World Health Organization

Background documentation for Day 2

This file contains the slides that were shown by the presenters during Day 2 of the meeting as well the background documentation shared with MPAG members ahead of the meeting.

Wednesday, 15 October 2025			
		Open	
13:00 – 13:05	Welcome back by the Chairperson, MPAG	Professor Dyann Wirth MPAG Chairperson	
	Session 5	**Open**	
13:05 – 14:00	Update on drug resistance activities (including information on the molecular marker compendium and implementation of Multiple First-line treatment) Background | Presentation	MPAG Sub-Committee malaria drug resistance Dr Charlotte Rasmussen Dr Peter Olumese	**for advice & information**
	Session 6	**Open**	
14:00 – 15:00	Vector control (GPIRM and Evidence underpinning guidelines for vector control) Background 1 | Background 2 | Presentation	MPAG Sub-Committee Vector Control Dr Emmanuel Chanda Dr Lauren Carrington	**for advice**
	Session 7	**Open**	
15:45 – 16:15	Malaria Big Push initiative to 2030 (updates and how can we lead to the changes needed in current context?) Presentation	Dr Michael Charles, Chief Executive Officer, RBM Partnership	**for information**
	Session 8	**Closed**	
16:15– 17:15	Finalization of conclusions	Professor Dyann Wirth MPAG Chairperson	**for advice**

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Update on the compendium of molecular markers

Antimalarial drug resistance remains a critical threat to malaria control and elimination. Of particular concern is artemisinin partial resistance, which has been confirmed in four countries and is suspected in an additional four. This evolving situation underscores the urgent need for reliable tools to track resistance, guide treatment policy, and support timely responses.

Compendium of molecular markers for antimalarial drug resistance

Molecular markers of antimalarial drug resistance – genetic alterations that reduce parasite susceptibility to medicines – are critical tools for detecting resistance, monitoring trends, and informing response strategies. However, validated markers remain lacking for several key drugs, and systematic genetic monitoring of known markers is not consistently implemented.

The Compendium of molecular markers for antimalarial drug resistance addresses this gap by consolidating evidence on genetic alterations in *Plasmodium falciparum* and *P. vivax*. Developed to guide national malaria programmes and researchers, the compendium provides a structured approach to prioritizing markers, improving the consistency of molecular surveillance, and identifying critical research gaps.

Purpose and scope

- **Target users**: national malaria programmes, researchers, and policy-makers.
- **Functions**:
    - Synthesizes current laboratory, clinical, and epidemiological evidence.
    - Establishes classification tiers (potential, candidate, validated markers).
    - Promotes consistent use of molecular markers in routine surveillance.
    - Identifies critical gaps for future research and validation.
    - Focuses on antimalarial drugs currently recommended by WHO.

Development process

The compendium was developed through a multi-step, expert-guided process:

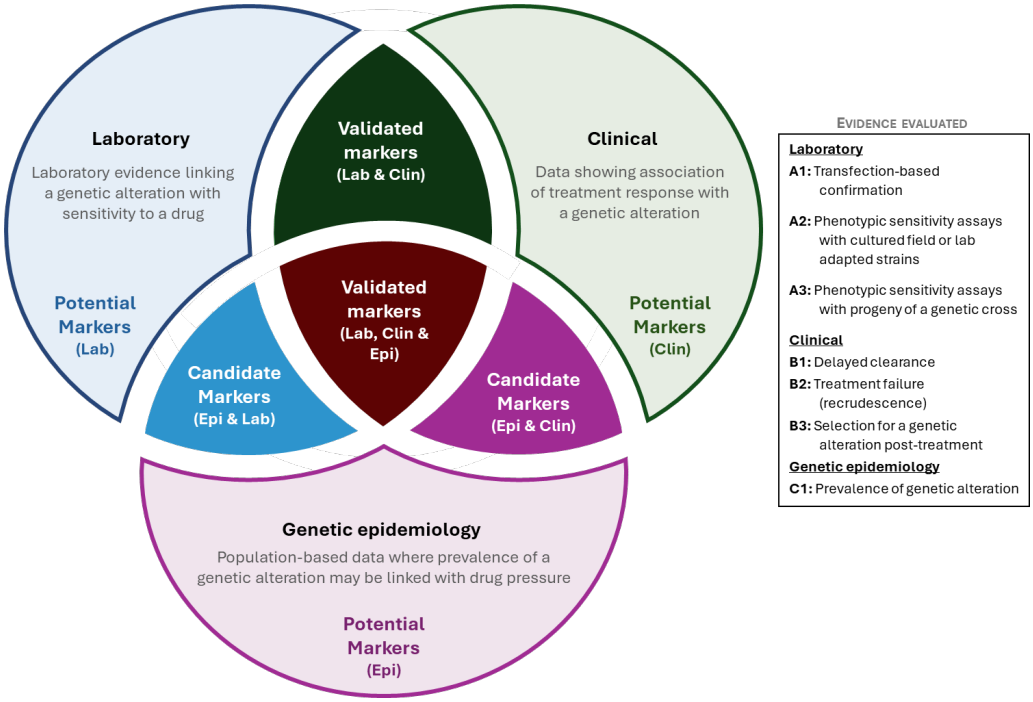
1. Establishing predefined criteria and thresholds for evidence evaluation.
2. Comprehensive literature review across laboratory, clinical, and genomic epidemiology studies.
3. Multi-round expert consultations to validate assessments and classifications.
4. Transparent documentation of evidence and reclassifications.

The result is a dynamic, evidence-based resource, intended to be **updated annually** to reflect evolving data and methodologies.

Classification framework

The classification system supports decision-making in both routine molecular surveillance and targeted research. Each level reflects the type of evidence linking a genetic alteration to drug resistance, enabling programmes to prioritize monitoring and research investments.

- **Validated markers**: Supported by laboratory and clinical data (with or without epidemiology). Highest priority for surveillance.
- **Candidate markers**: Supported by laboratory or clinical data plus epidemiological evidence. Priorities for validation studies and targeted surveillance.
- **Potential markers**: Supported by a single domain of evidence. Early signals, suitable for exploratory research and monitoring.



Next steps

This compendium should be seen as a first iteration – a foundation that will evolve as additional data are integrated, methodologies are refined, and expert feedback continues to guide development.

A major challenge during its development has been the lack of standardized approaches to reporting genetic alterations and their links with treatment response. Improving reporting standards and harmonizing data collection will be essential to strengthening future updates.

Another key priority is the identification and validation of markers for several important drugs where evidence remains insufficient. Of particular note is lumefantrine, the partner drug in the most widely used artemisinin-based combination therapy (ACT). Despite its central role in treatment, validated resistance markers for lumefantrine remain elusive, making this an urgent focus for research. To help accelerate progress, WHO will convene a dedicated meeting to advance the identification of molecular markers of resistance and align the global research agenda.

By acknowledging these limitations while providing a structured, evidence-based framework, the compendium sets the stage for more systematic molecular surveillance, clearer research priorities, and stronger responses to the evolving threat of drug-resistant malaria

Malaria drug resistance – update, compendium, and MFT implementation

Charlotte Rasmussen
Diagnosis, Medicine and Resistance
Global Malaria Programme

World Health Organization

Presentation outline

- Brief update on resistance status
- Molecular markers and the development of the compendium
- Focusing on lumefantrine
- MFT implementation

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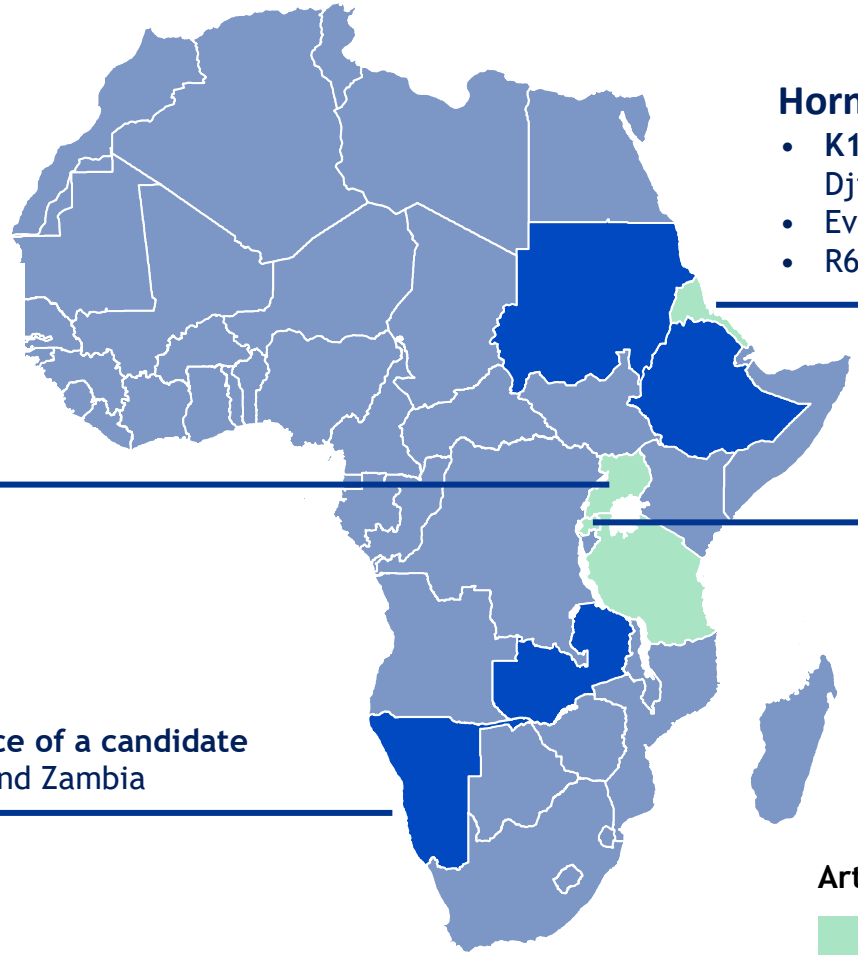
Drug resistance | Artemisinin partial resistance emerging and spreading



Horn of Africa

- **K13 mutation R622I** detected in several countries including Djibouti, Eritrea, Ethiopia, Sudan and Somalia
- Evidence of slow parasite clearance in Eritrea
- R622I has been detected in parasites *with Pfhrp2/3* deletions

Uganda

- **Different K13 mutations are spreading** with foci where parasites carry validated artemisinin resistance markers

Rwanda & Tanzania

- **K13 mutations, predominately R561H,** have been found at high prevalence in studies with evidence of delayed clearance in Rwanda and Tanzania

Southern Africa

- 2023 survey found **high prevalence of a candidate K13 marker (P441L)** in Namibia and Zambia

Artemisinin partial resistance:

Confirmed

(Evidence of delayed clearance in patients with validated markers)

Suspected

(Evidence of delayed clearance or >5% with validated or candidate markers)

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PfKelch13 R622I and *Pfhrp2/3* deletions

- R622I has been associated with delayed parasite clearance after a treatment containing an artemisinin while *Pfhrp2/3* deletions affects the ability to diagnose patients using a hrp2 – based RDT
- A statistically significant association between *R622I* and *Pfhrp2/3* deletions has previously been reported in Eritrea.
- Data collected in two hospitals in Sudan in 2017 found:
  - 21.8% carried 622I
  - 3.0% of the parasites carrying R622 (wild type) had also hrp2/3 deletions
  - 10.7% of the parasites carrying 622I (mutation) had also hrp2/3 deletions

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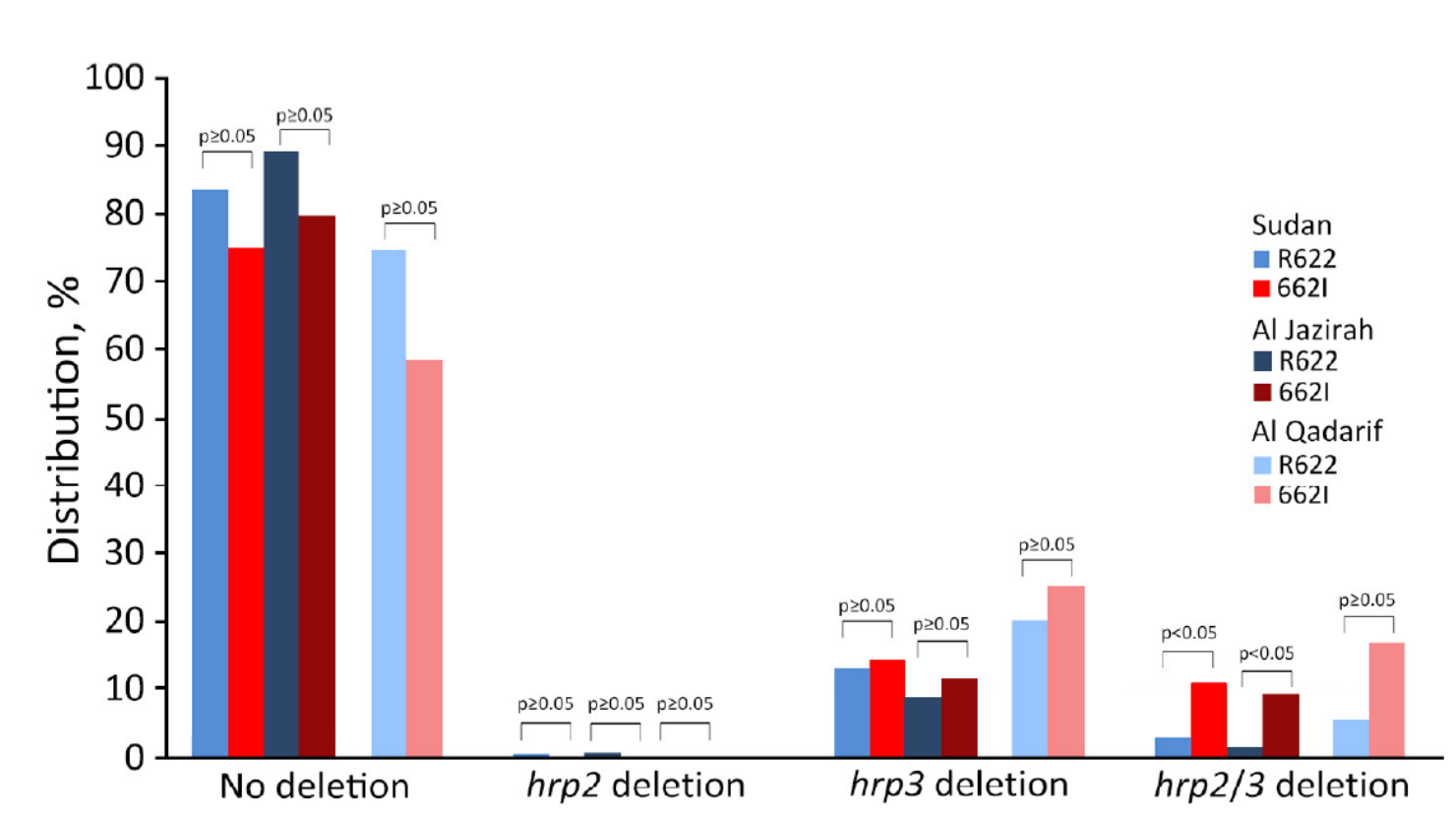
Percentages samples with *Pfk13 R622* and 622I P. falciparum parasites by hrp2/3 deletion status, in total and by the 2 study sites, Al Jazirah (n=170) and Al Qadarif (n=87) in 2017



Source: L'Episcopia et al. *High Prevalence of Artemisinin-Resistant Plasmodium falciparum, Southeastern Sudan*. Emerg Infect Dis. 2025 Jun; doi: 10.3201/eid3106.241810.

Presentation outline

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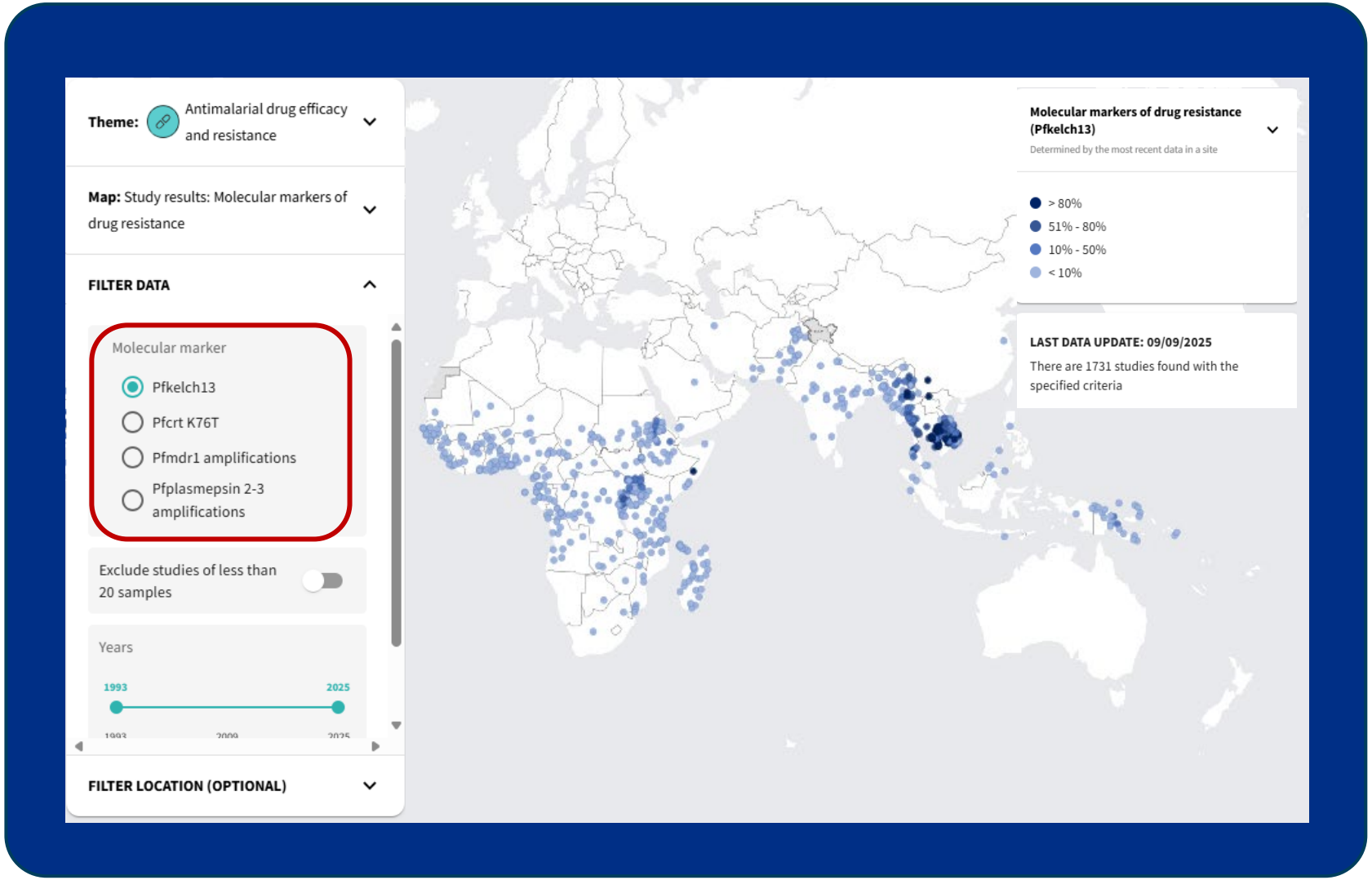
Tracking and reporting of molecular markers

- WHO has been tracking a small list of markers where there has been some evidence shown to associate these markers with antimalarial drug resistance.
- This information has been made available through the WHO Malaria Threat Maps

Malaria Threat Maps



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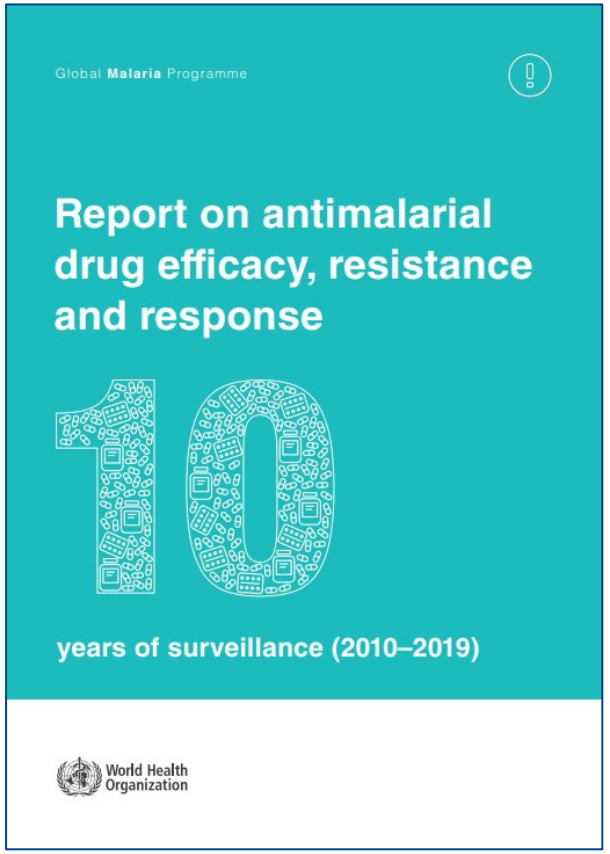
Tracking and reporting of molecular markers

- WHO have also periodically through reports provided overviews of different markers
- These are based on internal review of available information

WHO Report on antimalarial drug efficacy, resistance and response Global Malaria Programme years of surveillance (2010–2019)

TABLE 3
Molecular markers of resistance to antimalarial drugs for *P. falciparum*

Drug	Molecular markers	
	Gene	Mutation
4-aminoquinolines		
Chloroquine	*Pfcrt*	K76T + different sets of mutations at other codons (including C72S, M74I, N75E, A220S, Q271E, N326S, I356T and R371I)
	Pfmdr1 (in combination with *Pfcrt* mutations only)	N86Y, Y184F, S1034C, N1042D and D1246Y
Amodiaquine (mannich base)	Yet to be validated	Studies show that amodiaquine selects for *Pfmdr1* mutations (86Y)
Piperaquine	*Pfpm2–3*	*Pfpm2–3* increased copy number
	Pfcrt	Detected in vivo: T93S, H97Y, F145I, I218F and C350R
		Detected in vitro: T93S, H97Y, F145I, I218F, M343L and G353V
Antifolates		
Pyrimethamine	*Pfdhfr*	N51I, C59R, S108N and I164L
Sulfadoxine	*Pfdhps*	S436A/F, A437G, K540E, A581G and A613T/S
Proguanil	*Pfdhfr*	A16V, N51I, C59R, S108N and I164L
Amino-alcohols		
Lumefantrine	Yet to be validated	Studies show that lumefantrine selects for *Pfmdr1* mutations (N86)
Mefloquine	*Pfmdr1*	*Pfmdr1* increased copy number
Quinine	Yet to be validated	
Mannich base		
Pyronaridine	Yet to be validated	
Naphthoquinone		
Atovaquone	*Pfcytb*	Y268N/S/C
Sesquiterpene lactones		
Artemisinin and its derivatives	*PfK13*	List of candidate and validated markers developed (see Table 4)



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Markers of artemisinin partial resistance

- For markers of artemisinin partial resistance, definitions of candidate and validated markers were established by expert group based on data for:
  - The artemisinin specific Ring Stage Assay, and
  - Delayed parasite clearance times

***PfK13* markers of artemisinin partial resistance**

Validated markers

- F446I
- N458Y
- C469Y
- M476I
- Y493H
- R539T
- I543T
- P553L
- R561H
- P574L
- C580Y
- R622I
- A675V

Candidate markers

- P441L
- G449A
- C469F
- A481V
- R515K
- P527H
- N537I/D
- G538V
- V568G

Candidate: significantly associated with delayed parasite clearance in vivo or identified as having reduced susceptibility using Ring Stage Assay

Validated: significantly associated with delayed parasite clearance in vivo and identified as having reduced susceptibility using Ring Stage Assay

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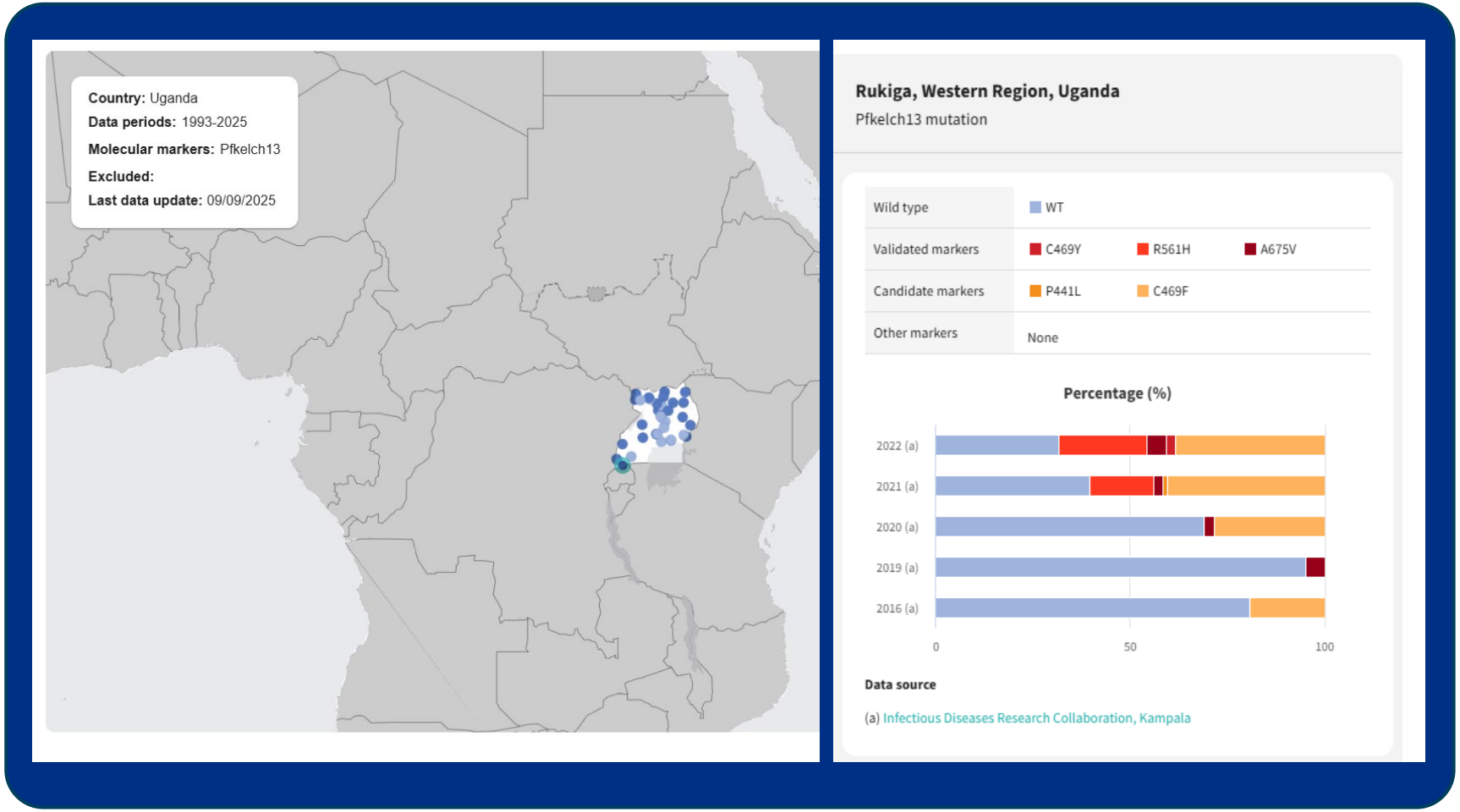
Tracking markers of artemisinin partial resistance

- The list of markers has help support the inclusion of the surveillance of these markers in most efficacy studies as well as surveys
- For some countries, frequent surveys allow us to track the rapid changes happening in the parasites sampled

Malaria Threat Maps



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Development of the **compendium of molecular markers of antimalarial drug resistance**

Objective of compendium

- To facilitate prioritisation of molecular marker surveillance and research by systematically categorizing drug resistance markers
  - Promotes consistent use of molecular markers in routine surveillance
  - Identifies critical gaps for future research and validation
  - Focuses on antimalarial drugs currently recommended by WHO for treatment

General challenges in the development

- No centralized repository for genotypic and phenotypic data; reliance on published studies.
- Published data are highly variable in methods and reporting, making cross-study comparison difficult.
- Association clearly doesn't mean causation; co-occurring mutations make it difficult to distinguish independent effects
- Haplotype context can be critical for interpretation and there is geographic specificities
- Drug specific challenges: where no confirmed resistance has been identified for a drug, markers are not available

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Process

Work undertaken

- Establishing predefined criteria and thresholds for evidence evaluation.
- Comprehensive literature review across laboratory, clinical, and genomic epidemiology studies.
- Multi-round expert consultations to validate assessments and classifications.

Moving forward

- What is being developed is the first iteration of a compendium
- The result is a dynamic, evidence-based resource, intended to be **updated annually** to reflect evolving data and methodologies

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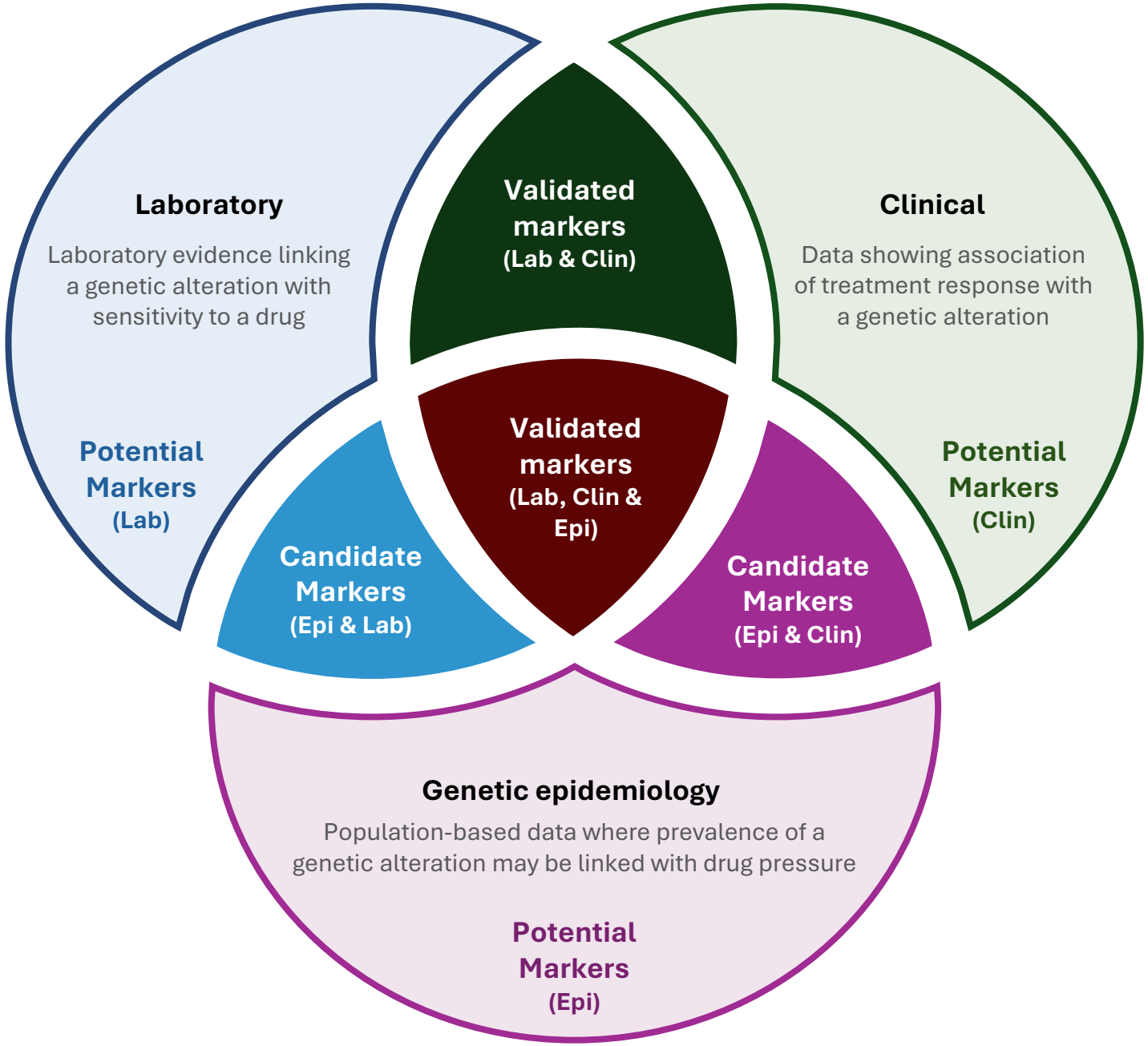
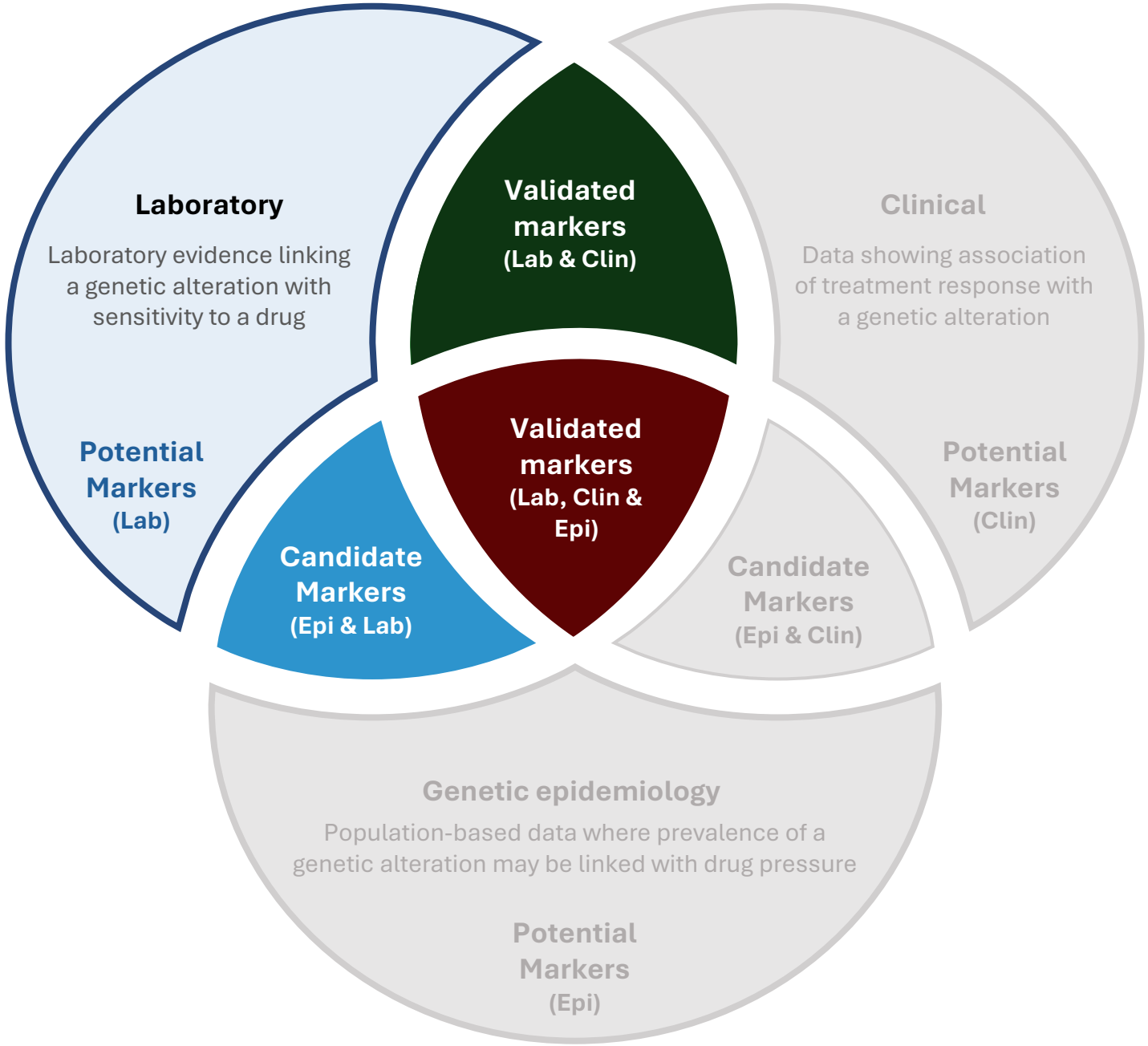
Compendium of antimalarial drug resistance

- Compendium being generated by review of data in three areas:
  - **Laboratory evidence** linking a genetic alteration with in vitro sensitivity to a drug
  - **Clinical evidence** showing association of treatment response with a genetic alteration
  - **Genetic epidemiological evidence** showing prevalence of a genetic alterations that could be linked with drug pressure
- Marker classification:
  - **Validated markers:** Supported by laboratory and clinical data (with or without epidemiology).
  - **Candidate markers:** Supported by laboratory or clinical data plus epidemiological evidence.
  - **Potential markers:** Supported by a single domain of evidence



Laboratory data

- Three types of evidence are considered in the assessment of laboratory data
  - **Transfection-based confirmation (given preference over other lab data):** comparing a strain incorporating the specific genetic alteration of the same strain.
  - **Phenotypic sensitivity assays:** Using cultured field or lab adapted strains with identified alteration compared with wild type
  - **Phenotypic sensitivity assays with progeny of a genetic cross:** Recombinant progenies expressing the genetic alteration of interest, compared with recombinant progeny expressing the wild-type allele or copy number
- Interpretation of in vitro assays is challenging due to the absence of IC_{50} threshold.
- Looking for a statistically significant increase IC50 or IC90 (For Ring Stage Assay (RSA) or Piperaquine Survival Assay (PSA) thresholds established)
- Some challenges in comparability of laboratory testing

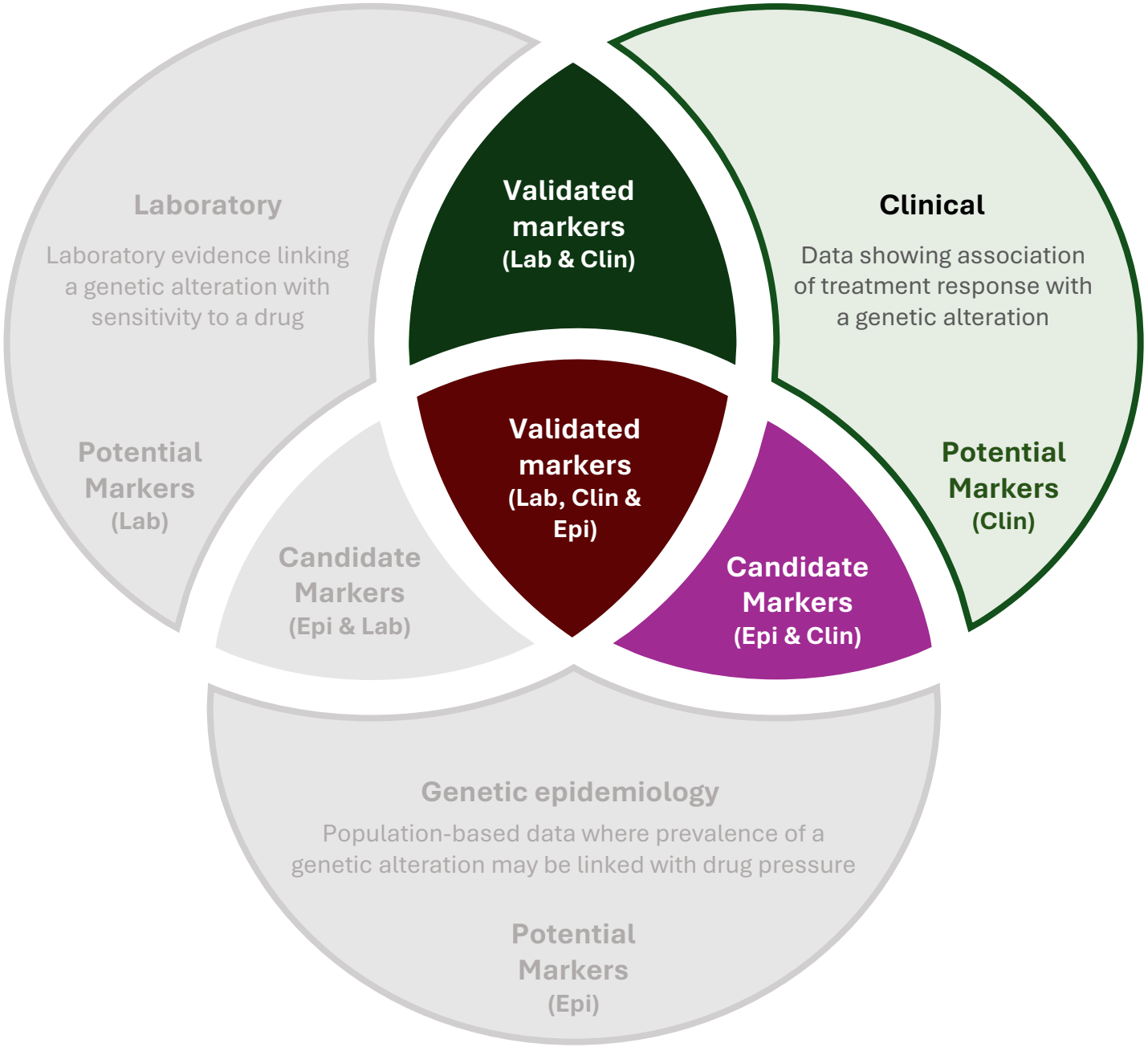


Clinical data

Three types of evidence are considered in the assessment of clinical data

- **Delayed clearance (relevant for artemisinins):** Statistically significant association between the presence of a mutation and delayed parasite clearance (parasite clearance slope half-life of ≥5 hours or the presence of parasitemia at 72 (± 2) hours
- **Treatment failure (recrudescence):** Treatment failures statistically associated with presence of a genetic alteration at start of treatment (PCR correction is a challenge)
- **Selection for a genetic alteration post-treatment:** A statistically significant increase in the prevalence of genetic alteration detected in parasites post-treatment compared to baseline (pre-treatment)

Clinical evidence outcomes influenced by host, drug, and study-design factors



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Genetic epidemiology

Selection influenced by factors, including fitness cost, all drugs used, transmission level

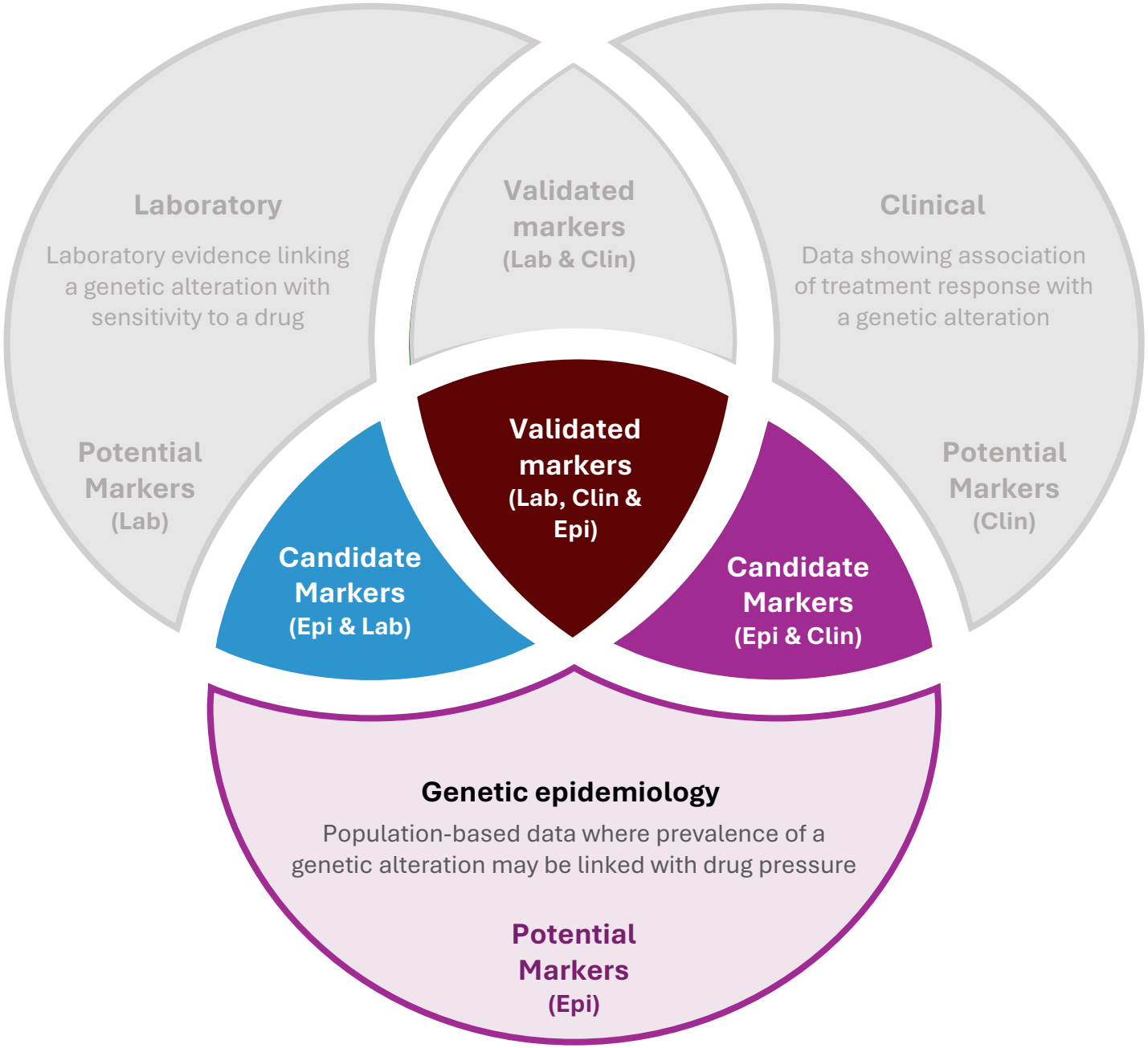
Assigning causality to a specific genetic alteration that is spreading is difficult.

Genetic epidemiology has been included as it can:

- give an indication of the potential for an alteration to spread
- Could highlight alterations worth studying

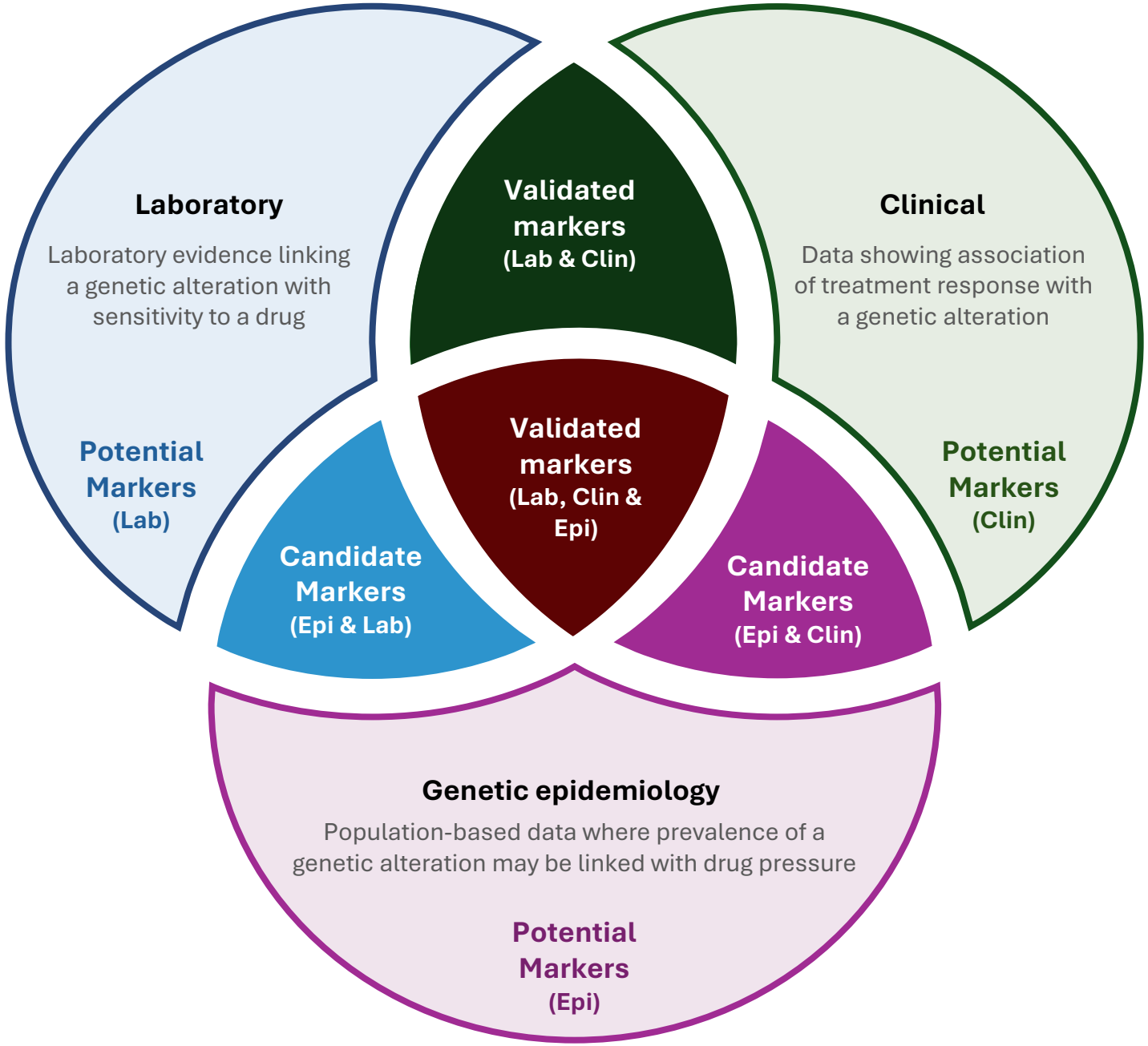
Thresholds

- **For markers already supported by clinical and/or laboratory data**: The genetic alteration has a prevalence ≥ 5% at a study site
- **For markers not supported by clinical and/or laboratory data:** studies demonstrating increase in prevalence over time following the introduction of the drug; or statistically significant higher prevalence in geographical areas where the specific drug is in use compared to other areas where the drug is not in use



Prioritization of markers in surveillance and research

- **Validated markers:** Supported by laboratory and clinical data (with or without epidemiology)
  - ➢ Represent the strongest case for an association with drug resistance and should be given the highest priority in molecular surveillance
- **Candidate markers:** Supported by laboratory or clinical data plus epidemiological evidence.
  - ➢ These are suitable for enhanced surveillance and should be prioritized for validation studies to confirm causality and track their potential spread
- **Potential markers:** Supported by a single domain of evidence
  - ➢ Important targets for research, including functional assays, clinical evaluations



Sharing of results

- Results will be shared online on dedicated website
- The website will provide background as will as overview **of validated and candidate** markers by drugs
- Online it will also be possible to download the excel table **also containing the list of potential markers and references**

Drug reviewed for *P. falciparum*

- Amodiaquine
- Atovaquone
- Artemisinin
- Chloroquine
- Cycloguanil
- Lumefantrine
- Proguanil
- Piperaquine
- Pyronaridine
- Quinine
- Sulfadoxine-pyrimethamine

+ Marker for P. vivax

Artemisinin example (online)

Category	Gene	Alterations
Validated marker (Epi., Lab. & Clin.)	*Pfk13*	F446I, N458Y, C469Y, M476I, Y493H, G533S, R539T, I543T, P553L, R561H, P574L, C580Y, R622I, A675V
Candidate marker (Epi. & Clin.)	*Pfk13*	E252Q, P441L, C469F, N537I, G538V, V568G

Artemisinin example (excel for download)

Gene	Alteration	A1	A2	A3	B1	B2	B3	C1	Category	PMID1	PMID2	PMID3	PMID4	PMID5	PM
pfk13	P441L				1			1	Candidate marker (Epi. & Clin.)	29378723	26911145	25927592	25075834	37611122	401
pfk13	C469F				1			1	Candidate marker (Epi. & Clin.)	28806957	37611122	40112841	32437557	34216470	
pfk13	N537I				1			1	Candidate marker (Epi. & Clin.)	34270459	25075834	30651111	28806957	25704894	306
pfk13	G538V				1			1	Candidate marker (Epi. & Clin.)	36437462	25075834	39929914	25704894	27313266	306
pfk13	V568G			2	1			1	Candidate marker (Epi. & Clin.)	35232492	29582728	30967148	30651111	25180241	306
pfk13	P413A	1	1						Potential marker (Lab.)	34606334	39902927				
pfk13	F495L	1							Potential marker (Lab.)	32098812					
pfk13	R515K	1							Potential marker (Lab.)	39816817	30651111				

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Next Steps and Planned Activities

- **Gaps identified**
  For several key drugs, no candidate or validated molecular markers have yet been identified.
- **Planned WHO meeting**
  WHO is planning a technical meeting to discuss activities needed to accelerate progress in identifying new molecular markers
- **Harmonization efforts**
  The meeting will also explore opportunities for harmonization reporting of results for studies
- **Framework refinement**
  Discussions will inform the second iteration of the review framework, including how geographic specificities are represented.

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Presentation outline

- Brief update on resistance status
- Molecular markers and the development of the compendium
- Focusing on lumefantrine
- MFT implementation

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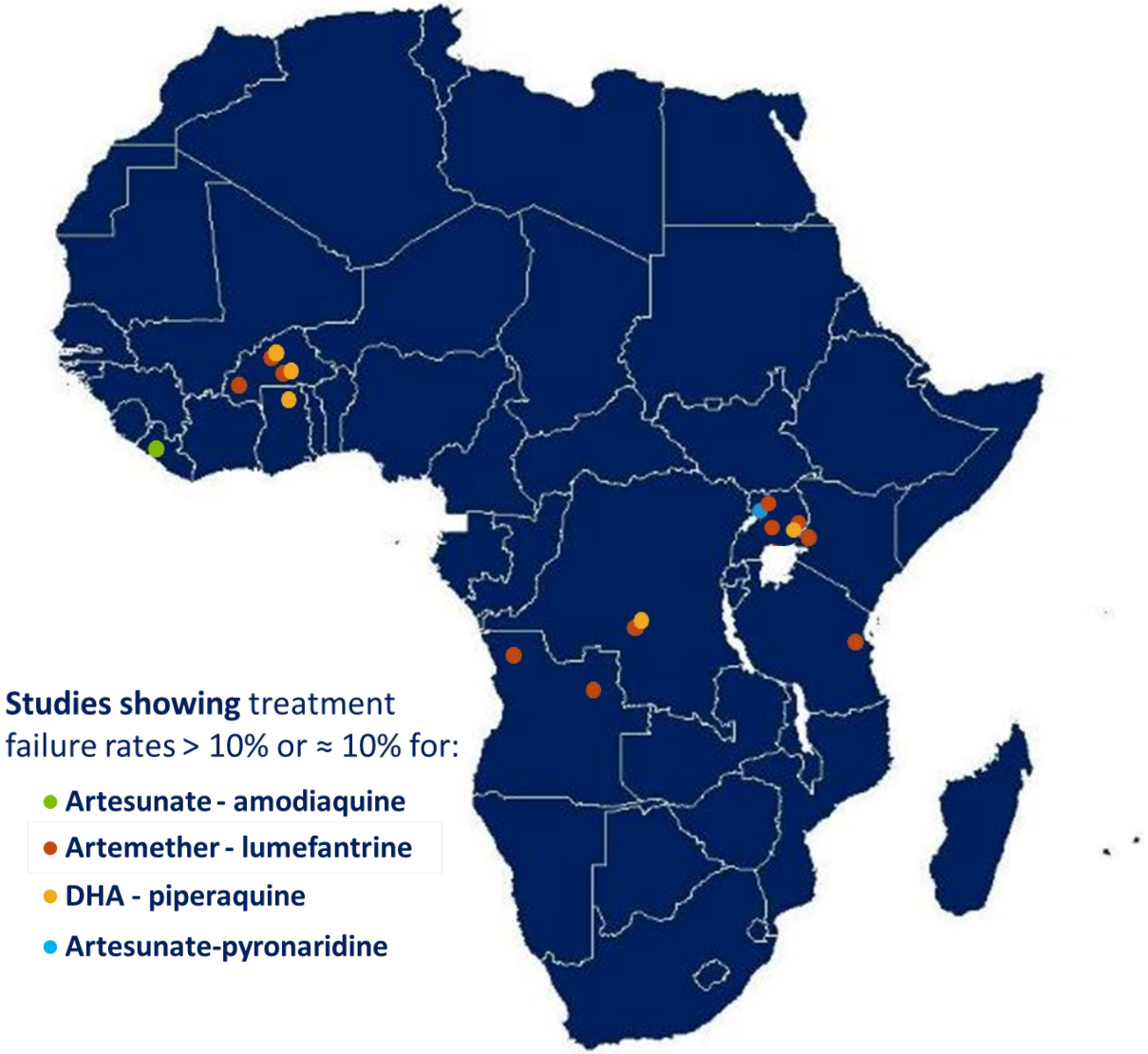
Gaps in information impede effective responses to resistance

- ACT partner drug resistance would result in high treatment failure rates
- Scattered reports of high treatment failure
- Identifying true decline in efficacy in the data is challenged by:
  - Molecular markers for resistance are missing for key ACT partner drugs.
  - Difficulties in distinguishing recrudescence from reinfection
  - Challenge related to adherence to standard TES protocol and quality of implementation
- Areas with no or limited data either due to no studies being done, or data not analyzed and shared.

TES with high failure rates from 2015 - 2024



Lumefantrine resistance? What is the evidence

Evidence	Unresolved questions and limitations in evidence
Data from efficacy studies:	
➢ **AL treatment failure rates of >10% have been reported in several countries** (including Angola, Burkina Faso, DR Congo, Kenya, Tanzania, Uganda)	➢ **Deviations from recommended protocol** ➢ **Deviation in molecular correction methods** ➢ Studies reporting **high failure rates of more than one ACT**.
Failures in returning travellers:	
➢ **AL failures reported for instance in travellers** returning from: ▪ Angola[1], Liberia[1], and Uganda[1,2] to the UK; ▪ Ghana, Gambia, Tanzania and SE Asia to Sweden[3]; and ▪ the Republic of Congo, Kenya, Malawi, and Zimbabwe to Prague[4]	➢ Patients are often **not receiving observed treatment**, and **lumefantrine blood levels not measured**
In-vitro and ex-vivo data:	
➢ **Decreased susceptibility to lumefantrine reported**: ▪ From Uganda[5]: lumefantrine IC_{50}* median 14.6 nM in northern Uganda vs. 6.9 nM in eastern Uganda ▪ Two cases to the UK from Uganda[2] with EC_{50} > 250 nM	➢ **No IC_{50} threshold** defined as lumefantrine resistance ➢ Uncertainty about the **meaning of outliers** ➢ In UK, **parasites were collected after treatment**. In-patient selection may have taken place

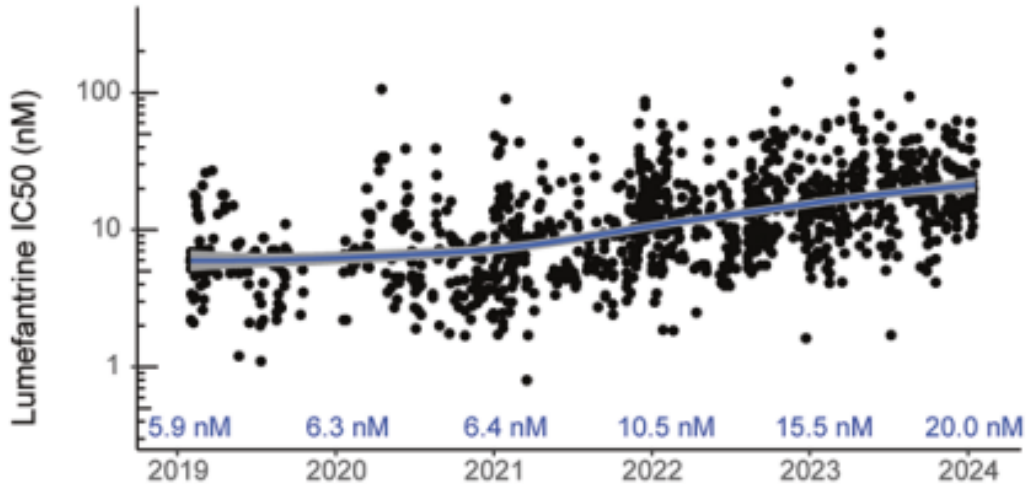
[1] Sutherland CJ et al. (2017) doi: 10.1128/AAC.02382-16
[2] van Schalkwyk et al. (2024) doi.org/10.1093/cid/ciad724
[3] Sonden et al. (2017) doi: 10.1093/cid/ciw710
[4] Grebenyuk et al. (2023) doi: 10.1016/j.tmaid.2023.102549
[5] *Tumwebaze, et al. (2022). https://doi.org/10.1038/s41467-022-33873-x*

**IC_{50} : Concentration required to inhibit 50% of the growth*

Focusing on susceptibility data from Uganda

Table 2 | Summary of drug susceptibility data (2019–2024)

Drug	IC_{50} (nM)								
	All sites			Eastern Uganda			Northern Uganda		
	N	Median	IQR	N	Median	IQR	N	Median	IQR
Chloroquine	1060	12.6	9.2–18.0	707	13.2	9.7–19.0	353	11.3	8.7–16.4
MDAQ	1062	7.8	4.9–10.4	708	7.6	4.8–10.1	354	8.2	5.2–10.8
Piperaquine	1062	5.4	3.6–8.2	708	5.5	3.6–8.3	354	5.2	3.5–7.8
DHA	1063	2.9	1.6–4.5	710	2.5	1.5–4.1	353	3.4	2.2–5.0
Lumefantrine	1060	11.3	6.1–19.5	706	8.7	5.2–17.2	354	15.3	10.4–21.7
Mefloquine	1058	15.2	9.6–24.8	709	14.9	9.4–25.2	349	15.8	9.9–23.2
Pyronaridine	1057	1.5	0.7–2.7	704	1.5	0.8–2.8	353	1.4	0.6–2.7
Quinine	770	115	75.1–173	625	117	76.8–178	145	106	72.1–153
Pyrimethamine	881	35,100	24,900–49,100	674	38,100	27,100–52,000	207	28,100	19,900–37,400



From Okitwi et al. *Changes in susceptibility of Plasmodium falciparum to antimalarial drugs in Uganda over time: 2019-2024.* Nat Commun. 2025 Aug 9;16(1):7353. doi: 10.1038/s41467-025-62810-x.

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MFTs implementation Guide

- A Guide to support adoption and implementation of MFT was published in November 2024.
- https://www.who.int/publications/i/item/9789240103603

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MFT: WHO implementation updates

- Support early use countries in planning, deploying, and evaluating the implementation, and document lessons.
  - Rwanda approved national implementation documents with procurements of commodities
  - Nigeria, DRC, Uganda, BF, Kenya are at various stages of developing their concept and implementation plans for adopting and deploying MFT policies.
- Support the UNITAID supported project (STOP-AMDR) through an Enabler grant

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STOP-AMDR Project

- A Unitaid-funded Scaling the Optimal Use of Multiple ACTs to Prevent Antimalarial Drug Resistance (STOP-AMDR) project (2025-2029) being implemented in six countries in SAA with a research component embedded aimed at assessing the feasibility, acceptability, and cost of implementing MFT.
  - Burkina Faso, DRC, Kenya, Nigeria, Rwanda and Uganda
  - Project was formally launched in July 2025.

- WHO involvement
  - Providing guidance on the development of research questions to ensure they generate relevant data needed to update MFT implementation guidance document.

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Evidence generation and guideline development in the context of vector control

Vector, Disease Control, Elimination and Eradication (VCE)

As is the case across all fields in public and global health, the quality of evidence is often variable and may not always reach the highest thresholds, but a GDG remains best placed within the evidence ecosystem to judge and interpret such collated evidence, within the dedicated framework that the guideline development process provides. That said, recommendations should be developed based on the *best available* evidence, and prioritize transparency in moving from evidence to recommendation, using established frameworks.

WHO guidance

WHO aligns with international evidence synthesis and appraisal methodologies, and remains actively engaged in the evolving field of guideline development. WHO has long recognized the role of non-randomized trials in evidence synthesis, particularly where RCTs are impractical or inappropriate (see *WHO Handbook for Guideline Development, 2nd edition,* 2014). While randomized controlled trials remain the 'gold standard' for clinical trials in public and global health, there is a recognition and understanding of the challenges associated with firstly, conducting such studies across all fields, and secondly, that the sole reliance on such trials would limit our capacity to generate recommendations for a range of interventions.

Evidence-to-decision framework

The GRADE approach (Grading of Recommendations Assessment, Development and Evaluation) is an established, internationally recognized method of assessing the certainty in evidence (also known as quality of evidence) and the strength of recommendations in health care. The GRADE approach is widely used amongst those developing guidelines within WHO, and is the approach that is used as part of developing the malaria vector control recommendations.

The approach emphasizes the need for assessment of both health-related effects (benefits and harms of an intervention) as well as contextual factors that might influence its uptake, such as acceptability, feasibility, resource considerations and equity. Evidence considered by the GDG is assessed for quality of evidence, with a recommendation being associated with an overall level of evidence certainty ranging from high to very low. For example, one of the latest published recommendations, for spatial emanators, is a *conditional recommendation* with *moderate certainty* evidence.

Fig 1. Explanations of the quality of evidence for trials, according to the GRADE approach (extracted from the WHO Handbook for Guideline Development 2nd Edition (2014)

Table 9.2. Quality of evidence in GRADE

Quality level	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

GRADE: Grading of Recommendations Assessment, Development and Evaluation.

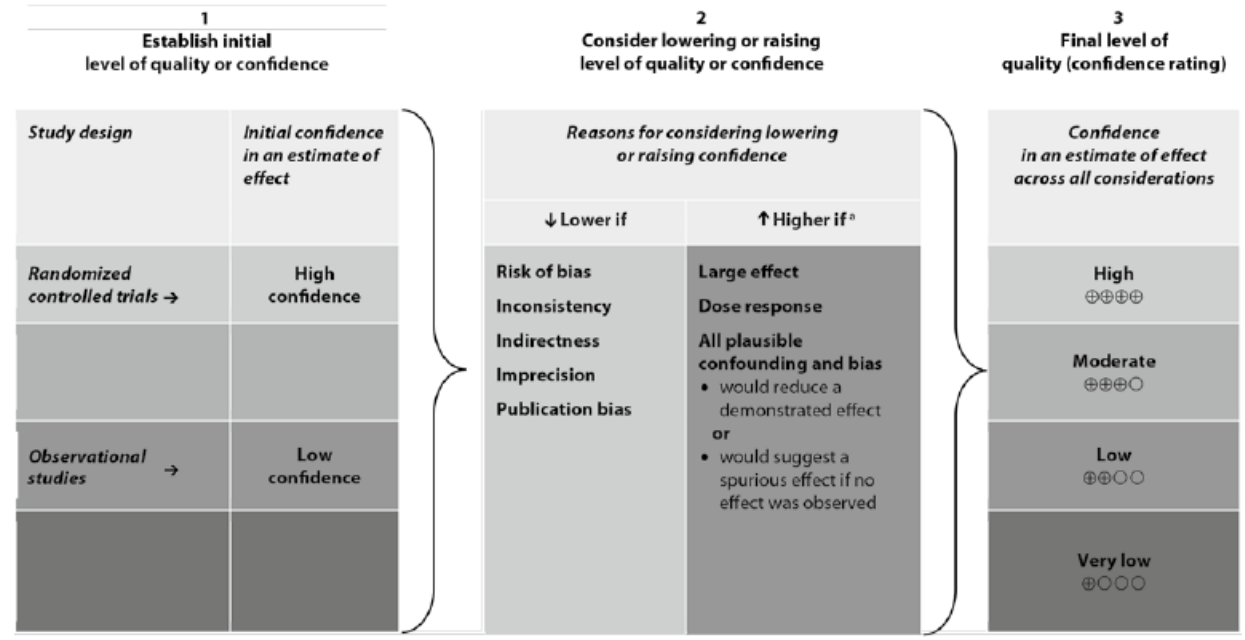
Trial designs and study appraisal

While randomized controlled trials are considered the gold standard for reducing the inherent risk of bias in clinical trials, it is also very common for non-randomized trials to be included within the body of evidence that underpins a recommendation. Indeed, all trials (randomized and non-randomized) are appraised for the certainty of evidence across five domains (see Fig 1; risk of bias, inconsistency, indirectness, imprecision or publication bias), using the GRADE approach, and even randomized trials often suffer from design limitations, and are appraised accordingly.

A range of scientific literature has been published on the topic of when one should include non-randomized controlled studies in evidence syntheses, and the considerations surrounding the use of such evidence. Inherently, non-randomized trials lack an important element of randomization, but as per the internationally recognized GRADE processes that WHO uses for guideline development, where non-randomized control trials are included in the analyses, the certainty of evidence generated from that trial will be assessed accordingly (downgraded), but still included in relevant analyses. Of note, under certain circumstances a study may be upgraded again, should there be a very large magnitude of effect or a dose-response effect observed, for example, but this is rare.

Fig 2. Summary of how the type of trial design and biases will influence the certainty of evidence that underpins a recommendation (extracted from the WHO Handbook for Guideline Development 2nd Edition (2014)

Fig. 9.1. **The GRADE approach to rating quality of evidence for each outcome**



GRADE: Grading of Recommendations Assessment, Development and Evaluation.
[a] Criteria for upgrading the quality are only applicable to observational studies without any reason for downgrading.

Specially designed tools to appraise the risk of bias have been designed for both randomized and non-randomized trial designs. These are standardly used by systematic review teams as part of the evidence appraisal process. For the latter, these tools include but are not limited to Newcastle-Ottawa, EPIQ, CASP and ROBINS-I.

Considerations for vector control

As vector control interventions (normally) target mosquitoes rather than humans, trials to assess efficacy of an intervention necessitate additional considerations. This may include mosquito movement and biology, the environment, and exposure to the intervention. This can mean that randomized controlled trials, and even *cluster* randomized controlled trials, may not always be appropriate for evaluation of an intervention's public health value. This challenge of undertaking high quality RCTs is well recognized in vector control, largely due to logistics of working with mosquitoes and thus the large clusters that are required to account for mosquito mobility (amongst other things), which can then amplify the already costly undertakings of conducting such trials. Such constraints are often prohibitive, and can lead to poorly implemented trials.

Alternate non-randomized trial designs are sometimes necessary to suitably evaluate an intervention. Depending on the intervention in question, such examples might include (but are not limited to) comparative controlled before-after, stepped wedge trials, interrupted-time series, cross-over studies, dose-response gradient studies, or observational prospective cohort studies. While it is clear that many of these study designs have inherent limitations and biases, such studies still have the capacity to demonstrate efficacy (or otherwise) of an intervention, and can build (or perhaps solidify) a body of public health evidence for an intervention.

Importantly, and especially for vector control, the decision to employ one trial design over another should bear in mind how the intervention is intended to be rolled out in programmatic situations, and thus use a trial design that allows the best chance for demonstrating success under real-world deployment conditions. An example of this is using a cluster RCT to evaluate the release of sterile males, where each individual cluster will face invasion of fertile males from all fronts and thus reduce the likelihood of vector population reduction. A more appropriate deployment strategy, and related study design might be a stepped wedge design with a 'rolling wave' of concentrated releases across a smaller interface, or wave front, between the fertile and sterile males. Another example might be a prospective cohort study for evaluation of spatial or even topical repellents, where cohorts might be at a household level to account for confounding of exposure.

Finally, the contextual factors that are considered as part of the GRADE approach are particularly important in vector control. How these factors affect the exposure of the intervention to the population (be it mosquitoes, or humans, depending on the intervention) can influence the strength of a recommendation. For example, when assessing feasibility, one might consider how easy it is to deploy a new intervention – taking spatial repellents as an example, one could take advantage of established pre-planned community visits as part of regular SMC activities to distribute and replace the units to households, rather than initiating whole new programmatic operations for deployment. Such integration could increase the feasibility of deployment, as well as rendering the visits overall more cost-effective per prevention activity completed. Considering another contextual factor, acceptability, one could contemplate different types of residual surface treatment, where longer lasting active ingredients are more acceptable to end users. To exemplify the point, a single visit from a programme worker to install a long-lasting insecticide-impregnated wallpaper in a household would possibly be more acceptable to households than regular seasonal visits for IRS application, requiring vacation of the premises and protection of furniture with each application.

Ultimately, with the goal to ensure interventions are used in the intended fashion, to illicit the desired effect, it is critical to also reflect on how contextual factors may influence success, or failure. Evidence promoting equity, increased cost effectiveness, feasibility and acceptability are therefore key elements that must be considered in deliberations of the direction and strength of recommendations.

As part of all ongoing and future work in the malaria vector control guidelines, the GRADE approach is being applied to any and all studies that are being considered a part of the systematic reviews underpinning GDG deliberations. Depending on the *a priori* PICO question in the systematic review protocol, this may indeed include non-randomized controlled trials as part of that evidence basis.

Summary

RCTs remain the benchmark for internal validity and certainty of evidence; however, in vector control, well-conducted non-randomized studies are often indispensable to complement or, where necessary, substitute for RCTs. WHO applies internationally recognized standards for evidence appraisal and recommendation development, ensuring that all studies – whether randomized or non-randomized – are rigorously assessed for their contribution to the evidence base. In the absence of RCT data, evidence from non-randomized studies can appropriately inform GDG deliberations when transparently appraised. Ultimately, recommendations should rest on the best available evidence, integrating both health effects and contextual considerations, to ensure they are robust, relevant, and implementable in real-world settings.

Malaria Policy Advisory Group Meeting
Virtual meeting, 14–16 October 2025 (13:00-17:00 GMT+1)
Background document for Session 6

World Health Organization

Updating the Global Plan for Insecticide Resistance Management in Malaria Vectors

Vector, Disease Control, Elimination and Eradication (VCE)

The Global Plan for Insecticide Resistance Management in Malaria Vectors (GPIRM), published by WHO in 2012, set out the first comprehensive global strategy to address the growing threat of insecticide resistance in malaria vectors. Its goal was to preserve the effectiveness of core vector control tools – particularly LLINs and IRS – by promoting coordinated resistance management strategies, strengthening monitoring systems, and driving research into new insecticides. At the time, the intended impact was to avert control failures, sustain recent gains in malaria reduction, and safeguard the long-term effectiveness of malaria vector control.

The GPIRM was a landmark strategy, but it is now somewhat out of date. Thirteen years on, the field of malaria vector control has changed significantly: new invasive species have emerged, other vector-borne diseases have increased incidence, there is a strong, renewed push for integrated vector management across diseases and vectors. While the assays used to evaluate resistance remain consistent, the range of available tools to combat vectors has grown (including non-insecticide based tools). At the time of publication, GPIRM focused on core tools, being pyrethroid-only LLINs and IRS, with only four insecticide classes prequalified, whereas today multiple new insecticide classes (including dual-active ingredient nets, broflanilide, chlorfenapyr, isocycloseram), as well new interventions themselves (for example spatial repellents) are available, and ripe for integration. Moreover, technologies and platforms to support monitoring, surveillance and evaluation of insecticide resistance, and vector control implementation more generally, are almost unrecognizable compared with those available in 2012. Insecticide resistance has also become more widespread, with clearer evidence of its operational impact. Finally, financial projections are outdated, and at over 100 pages, the GPIRM is too dense for rapid uptake by the intended audience, largely being control programme managers.

An updated, streamlined plan – illustrated with case studies and digestible graphics, and aligned with WHO's current guidance and guideline frameworks – is now essential.

Proposed approach for updating the GPIRM

The update of the GPIRM will follow a structured and consultative process to ensure that the revised document is relevant, practical, and aligned with current priorities in vector control.

- **Consultation with MPAG**: Early engagement with the MPAG will help define the scope, content, and key issues to be addressed, ensuring the document meets the needs of end users.
- **Engagement with country programme managers and manufacturers/industry in a two-step process**: First engage to understand impact and use of current document by respective end users. Second, following feedback, share an advanced draft with interest holders, including national programme managers who are familiar with the original GPIRM. Use focus groups or similar mechanisms to gather feedback on the value and applicability of the proposed changes.

- **Broader stakeholder input**: The draft will also be circulated to stakeholders working on other relevant neglected tropical diseases (including but not limited to arboviruses, leishmaniasis, lymphatic filariasis), ensuring the updated plan resonates beyond malaria and strengthens integrated vector management approaches.
- **External review**: A revised version will undergo external peer review, drawing on both contributors to the original GPIRM and new experts, to ensure a balance of continuity and fresh perspectives.
- **Internal review within WHO**: The final draft will be reviewed internally by the newly merged Department of Malaria and Neglected Tropical Diseases (MNT), reflecting the relevance of the updated GPIRM to all vector-borne diseases and highlighting its role in advancing integrated vector management across the department.
- **Consultation with MPAG**: Reviewing the final document with (MPAG) to ensure review key issues are addressed, and that the document meets the needs of end users.

This inclusive approach is designed to ensure the updated GPIRM is evidence-based, forward-looking, and widely owned by the malaria and broader vector control community.

Proposed updates to the GPIRM

Overall, the revised document should shift from being a dense technical report to a practical, guidance-oriented tool with strong visuals, clear country-level recommendations, and illustrative case studies.

Topic	2012 content	Update proposed
Revisit pillars	**2012 pillars and timeline**: strategic goals and visions for next 10 years	○ Review and evaluate progress against the short-, mid- and long-term goals listed within the document (preserve susceptibility, improve management of IR, and look to innovation for sustainability) ○ Focus on evidence-based decision making and capacity building ○ Revisit the pillars and ensure relevance for current landscape (including new molecules, exemplify case studies) ○ Ensure continued alignment with current WHO documentation (especially GVCR, which was published after GPIRM, but also IVM, other IRM guidance) ○ Strengthen push to intersectoral collaboration between agriculture, health, and infrastructure development/local authorities (case studies) ○ Promote collaborations, including with WHO CCs, for tracking mechanisms to implement rational IRM, via complementary work with academia and other institutions

Scope of vector control tools	**2012 limitation**: focused only on LLINs (all pyrethroid-based at the time) and IRS with four insecticide classes.	○ Incorporate the fact that there are now more than four classes of insecticide available for adult vector control. ○ Pyrethroids are no longer the only ITN insecticide; dual-active ingredient nets (e.g., pyrethroid–PBO, pyrethroid–chlorfenapyr) are now widely deployed. ○ Expand to include IRS insecticides newly recommended by WHO (e.g., broflanilide, isocycloseram, chlorfenapyr). ○ Integrate novel interventions already in WHO guidelines (e.g., spatial emanators) and highlight interventions nearing the end of the evaluation pipeline. ○ Ensure the framework is adaptable to future tools in the pipeline.
Insecticide resistance landscape	**2012 context**: resistance confirmed in 64 malaria-endemic countries, with patchy monitoring.	○ Reflect the current number of countries reporting resistance (substantially higher now). ○ Integrate evidence of broader and stronger resistance across regions and species. ○ Highlight genetic and molecular tools now used for resistance detection. ○ Showcase studies where monitoring enabled timely IRS rotations or adjustments in national insecticide use plans to preserve susceptibility. ○ Issue of cross resistance that needs to be highlighted, and emphasise that understanding of the mechanistic basis for resistance needs to be investigated to mitigate this phenomenon ○ Highlight the modalities for management of resistance currently available, including emphasis on non-insecticide approaches (in line with the long-term plan of the original GPRIM) ○ Case studies on impact of resistance on disease burden
technical recommend-ations for countries	**2012 approach**: IRS rotations emphasized, limited guidance for LLINs.	○ Update guidance around rotations for classes of ITNs, IRS insecticides, and insecticide-based interventions ○ Embed guidance for using combinations of interventions (LLINs, IRS, emanators, larval source management). ○ Greater advocacy for the sustainability and responsibility of community-based vector control (case studies) ○ Strengthen links to WHO's consolidated vector control guidelines and IVM.

Research & development agenda	**2012 priorities**: mainly new active ingredients for LLINs and IRS.	○ Reflect progress made in insecticide discovery and product development (e.g., IVCC-supported pipeline). ○ Expand to include evaluation of new classes of LLINs, IRS products ○ Further emphasis needed on non-insecticide-based tools, to prolong susceptibility to insecticides (for emergency uses) and to support the minimal resources available for commodity-based tools/approaches. ○ Address assessment frameworks under WHO guideline development (GRADE-based evidence).
Monitoring and data systems	**2012 situation**: inconsistent, ad hoc resistance monitoring; no global system.	○ Reference current data platforms (e.g., IR Mapper, WHO databases). ○ Strengthen emphasis on routine entomological and epidemiological surveillance integration. ○ Include case studies where real-time monitoring has triggered policy change at national level. ○ Highlight the potential for AI to support monitoring evaluation?
Costing and financing	**2012 estimates**: ~US$200 million per year for GPIRM implementation.	○ Revise cost estimates, including experience with dual-active ingredient nets, IRS with new insecticides, and combined approaches. ○ Incorporate economic evaluations of new tools and long-term cost-effectiveness of IRM. ○ Address sustainability in financing, including transitions in donor support.
Cross-sectoral and enabling mechanisms	**2012 framing**: collaboration across malaria and agriculture sectors; call for advocacy.	○ Reinforce One Health approaches, especially agriculture–public health pesticide links. ○ Update capacity-building priorities, including entomology workforce development. ○ Ensure advocacy and communication messages align with today's Global Technical Strategy for Malaria and WHO's 2023 consolidated vector control guidelines.

Streamlining the document (~50% reduction)

The 2012 GPIRM runs long, with extensive annexes and technical background. To make a new version more user-friendly while retaining value, it is proposed to streamline or cut some sections, while retaining, and even strengthening others.

Overall, the goal would be to keep the document concise, specifically relating to the roles of the audience of the document (so they know what they can do and how it can be done), and to augment the visually supports throughout the document (charts/figures to support key concepts).

Streamline or cut	Retain or strengthen
• Annexes with historical background (e.g., Annexes 1–3 on past use of DDT, history of resistance): these could be condensed into a short historical overview box. • Detailed modelling assumptions (Annexes 7–8, 11): these could be replaced with summary tables/graphics and link to technical reports online. • Narrative repetition (e.g., introduction to IRM concepts appears in multiple places): condense into one clear section with definitions, and support this with key reference graphics	• Executive summary and "Five Pillars" framework (still useful, but these require a solid update). • Country guidance (Part 3) — to retain, but should be condensed into scenario-based tables or decision trees. • Case studies — add as illustrative boxes instead of long annexes. • Use of graphics and illustrations to support the explanation of key concepts.

Key takeaway for the concept note

The 2012 GPIRM was visionary but is now outdated because the toolbox has expanded, the resistance problem has intensified, and WHO's evidence and guideline frameworks have evolved. Updates should focus on:

- Highlight the need to link agile guidance with regularly updated guidelines
- Incorporating new tools/interventions (LLINs with multiple active ingredients, spatial emanators, others).
- Reflecting the current resistance evidence base and improved surveillance systems.
- Providing updated country guidance that integrates both insecticide-based and non-insecticidal tools under a unified IRM/IVM framework supported by case studies
- Aligning with current policy, funding realities, and innovation pipelines.

Key questions for MPAG

1. **Reflection:** Has the document been used by the intended end users (largely programme managers), and how helpful has it actually been? Has it been used by other users (manufacturers/industry), and what value has it provided?
2. **Scope**: Do you agree with the proposed scope of the GPIRM update, including expansion beyond malaria to support integrated vector management across diseases and vectors? Are there additional areas you believe should be included to strengthen its value?
3. **Content priorities**: Which elements of the revised GPIRM should be emphasized most strongly to ensure it is actionable for national programmes (e.g., decision-support tools, practical case studies, updated monitoring and resistance management guidance, or costing considerations)?
4. **Evidence gaps**: From your perspective, what are the most critical evidence gaps (e.g., operational impact of resistance, cost-effectiveness of new tools, resistance mechanisms, cross resistance, implementation research) that the updated GPIRM should highlight as priorities for further research and investment?

5. **Cross-disease alignment**: How can the updated GPIRM best reflect and advance the broader shift toward integrated vector management, ensuring relevance not only for malaria but also for arboviral and other vector-borne diseases?

Vector control

Emmanuel Chanda
Lauren Carrington

World Health Organization

Outline

- Evidence underpinning guidelines for vector control
- Global plan for insecticide resistance management

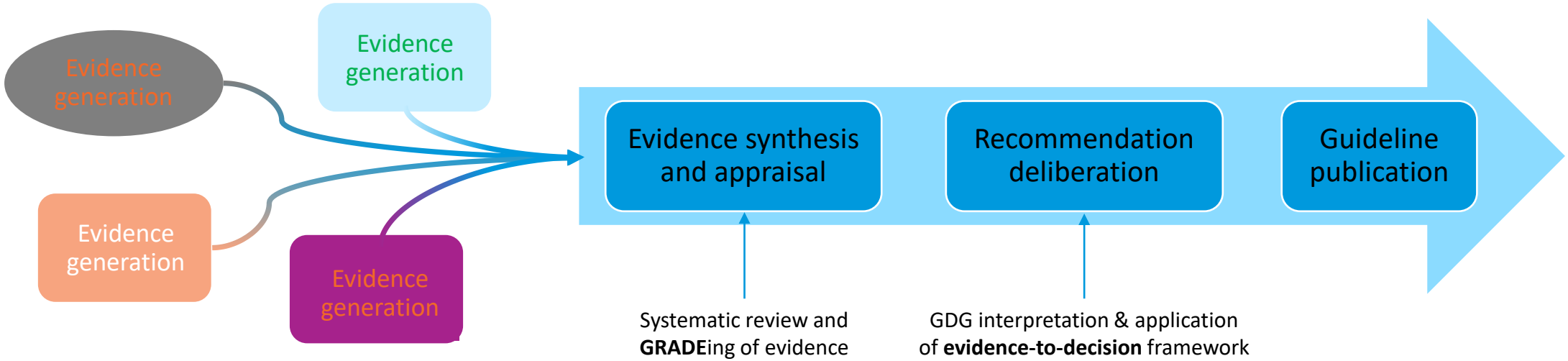
Evidence underpinning guidelines for vector control

Lauren Carrington

World Health Organization

Evidence and Guideline Development at WHO

- Recommendations must be based on the best available evidence
- WHO follows standard processes and uses internationally recognised appraisal methodologies
  - Systematic reviews synthesize evidence
  - Multiple types of evidence can be included, all evidence appraised for quality and analyzed
  - GDGs interpret evidence within a structured, documented, transparent process
- Aim: ensure credible, transparent, and practical guidance



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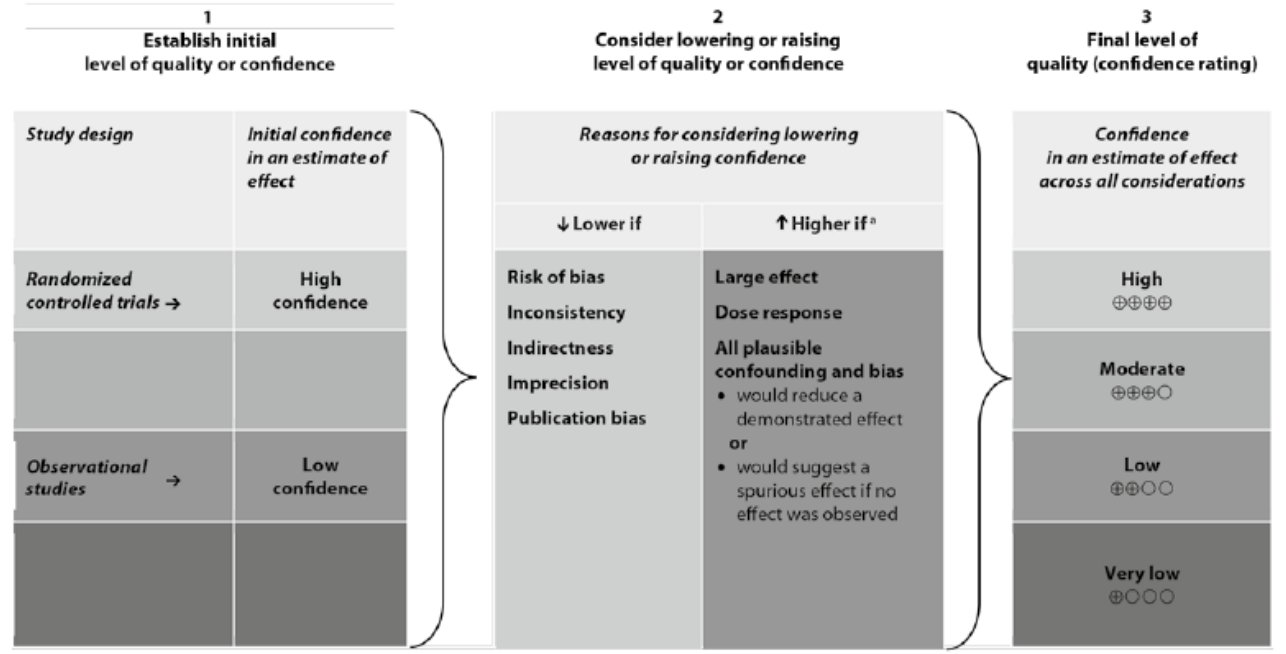
Appraisal of evidence for different types of trial designs

- WHO recognises the role of non-randomised studies in evidence synthesis
- RCTs are the benchmark for providing high certainty of evidence
  - ...but may still suffer from limitations
- Both trial types are appraised using the GRADE framework

Fig. 9.1. The GRADE approach to rating quality of evidence for each outcome



GRADE: Grading of Recommendations Assessment, Development and Evaluation.

[a] Criteria for upgrading the quality are only applicable to observational studies without any reason for downgrading.

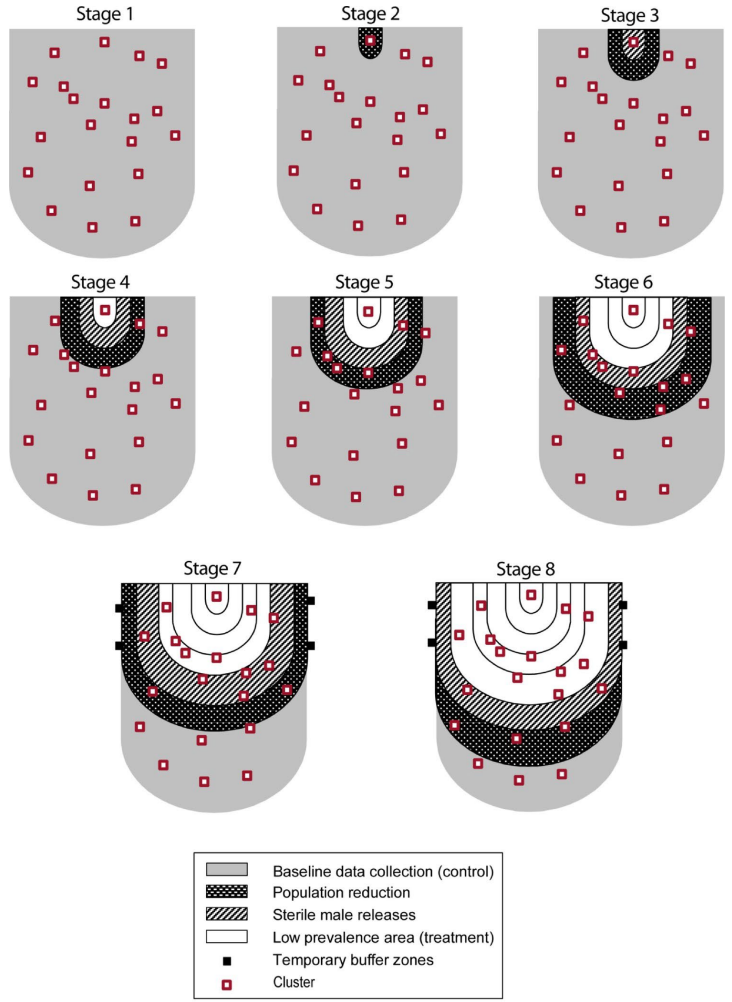
Summary of how the type of study design and other factors can influence the certainty of evidence that underpins a recommendation (extracted from the WHO Handbook for Guideline Development 2nd Edition (2014)

Resources:
1. WHO Handbook for Guideline Development 2nd edition (2014)
2. GRADE working group: https://www.gradeworkinggroup.org/

World Health Organization

Considerations for Vector Control

- In vector control, RCTs may be impractical, inappropriate or insufficiently funded
- Challenge to traditional RCT designs: vector biology, mobility, environment, buffer zones…
- Alternative designs may include (but are not limited to):
  - Controlled before–after, stepped wedge, interrupted time series
  - Prospective cohorts, dose–response studies
- Selection of trial design should ideally:
  - Support the *capacity* for the intervention to demonstrate efficacy
  - Reflect real-world programmatic deployment
- Contextual factors can influence both uptake and therefore impact
  - Feasibility, acceptability, cost-effectiveness, equity



Bouyer et al, 2020. Trends in Parasitology
https://www.sciencedirect.com/science/article/pii/S1471492220300143#f0015

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Summary

- RCTs remain the benchmark, but non-randomised studies/other study designs should be considered, especially in the context of vector control
- WHO processes ensure and *require* rigorous appraisal of all evidence – using internationally recognised approaches (for vector control, we use GRADE)
- Inclusion of trial designs other than randomized controlled trials is well established within WHO guideline processes
- Recommendations must be founded upon on health outcomes + contextual realities, while transparently documenting the evidence-to-decision process

World Health Organization

GPIRM 2.0

Emmanuel Chanda

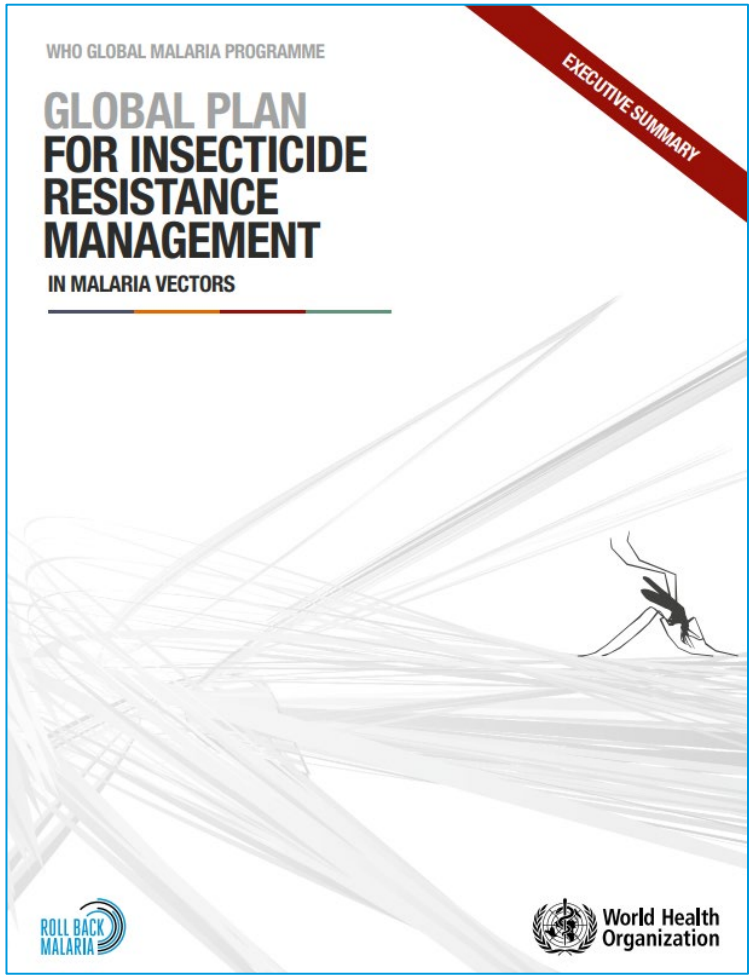
World Health Organization

Background

- Major vector control tools remains insecticide-based
  - ITNs
  - IRS
  - Larvicides
  - Spatial emanators
- It is important to remember that we have non-insecticidal vector control tools as well
  - Source reduction
  - House screening
- For insecticide-based tools to remain effective, insecticide resistance must be managed
- Insecticide resistance management (IRM) has prolonged historical importance in agriculture
- IRM in malaria vector control is more recent – but increasingly necessary

Global plan for insecticide resistance management

- Published in 2013
- Landmark document for the malaria vector control community
- Informed development of national insecticide resistance management plans
    - implementation issues persisted....



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Reasons for update

- Document does not sufficiently focus on **integration** across diseases
- **Increased number of insecticide classes** available now across numerous intervention classes
    - 3 classes for ITNs
    - 8 classes for IRS
    - 6 classes for larvicides
    - 1 class for spatial repellents
- Increased **diversity of interventions** now assessed for public health value
- Improved **molecular tools** available for resistance monitoring
- Case studies are out of date
- Updated **economic estimates** and analyses needed
- Reinforce One Health, Integrated Vector Management, and Global Vector Control Response
- Potentially limited use of current document due to **length (132 pages)**

World Health Organization

Consultative approach for updating the document

1. Initial consultation with MPAG
2. Engagement with country programme managers and manufacturers/industry
3. Broad interest holder inputs – *Aedes*, and beyond….
4. WHO standard review
   - External
   - Internal
5. Final presentation to MPAG

World Health Organization

Streamlining and strengthening the guidance

Improving usability and practical nature of document

- Historical backgrounds condensed into overview boxes
- Detailed modelling assumptions → summary tables/graphics & links to technical reports.
- Condense and simplify concepts with key graphics
- Enhance executive summary and “Five Pillars” framework
- Country guidance to be retained, supported by decision trees
- Improved case studies + illustrative boxes
- Supplementary visual aides

World Health Organization

Proposed updates

Revisit pillars and goals

- Review progress against short- mid- and long-term goals & review for continued relevance
- Strengthen alignment with IRM, IVM, GVCR, capacity building, evidence-based decision making

Scope of vector control tools

- Previous focus on ITNs and IRS → increased diversity of tools, and insecticide classes now available

Insecticide resistance landscape

- Issues of cross-resistance more prevalent, investigative assays needed to understand mechanisms
- Current technologies to monitor & evaluate IR have evolved dramatically (online platforms, etc)
- Re-emphasise previous goal of moving away from insecticide-based tools also

Technical recommendations for countries

- Greater advocacy for sustainable and community-based vector control
- Update guidance around rotations for classes of ITNs, IRS insecticides, and insecticide-based interventions

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Proposed updates

Research and development agenda

- Reflect progress made in R&D pipeline, and that forthcoming
- Further emphasis on non-insecticide-based tools to prolong susceptibility to insecticides

Monitoring and data systems

- Reference current platforms for M&E (IR mapper, Malaria Threats Map, WHO databases)
- Strengthen emphasis on routine ento + epi surveillance integration
- Highlight potential for AI to strengthen/automate existing platforms (?)

Costing and financing

- Revised costs estimates must reflect available tools (eg: dual AI nets, new insecticide classes)
- Encourage economic evaluations and advocate for long-term cost-benefits of managing resistance, address sustainability in financing and transitions in donor support

Cross-sectoral and enabling mechanisms

- Reinforce agriculture-public health pesticide links and the need for sustained engagement from outside of the health sector, community engagement
- Update capacity building priorities, including entomology workforce

World Health Organization

The Big Push: Aligning Global Health Financing and Governance for Impact

MPAG Update

October 2025

RBM Partnership to End Malaria

Agenda

01 Setting the scene

02 Engagement & Realignment

03 Country Focus & Data

04 Resource Mobilization

05 The Big Push & Next Steps

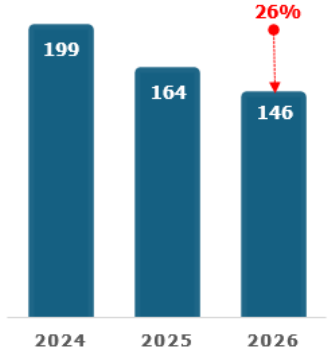
Setting the scene - beyond the perfect storm

Malaria progress is stalling; but countries are showing ownership and innovation against funding instability and rising threats.

- **Evolving global health ecosystem** will require further partner alignment, resource optimization and country ownership, integration, and new financing models
- **Converging threats** need continued agility (drug/insecticide resistance, adverse weather patterns)
- **Shrinking ODA** vs country ownership/response

Shrinking aid landscape

Projected **ODA loss** (billions) from largest 17 donors



Global ODA projected to fall 26% by 2026

Source: donortracker.org

Sustain progress | Adapt to fiscal space | Unify in action

Turning challenges into opportunity

The Partnership is positioning the Big Push as a mechanism to align and amplify country priorities — ensuring malaria is a united, high-impact agenda.

Aligning resources	Turning policy to action	Unifying the ecosystem
		
Broker, not duplicator–focus on filling gaps, not creating silos.	**Catalyst for collective action–** turning country priorities into collective delivery.	**Whole-of-ecosystem convener–** aligning global, regional, and national efforts.

RBM Partnership To End Malaria

Agenda

01 Financing for Malaria

02 The Big Push

03 Country Focus & Data

04 Resource Mobilization

05 The Big Push & Next Steps

Big Push: Shifting from theory to practice

The Big Push is no longer theory — it is the anchor of RBM's strategy and governance.

As we shift from theory to practice, RBM has been focusing on:

- **Strategic alignment:** Embedding Big Push across Partnership's workplan and in 2026–2030 Strategic Framework as the mechanism for convening and collective action.
- **Governance shift:** Simplifying oversight and strengthening country voice in Big Push governance.
- ***F ocus*:** Coherence, efficiency and country-led delivery.

Core principles to create an eradication ready ecosystem:

Countries need to be at the center
No one partner can accomplish massive change on their own
The Big Push succeeds only when many small pushes move in the same direction

The Big Push: Core Value Proposition

- Mobilises collective action and sustained investment behind shared priorities
  → e.g. *Nigeria meeting catalysed National leadership, country ownership and domestic financing pledges*

- Anchors financing within broader *governance reforms* (COOPs, joint reviews, scorecards).

- Reinforces *country ownership* while leveraging *regional leadership platforms* (AU, Africa CDC, EAC, SADC).

Core principles to create an eradication ready ecosystem:

Countries need to be at the center
No one partner can accomplish massive change on their own
The Big Push succeeds only when many small pushes move in the same direction

RBM Partnership To End Malaria

10 KEY PERFORMANCE INDICATORS

Agenda

01 Financing for Malaria

02 Engagement & Realignment

03 (title on Support for GHA evolution)

04 Resource Mobilization

05 The Big Push & Next Steps

Aligning with the new global health architecture

The Big Push adds value to bilateral agendas by promoting efficiency and accountability through country-led delivery.

- **One Plan, One System:** CRSPC aligns malaria partners behind Country Optimized Operational Plans (COOPs) — demonstrating efficiency and reducing the parallel systems.
- **Integrated Data & Surveillance:** strengthens data integration across national systems, WHO platforms, and partner dashboards enabling real-time visibility, joint analytics, and evidence-driven decision-making from national to regional levels.
- **Private-Sector Synergy:** connects African and U.S. private sector – linking America First's commercial goals with Africa's manufacturing drive.

Core principles to create an eradication ready ecosystem:

Countries lead with one integrated plan.
Partner alignment reduces duplication and maximises frontline impact.
Coordination across CRSPC, Working Groups, and ARCPC ensures coherent delivery from policy to community.

Big Push: Nigeria country ownership

Nigeria meeting provided a blueprint for convening to mobilize national commitment and drive toward malaria elimination under the Big Push.

Key outcomes of the meeting included:

The *Abuja High-Level Meeting (Sept 2025)* demonstrated the Big Push in action: Unified ministers, parliamentarians, and private

Aligning with Global Health Governance Reform:

Connecting the Big Push to Global Reform Agendas

Initiative	Focus	RBM's Role / Added Value
America First GHS	Reconfiguring global health architecture for accountability & efficiency	RBM adds value by demonstrating a functional country-driven coordination model through COOPs
Lusaka Agenda	Integration & alignment	RBM's COOP process and CRSPC demonstrate operational alignment
Yaoundé Financing Compact	Sustainable domestic & regional financing	RBM Board sub-committee on Financing for Impact established
Accra Reset	Health sovereignty & regional production	RBM linking to market shaping and local manufacturing dialogues
Abuja 2025	Political leadership & accountability	Ministers endorsed Big Push compact and quarterly review platform

Agenda

01 Financing for Malaria

02 Engagement & Realignment

03 Country Focus & Data

04 Strategic Opportunities for Big Push

05 The Big Push & Next Steps

Global Implementation | *Translating Big Push Pillars into an agenda for action*

Strategic areas → **Ecosystem engagement** → **Agenda for Priority Action**

1: Coordination

2: National Leadership

3: Data Systems

4: Accessibility/availability

5: New Tools

6: Financing

Ecosystem coordination
Global AMDR Consultation

Country-led prioritization
GC7/G78 Optimization Dialogue

Crisis response & alignment
Data & Incident Management LG

Data Driven Solutions
New data products designed for users

- **Optimized National Plans**
- **AMDR**
- **Market Shaping & local manufacturing**
- **Strategic Information & Data**
- **Outbreak Preparedness and Response**
- **Vaccines**
- **Financing**

Malaria Eradication Ready Ecosystem

Framework → **Dialogue** → **Action**

Partnerships that Work: RBM & WHO Collaboration

WHO provides technical leadership and normative guidance.

RBM ensures partner alignment and collective delivery behind WHO frameworks.

Joint initiatives: COOP rollout, data alignment, joint reviews, and regional coordination platforms.

Illustration: "WHO sets the course — RBM builds the convoy."

Looking Ahead: 12-Month Roadmap

Quarter	Milestones
Q4 2025	Market shaping & Local manufacturing Dialogue
Q1 2026	COOPs finalized in 10 initial countries
Q2 2026	Regional AMDR Ministerial meetings (EAC & SADC)
Q3 2026	Big Push Compact mid-year review
Q4 2026	Launch of RBM Strategic Framework 2026-2030

Agenda

01 Financing for Malaria

02 Engagement & Realignment

03 Country Focus

04 Data & Resource Mobilization

05 Call to Action & Next Steps

Call to Action

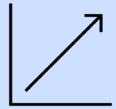
Financing and Governance aligned under Big Push

- Financing & governance reforms sustain impact
- Country-led mechanisms drive alignment across partners and regions

Champion Lusaka, Yaoundé, Accra, & Abuja

- Complementary, mutually reinforcing agendas
- Demonstrate African-led coordination and accountability in action

Political Commitment



- Coherent global health architecture fit for the post-pandemic era
- Collective leadership to ensure malaria remains central to health security and UHC

"The Big Push is Africa's collective declaration that malaria will no longer dictate our destiny."

Call to Action for MPAG

MPAG Members are invited to:

1. **Endorse** the alignment of *financing reforms* with *governance reforms* through the Big Push.

2. **Champion** Lusaka, Yaoundé, Accra and Abuja as complementary, mutually reinforcing agendas.

3. **Signal** political commitment to a coherent global health architecture that it fit for purpose in the post-pandemic era.

4. **Support** WHO-RBM collaboration for country-driven delivery.

Closing line: *"The Big Push is the Partnership's contribution to a smarter, united and accountable malaria response."*