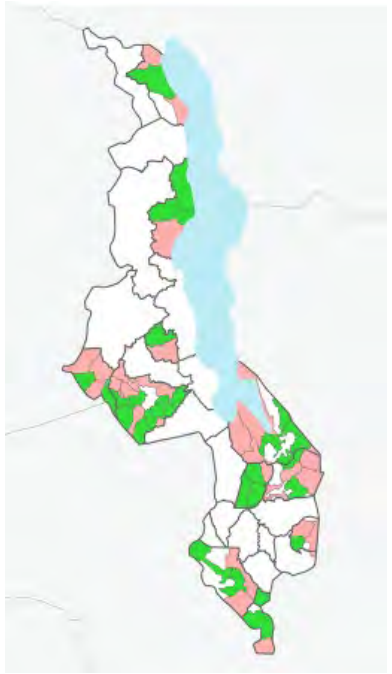
Using vaccine doses donated by GSK & funding from US-based Open Philanthropy to PATH

World Health Organization

Malawi

First introduced: 23 April 2019

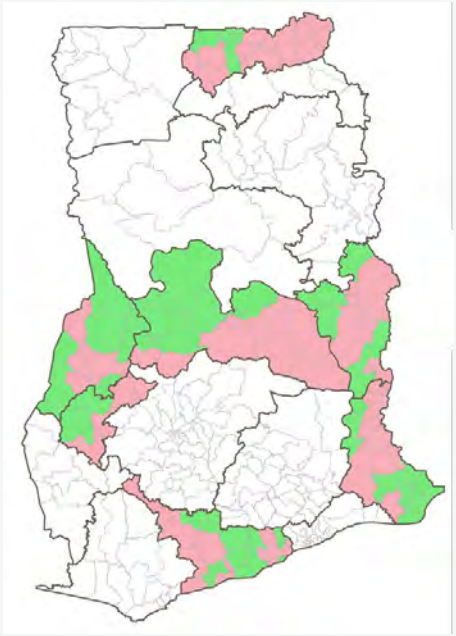
Expanded: 29 Nov 2022



Ghana

First introduced: 30 April 2019

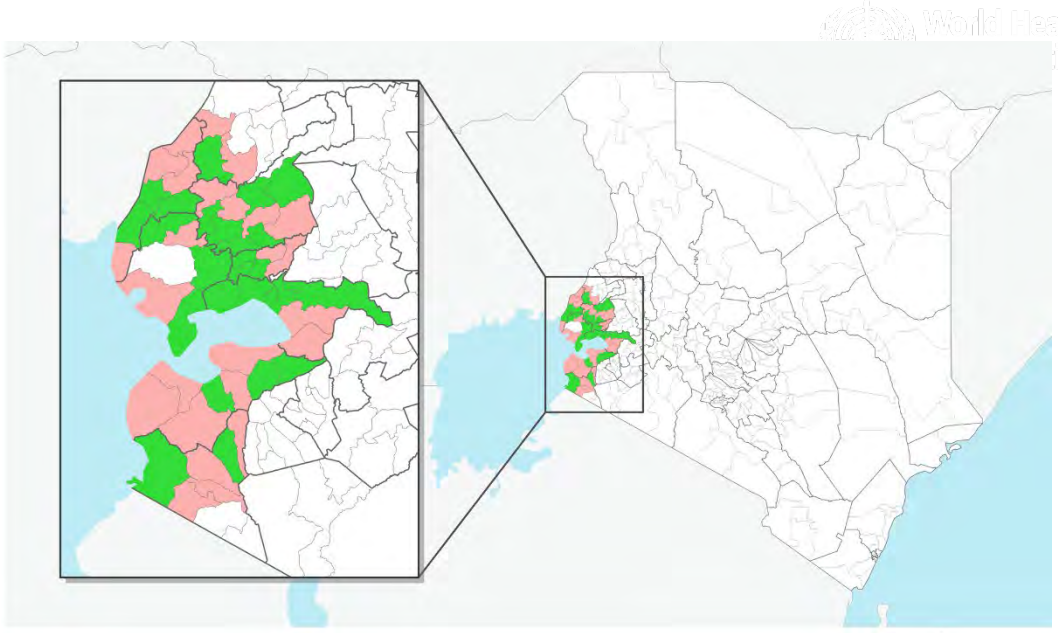
Expanded: 20 Feb 2023



Kenya

First introduced: 13 Sept 2019

Expanded: 7 March 2023



MVIP vaccinating district

MVIP comparator district (**initially non-vaccinating – now introducing using donated vaccine doses available until end of MVIP**)

Non MVIP district

Planning for end of MVIP (July 2017 - Dec 2023)

- Hospital and mortality surveillance reached 46 months in February 2023 in Ghana and Malawi; July 2023 in Kenya
- Analysis of the pilot evaluation (Q4 2023)
  - Feasibility of vaccine introduction, including uptake of the 4th dose
  - Safety after more than 4 million doses given
  - Impact on severe malaria and mortality, with the level of coverage achieved; any indication of rebound in the population age-eligible for vaccination
- PATH-led qualitative findings; mathematical modeling on cost-effectiveness and impact (2024)
- EDCTP-funded case-control study nested in MVPE (2024)
  - Measure added benefit of 4-dose over 3-dose schedules and individual measures of safety
  - **At risk** due to end of hospital surveillance while severe malaria cases still need to be identified; US$ 2M funding gap

Planning for end of MVIP: December 2023

Credit: WHO/Fanjan Combrink

Document and disseminate results and wide variety of lessons learned

- Plan for wide dissemination in country; regionally; globally through presentations, scientific symposia, regional conference
- Many lessons learned incorporated into Vaccine Introduction Guide and related tools / materials (e.g., updated generic WHO training modules)
- Lessons learned for future malaria vaccine review, incorporated into policy/recommendation pathway, including for R21/MatrixM review
- Document through publications, including comparing introduction strategies and results; MVPE analysis on safety, impact, feasibility; Framework for Policy Decision; Allocation Framework; lessons learned; among others
- Support cross-country engagement with MoH and partners from pilot countries – providing opportunities to incorporate lessons learned in pilot countries into new vaccine introductions

Malaria vaccine access

Ms Eliane Furrer

Malaria vaccine supply

Current situation

First Malaria Vaccine RTS,S/AS01

WHO pre-qualified since 15 July 2022

Manufacturer	GSK
Price	EUR 9.30/dose (initially)
Current availability	18M doses for 2023-2025
Allocation	Based on Framework for Allocation of Limited Malaria Vaccine Supply

Medium to long term outlook

- RTS,S/AS01 to be supplied by Bharat Biotech (India), product transfer underway
- Potential market entry of R21/Matrix-M, currently in Phase 3 trials, data review by SAGE/MPAG WG started
- Weighted Average Price reduction expected with more supply and scale up of production capacity

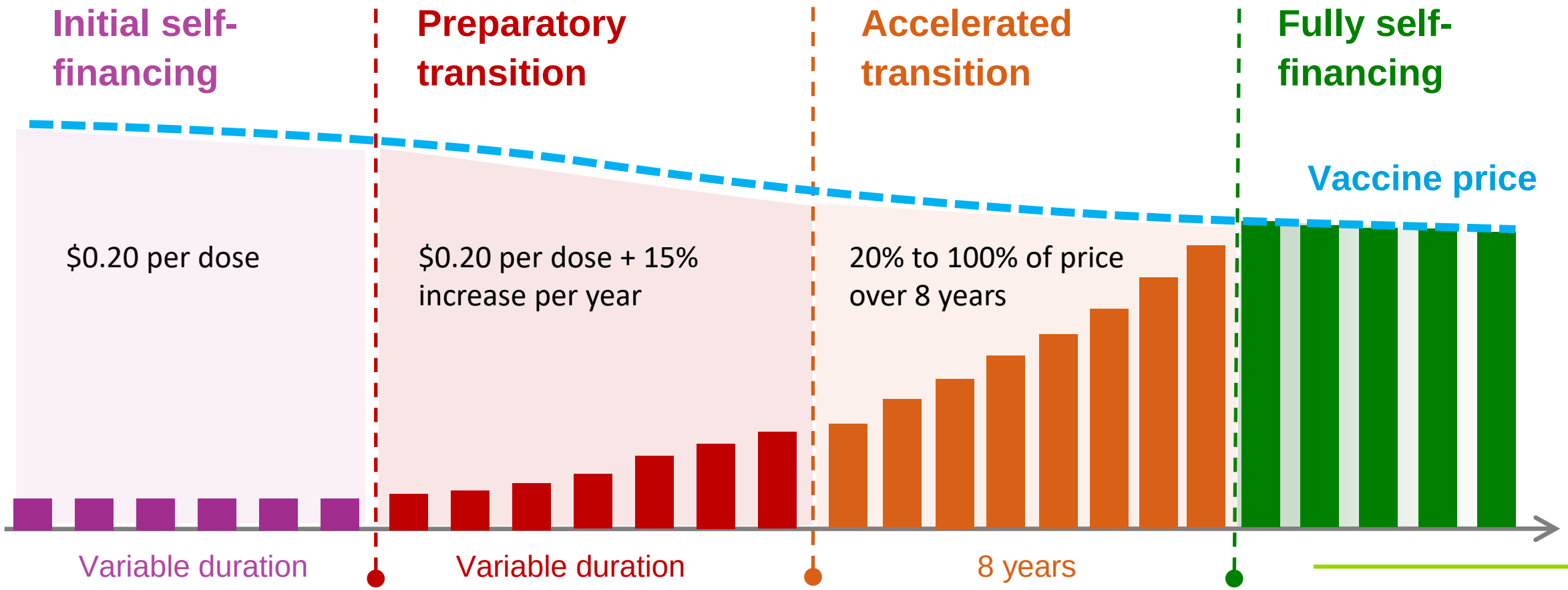
Useful links

Mi4A – WHO Malaria Vaccine Global Market Study – Sept 2021
https://www.who.int/publications/m/item/who-malaria-vaccine-global-market-study-september-2021

UNICEF Q&A on malaria vaccines supply, price and market-shaping efforts
https://www.unicef.org/supply/documents/malaria-vaccine-questions-and-answers

Gavi Market Shaping Roadmap – Malaria Vaccines
https://www.gavi.org/sites/default/files/document/Malaria-Roadmap-Public-Summary.pdf

Gavi co-financing: exeptional time-limited approach for malaria vaccines to facilitate affordability and uptake*



As a country GNI per capita increases, the level of its co-financing rises

*To be reviewed no later than 2027

Gavi, the Vaccine Alliance, confirms unprecedent demand

- At least 28 countries expressed interest in applying for Gavi support to introduce
- To date, 14 country applications approved by Gavi's Independent Review Committee (IRC)
- Next critical step: supply allocation based on Framework for allocation of limited supply

September 2022 deadline

Approved support to continue immunization in the MVIP areas after the end of the MVIP (Dec 2023)

Ghana – pilot areas
Kenya – pilot areas
Malawi – pilot areas

Vaccine requirements: ~6.9M
(of 18M from 2023-2025)

January 2023 deadline

- 13 applications submitted
- **11 applications recommended for approval by IRC**

Next step:
- Supply allocation decisions based on **Framework** for allocation of limited supply
- Some IRC approved countries will <u>not</u> get a supply allocation immediately

Future application windows

- Up to 15 additional applications expected for next windows in 2023: April, July, October deadlines
- Typically, 3-4 application opportunities per year

Framework for the allocation of limited malaria vaccine supply

Available on WHO website

Governance principles

Transparency

Inclusiveness & participation

Accountability

Ethical principles for allocation

First priority principle: Greatest need
Allocate the vaccine to countries with areas of greatest need, where the malaria disease burden in children and the risk of death are highest

Second priority principle: Maximize health impact
Allocate the vaccine to countries for use in areas where the expected health impact is greatest

Third priority principle: Equity (Equal Respect)
Prioritize countries that commit to fairness and addressing the needs of marginalized individuals and communities in their malaria vaccination programmes

Fourth priority principle: Fair benefit sharing
If everything else is equal, the country with a prior contribution to the vaccine's development should get priority

Additional key considerations

Honour commitments to MVIP countries: MVIP areas continue to get priority access to vaccine

Ensure continuity / sustainability of access to vaccine once a programme has started

Minimize risk of vaccine wastage and delayed use of available doses

Allocation should not perpetuate pre-existing structural injustices

Foundational value: solidarity

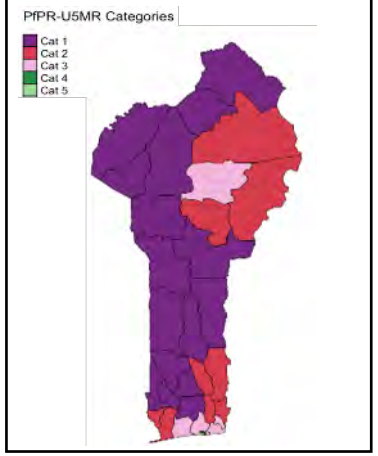
Thinking as a community and standing in solidarity with those most in need:
Initially, if there are unmet vaccine requests for greatest need (category 1) areas across multiple countries, no single country should receive more than 20% of the total available supply

Stratification of areas by category of need

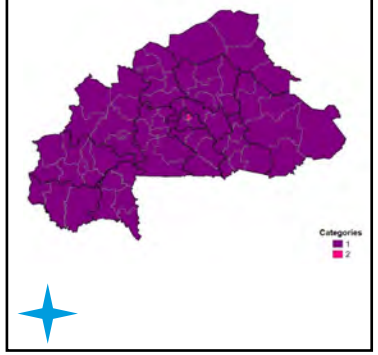
Done by countries that applied for Gavi support in January 2023

World Health Organization

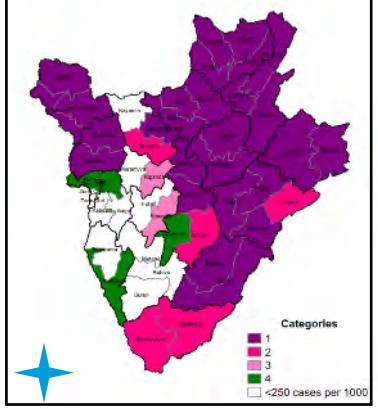
Benin



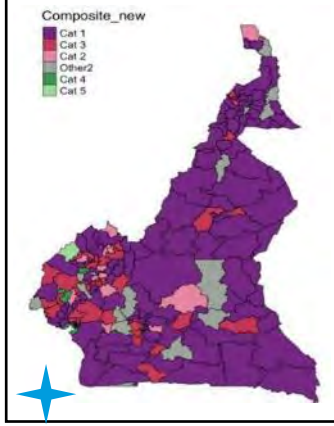
Burkina Faso



Burundi



Cameroon



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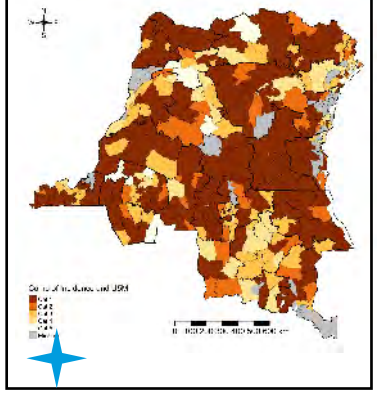
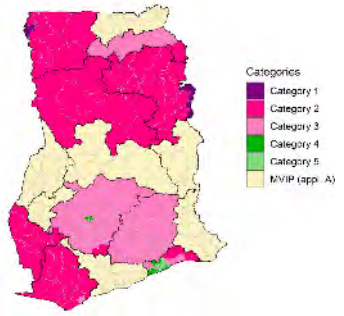
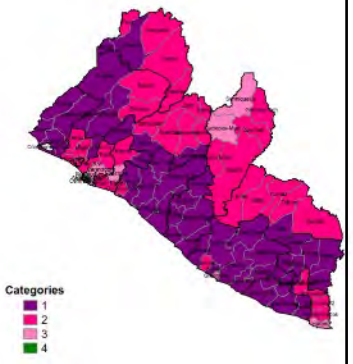


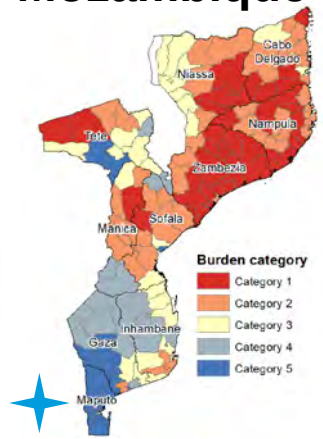
Ghana



Liberia

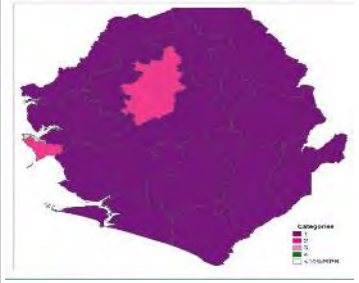


Mozambique

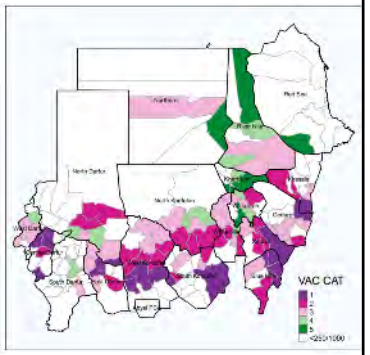


Niger

Sierra Leone



Sudan

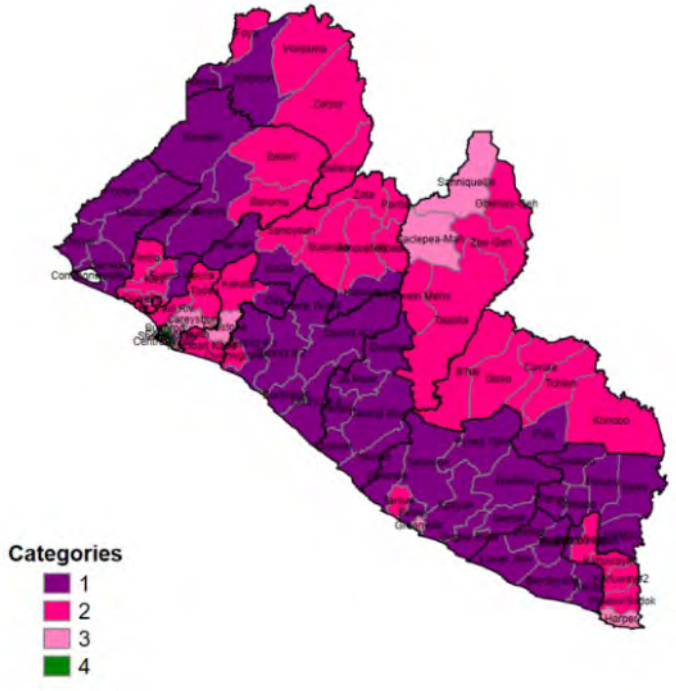


Uganda

= country affected by solidarity cap (max. 1 million vaccine doses / year ; requiring further prioritization within category 1 areas)

Illlustration 1: Liberia's stratification and proposed first phase of roll-out in line with the Framework for allocation of limited supply

Stratefication by categories of need



Cat.	Target population Surviving infants (2024)
1	44,954 (48 districts)
2	61,385 (34 districts)
3	50,508 (9 districts)
4	15,692 (1 district)
5	--
Total	**172,539**

First phase of roll-out

World Health Organization

All category 1 areas

Target population: ~44,954 children in 2024

In 48 of 93 districts

Allocation of limited vaccine supply: Key implications for countries

- All countries will have to consider **a phased approach** to vaccine implementation, starting in areas with highest need, with expansion after supply increases
- **Interested countries are not guaranteed** access to the malaria vaccine during the initial period of rollout. Applying the Framework ensures that allocations adhere to values and principles of solidarity, greatest need, impact, and equity.
  - **Currently available supply will be exhausted after allocations to a sub-set of the 11 countries approved by Gavi IRC in March for their phase 1** (= category 1 areas; for some countries: further prioritized to fit below the cap of 1 million doses per year)
  - Some of the IRC approved applications will not receive a supply allocation immediately and will go on a wait list
- Supply allocation decisions will be communicated in coming weeks
- The Framework is **dynamic to accommodate more supply** and may be updated if needed

Malaria Vaccine Coordination Team (MVCT)

Organizations currently represented:

- Co-chaired by WHO and Gavi Secretariat, created in early 2022
- MVCT provides a platform for coordination and information sharing
- Initial focus on support to design of the Gavi malaria vaccine programme
- Overtime, expected to support the ongoing implementation of the Gavi programme & coordination among partners

Malaria vaccine R21
Evidence review and recommendation processes

Mary Hamel and Lindsey Wu, WHO

Credit: WHO/Panjan Combrink.

Introduction

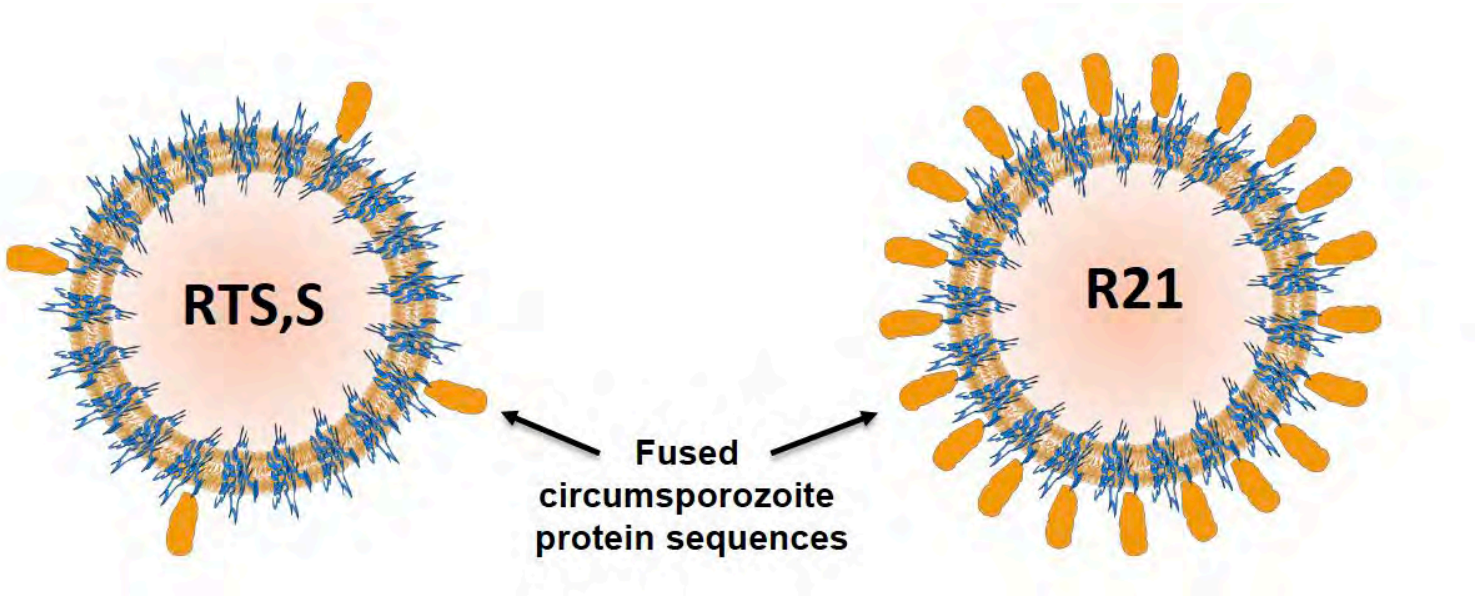
- October 2021, WHO recommended the first malaria vaccine (RTS,S/AS01) to be used for the prevention of *P. falciparum* malaria in children living in regions with moderate to high transmission
- R21/MatrixM malaria vaccine will be the second malaria vaccine reviewed by WHO for a potential recommendation for use
- WHO policy recommendation for malaria vaccines is already in place
- Therefore, pathway for review will depend on whether R21/MatrixM can be recommended under the current WHO policy for malaria vaccines or whether a new WHO policy recommendation is required

Background on R21/MatrixM

- Similar to RTS,S/AS01 in construct
- Pre-erythrocytic stage vaccine, indicated for reduction of clinical malaria in infants and children
- Targets *P. falciparum* pre-erythrocytic circumsporozoite (CS) protein
  - Similar target as RTS,S/AS01
  - Functional protein in sporozoite development and hepatocyte invasion
  - Anti-CS Abs should reduce liver cell invasion & prevent merozoites from reaching blood from liver, thus preventing blood stage infection
- Matrix M adjuvant – saponin extract (similar to AS01) manufactured by Novavax AB
  - Has been used in vaccines against RSV, influenza and COVID-19
  - Administered safely to >1200 children aged 2-11 years as a COVID-19 vaccine

Background on R21/MatrixM (2)

- Virus-like particle (VLP) - fusion of CS protein + hepatitis B surface antigen (HBsAg)
- Similar to RTS,S VLP, but with unfused HBsAg absent, allowing higher expression/concentration of R21 fusion protein alone and lower dose



Background on R21/MatrixM (3)

Potential positive characteristics of R21/MatrixM

- Matrix M adjuvant less complex than AS01, more straightforward production with commitment from Novavax to match R21 supply (transfer of MatrixM technology to SII)
- Planned large scale supply of >150 million doses per year by Serum Institute India
- Ongoing studies on two-dose single-vial formulation
    - If successful, likely to be appealing to programs – ease of administration, less bulky
- Publicly stated vaccine price by SII is lower than current malaria vaccine

R21/MatrixM marketing authorisations by national regulatory authorities

- (September 2022) Drugs Controller General India (DCGI) license to SII for export
- (28 March 2023) Ghana Food and Drugs Authority (FDA) approval for use for the immunization of children aged 5 to 36 months against malaria caused by *P. falciparum.*
- (17 April 2023) Nigerian National Agency for Food and Drug Administration Control (NAFDAC), provisional approval
  - Need for phase 4 clinical trial/pharmacovigilance to be conducted in Nigeria.
- WHO has not seen the dossiers submitted to NRAs for approval.
- Intended use by Ghana's and Nigeria's MOH (Immunization Programmes) not yet known.

R21 Phase 1-2b studies show good safety profile and 2b positive efficacy

Study and phase	Description
Phase 1, VAC053 (completed)*	Safety, immunogenicity of R21/Matrix M, **healthy UK adults**
Phase 1, VAC056 (completed)	Safety, immunogenicity of R21/AS01B, **healthy UK adults**
Phase 1/2, VAC060 (completed)*	Safety and immunogenicity of R21/Matrix M, **healthy adults Burkina Faso**
Phase 1/2a, VAC065 (completed)	Safety, immunogenicity, efficacy R21/Matrix M (standard and high dose) +/- ChAd63/MVA ME-TRAP, **healthy UK adults (CHMI)**
Phase 1/2a, VAC072 (completed)	Safety, immunogenicity, efficacy of R21/Matrix M, different dose schedules, **healthy UK adults (CHMI)**
Phase 1/2, VAC073 (completed)	Safety and immunogenicity, age de-escalation study and dosing in **Kenyan adults, young children, infants**
Phase 2b, VAC076 (ongoing season 3 randomize +/- boost)*	Safety, efficacy R21/Matrix M **seasonal administration**, **children Burkina Faso**

***Published**

R21 Phase 1-2b studies (underway and planned)

Study and phase	Description
Phase 1, VAC088 (underway)	Safety, immunogenicity in children of R21/Matrix M, single and two-vial presentation, different immunisation schedules (delayed 3rd dose), **co-administration with EPI Mali**
Phase 2b, VAC074 (underway)	Safety, immunogenicity, efficacy of R21/Matrix M and **ChAd63/MVA ME-TRAP in Kenyan adults (CHMI)**
Phase 2, MAL22001 (underway)	Safety, immunogenicity of R21/Matrix M **co-administration with DHA-PQP + primaquine in Thai adults**
Phase 1b, VAC086 (planned)	Safety, immunogenicity of **multi-stage vaccine Rh5.2/Matrix M VLP (blood stage) and R21/Matrix M alone and in combination, adults and infants Gambia**
Phase 1b, VAC092 (underway)	Safety, immunogenicity of **R21/Matrix M in African children living with HIV, Uganda**

R21/MatrixM Phase 3 trial

- Multi-centre trial began January 2021, evaluating efficacy of 5µg R21 / 50µg Matrix M
- Total 4,800 children aged 5-36 months 2:1 randomization (R21/MatrixM vs. Rabies vaccine)
- **Two administration regimens:**
  - **Seasonal administration/ highly seasonal transmission** (2,400 participants at 2 sites)
    - **3-dose primary series** (April/May – June/July prior to malaria season); dose-4 given annually in June/July the following year
      - Bougouni, Mali and Nanoro, Burkina Faso
  - **Standard (age-based) administration** (2,400 participants 5-36 months of age at 3 sites)
    - 3-dose primary series with 0,1,2 M dosing; dose-4 given 12 months after dose-3
      - Dande, Burkina Faso (highly seasonal transmission - low or low/moderate),
      - Kilifi, Kenya (low transmission),
      - Bagamoyo, Tanzania (low transmission)
    - No assessment of vaccine efficacy or duration in areas of high perennial transmission

R21/MatrixM Phase 3 trial (3)

- **Primary objectives**
  - Vaccine efficacy against clinical malaria **12 months after dose-3** for standard or seasonal administration, separately
  - Safety in the month following each vaccination and 12 months after dose-3
- **Secondary objectives (partial list)**
  - Vaccine efficacy against clinical malaria 12 month after dose-3, standard and seasonal combined
  - Vaccine efficacy against clinical malaria, 12 months after dose-4, standard and seasonal analysed separately and combined
- All participants will be followed up for **2 years after dose-3**

Overview of review process and groups involved

The **SAGE Steering Group on vaccination policy guidance (SG)** assesses whether a new product can be accommodated **under an existing WHO recommendation or position**

SG is an internal WHO group comprised of Immunization, Vaccines & Biologicals (IVB) department and Global Malaria Programme

- The **SAGE/MPAG Working Group on Malaria Vaccines** has been asked to review the evidence and provide recommendations to the SG on whether the R21/MatrixM vaccine is:
  - Sufficiently similar to the currently recommended malaria vaccine (RTS,S/AS01) and therefore may be recommended under the current WHO malaria vaccine policy
  - Not sufficiently similar– then a full evidence review by SAGE/MPAG will be requested to consider a new WHO malaria vaccine recommendation
  - More data/analysis required to determine the pathway and/or recommendation for use

Example disease and vaccine areas that have not required SAGE review prior to inclusion in existing recommendation

Pneumococcal conjugate vaccine (PCV)

- https://apps.who.int/iris/handle/10665/344915

Rotavirus vaccine

- https://www.who.int/publications/i/item/WHO-IVB-2021.03

Typhoid conjugate vaccines

- https://apps.who.int/iris/handle/10665/345367

HPV vaccine: guidance being developed

Members of the SAGE/MPAG Working Group on Malaria Vaccines

- **Chair: Prof Peter Smith**, London School of Hygiene & Tropical Medicine, United Kingdom
- **Co-chair: Dr Eusebio Macete**, Centro de Investigação em Saúde de Manhiça, Mozambique

- **Prof Nick Andrews**, UK Health Security Agency, United Kingdom
- **Prof Graham Brown**, University of Melbourne, Australia **(MPAG member)**
- **Dr Dafrossa Cyrily Lyimo**, Independent consultant (and former National Immunization and Vaccine Development Programme Manager), Tanzania
- **Dr Corine Karema**, Interim CEO of RBM Partnership to End Malaria (and former Director of the Rwanda National Malaria Control Programme), Rwanda
- **Prof Kim Mulholland**, Murdoch Children's Research Institute, Australia **(SAGE member)**
- **Prof Kathleen Neuzil**, Center for Vaccine Development and Global Health (CVD), University of Maryland School of Medicine, USA **(SAGE member)**
- **Prof S. Patrick Kachur**, Mailman School of Public Health, Columbia University, USA **(MPAG member)**
- **Observers: Prof Faith Osier,** Co-Director Institute of Infection, Imperial College London, United Kingdom

SAGE MPAG WG initial evidence review 7-8 March 2023

- **To confirm pathway forward for evidence review, on 7-8 March 2023, SAGE/MPAG WG conducted *initial* evidence review based on *currently available data***
  - ~90% participants completed 12-months follow-up post dose-3 in standard sites
  - ~90% participants have completed 18-month follow-up post dose-3 in seasonal sites
  - Presented by University of Oxford / Serum Institute India
- **Key topics discussed by WG:**
  - Study design, transmission intensity and patterns, seasonal vs. standard administration
  - Vaccine efficacy against clinical malaria (not powered for severe malaria, very few cases)
  - Duration of protection and waning vaccine efficacy
  - Safety
  - Recommendation pathway (is the vaccine sufficiently similar to come under current recommendation)

SAGE MPAG WG conclusions from initial data review

- The initial results presented on the R21/MatrixM candidate vaccine appear promising
- Vaccine efficacy is high during nearly 18 months follow-up when the vaccine is provided seasonally in a 4-dose schedule in areas of highly seasonal transmission
- Vaccine efficacy against clinical malaria is good thus far, during less than 12 months follow-up, in areas of low or low/moderate transmission, when the vaccine is provided in a “standard” or age-based administration
    - Not powered to measure VE against severe malaria and very few cases
- WG emphasized that because RTS,S/AS01 and R21/MatrixM are not being compared in a clinical trial and have been tested in different transmission settings and contexts, it is not possible to determine whether one vaccine is more efficacious than the other
- The review of the currently available data is limited by:
    - Lack of completed follow-up of the participants in the trial
    - No trial sites with high perennial transmission

Additional conclusions from 18-21 March meeting of Strategic Advisory Group of Experts on Immunization (SAGE)

- Need for data on vaccine efficacy in high perennial transmission settings, potentially in post marketing studies
- Countries should not delay introduction/applications in anticipation of R21 because the recommendation and PQ timeline is uncertain
- Important to understand interchangeability between RTS,S/AS01 and R21 to facilitate potential future scale up
- Might be useful to have immunogenicity studies to compare response of RTS,S/AS01 vs R21 (noting there is no validated correlate of protection)
- Post-marketing safety monitoring for R21/MatrixM (particularly of MatrixM) will be important in the target age group, where little data are available
- Exploration of ways to strengthen supply security for African countries was encouraged, including through local manufacturing

SAGE MPAG WG next steps after initial data review

- SAGE/MPAG WG will next review the data when
  - 18-month follow-up is complete for the seasonal administration sites, and
  - 12-month follow-up is complete for the “standard” or age-based administration sites
- During the next data review, the SAGE/MPAG WG will determine what additional observations and data might be required before a recommendation for use might be made under the current WHO malaria vaccine policy (for seasonal use, or for both seasonal and perennial use)

Global Advisory Committee on Vaccine Safety (GACVS) to review safety data and WHO Prequalification Team (PQT) review

- Global Advisory Committee on Vaccine Safety (GACVS) will conduct a safety review for R21/MatrixM
  - Anticipate review in May/June 2023, depending on availability of data from SII
  - Recommendations of GACVS will be provided to SAGE/MPAG WG
- WHO Prequalification (PQ) screening underway
  - Per ordinary processes, 9-12 months required for PQ review after acceptance of dossier
  - PQ required for procurement through UNICEF with Gavi support

Thank you.

Credit: WHO/F.Combrink

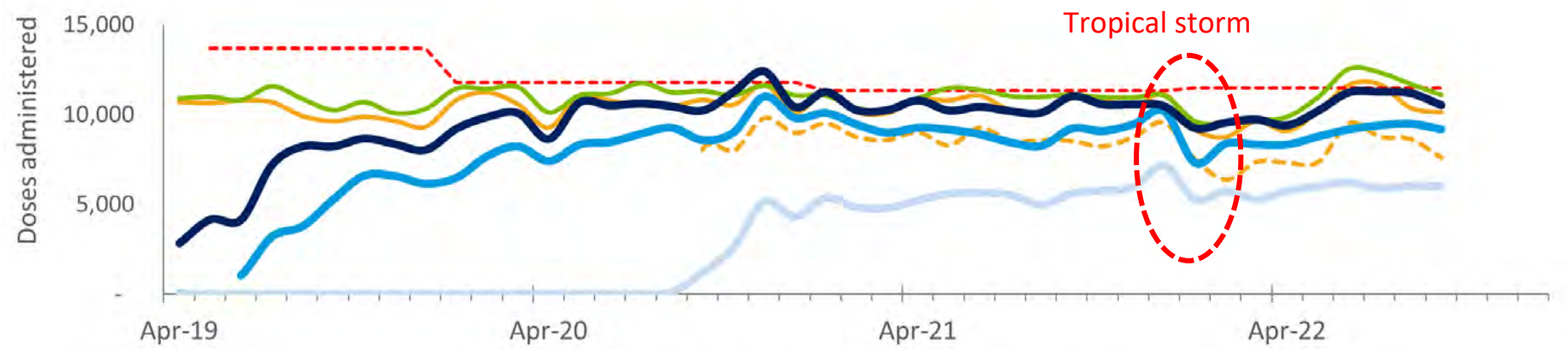
Additional slides for reference

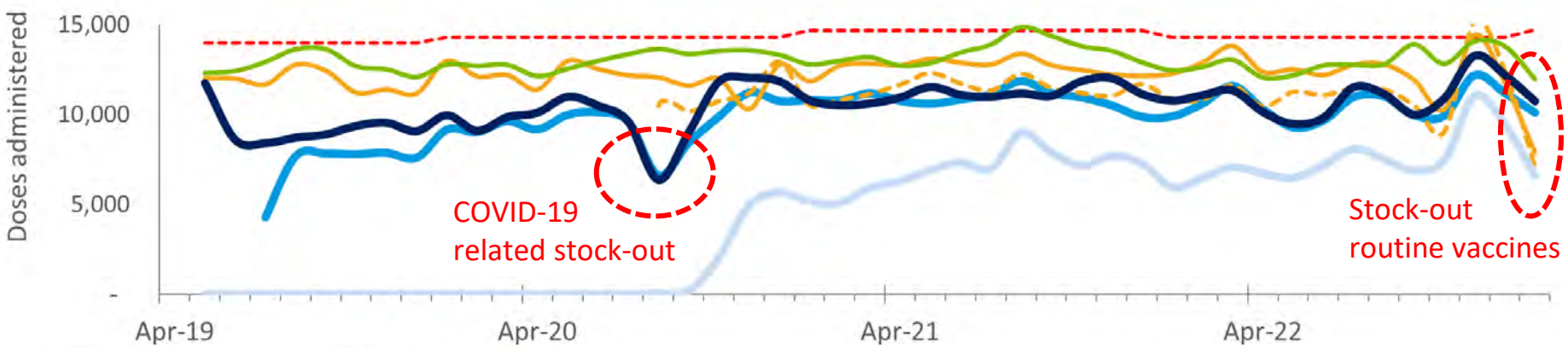
Immunization coverage in MVIP areas: monthly administrative data reports (through Jan 2023)

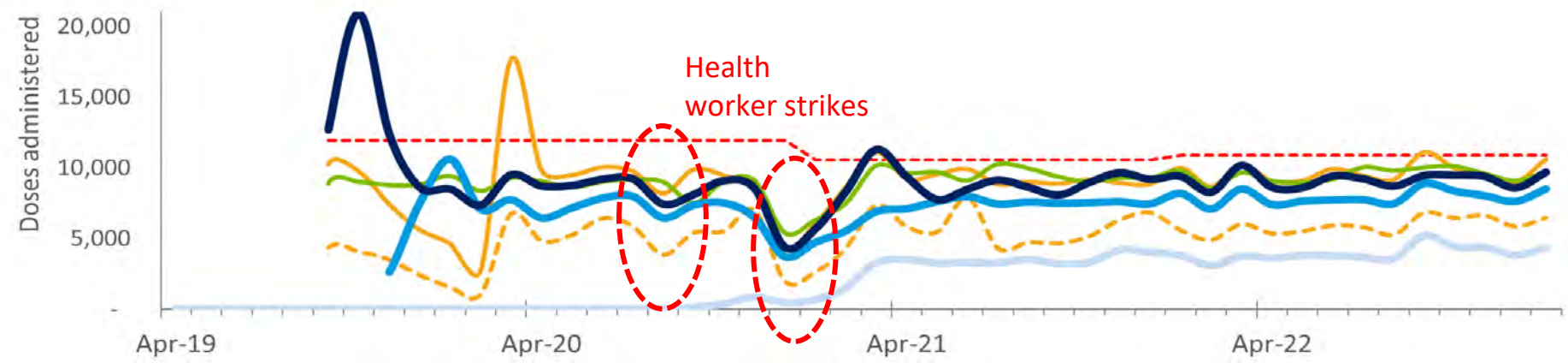
Malawi	2020	2021	2022*
Penta-3	95%	97%	94%
RTS,S -1	88%	93%	89%
RTS,S -3	73%	81%	76%
MR-1	90%	94%	87%
MR-2		77%	68%
RTS,S-4		49%	50%

Ghana	2020	2021	2022
Penta-3	92%	92%	90%
RTS,S -1	71%	76%	76%
RTS,S -3	66%	74%	73%
MR-1	85%	86%	87%
MR-2		78%	79%
RTS,S-4		47%	52%

Kenya	2020	2021	2022
Penta-3	72%	87%	87%
RTS,S -1	69%	82%	83%
RTS,S -3	60%	67%	72%
MR-1	73%	86%	88%
MR-2		52%	53%
RTS,S-4		29%	36%







[#] Malawi data from Jan to Sept 2022