Strategy to Respond to Antimalarial Drug Resistance in Africa

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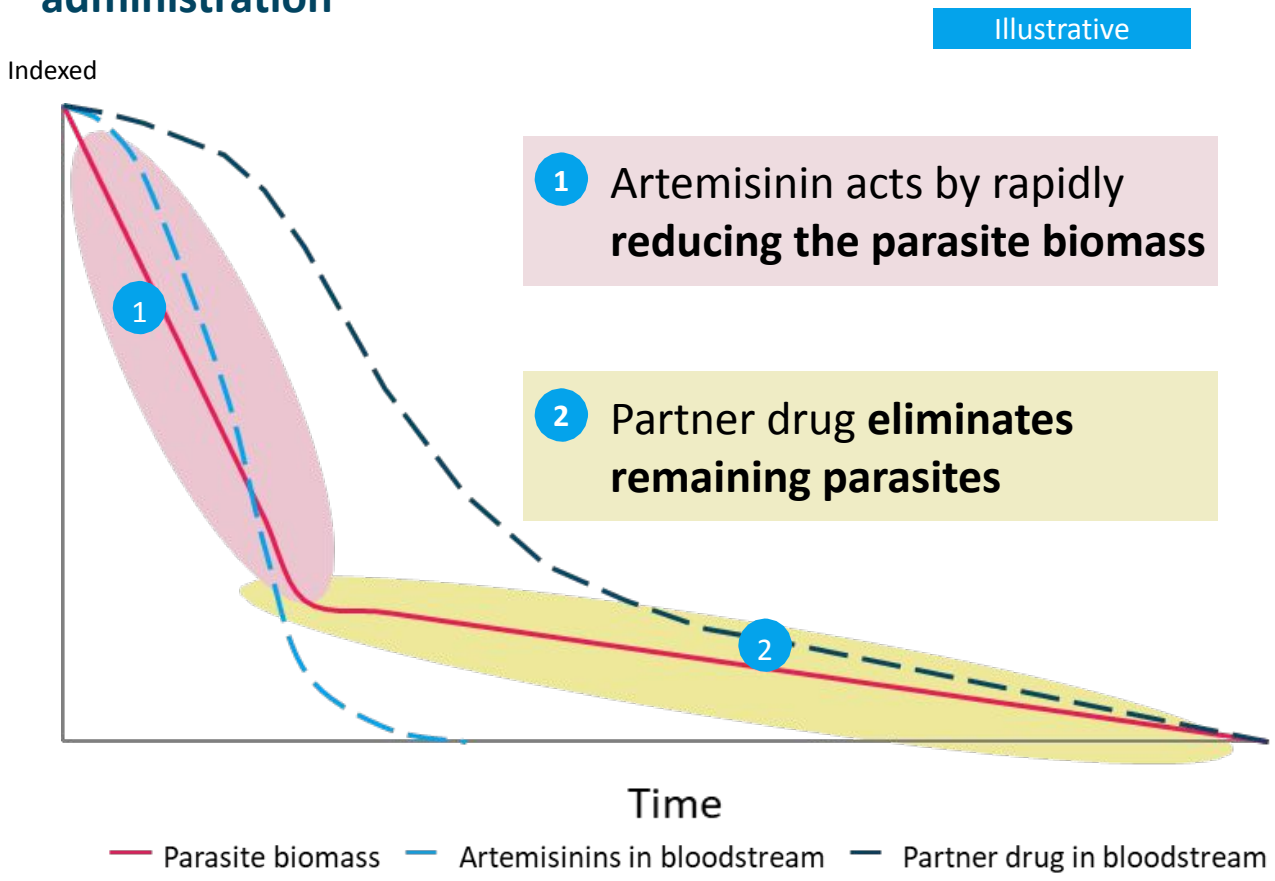
Artemisinin-based combination therapies at the heart of the response

- After the spread of chloroquine and SP resistance, artemisinin-based combination therapies (ACTs) became the main treatment of uncomplicated *P. falciparum* malaria
- ACTs combine an artemisinin and a partner drug
- The efficacy of ACTs is dependent on the efficacy of both components
- All 6 partner drugs highly efficacious as monotherapies in the absence of resistance
- Artemisinin rapidly lower the parasite biomass while partner drug completes the elimination of the parasites

Evolution of parasite biomass in the body following ACTs administration



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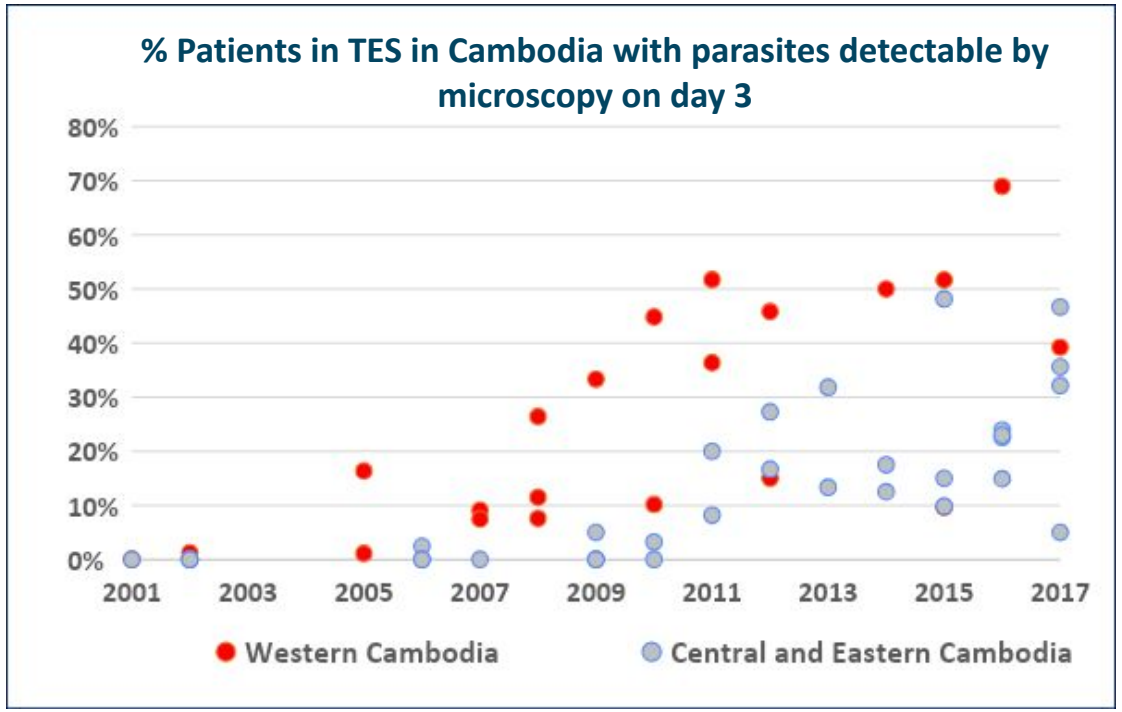
Artemisinin partial resistance

- **Artemisinin partial resistance** seen as delayed parasite clearance following treatment with artemisinin-based monotherapy or with an ACT



- Delayed clearance alone does not lead to ACT treatment failure
- In combination with partner drug resistance, very high failure rates have been seen
- Artemisinin partial resistance have been associated with different mutations of *Pfkelch13*. List of validated and candidate markers available on GMP website (*https://www.who.int/news-room/questions-and-answers/item/artemisinin-resistance*)
- 7-day artesunate treatment showed > 90% efficacy even in areas of high prevalence of mutant *Pfkelch13*
- For artemisinin partial resistance to be confirmed in a site, quality evidence is needed on:
  - Presence of validated marker (≥5%) (PfK13 mutations)
  - Evidence of delayed clearance (Day 3 + or parasites clearance half-life)

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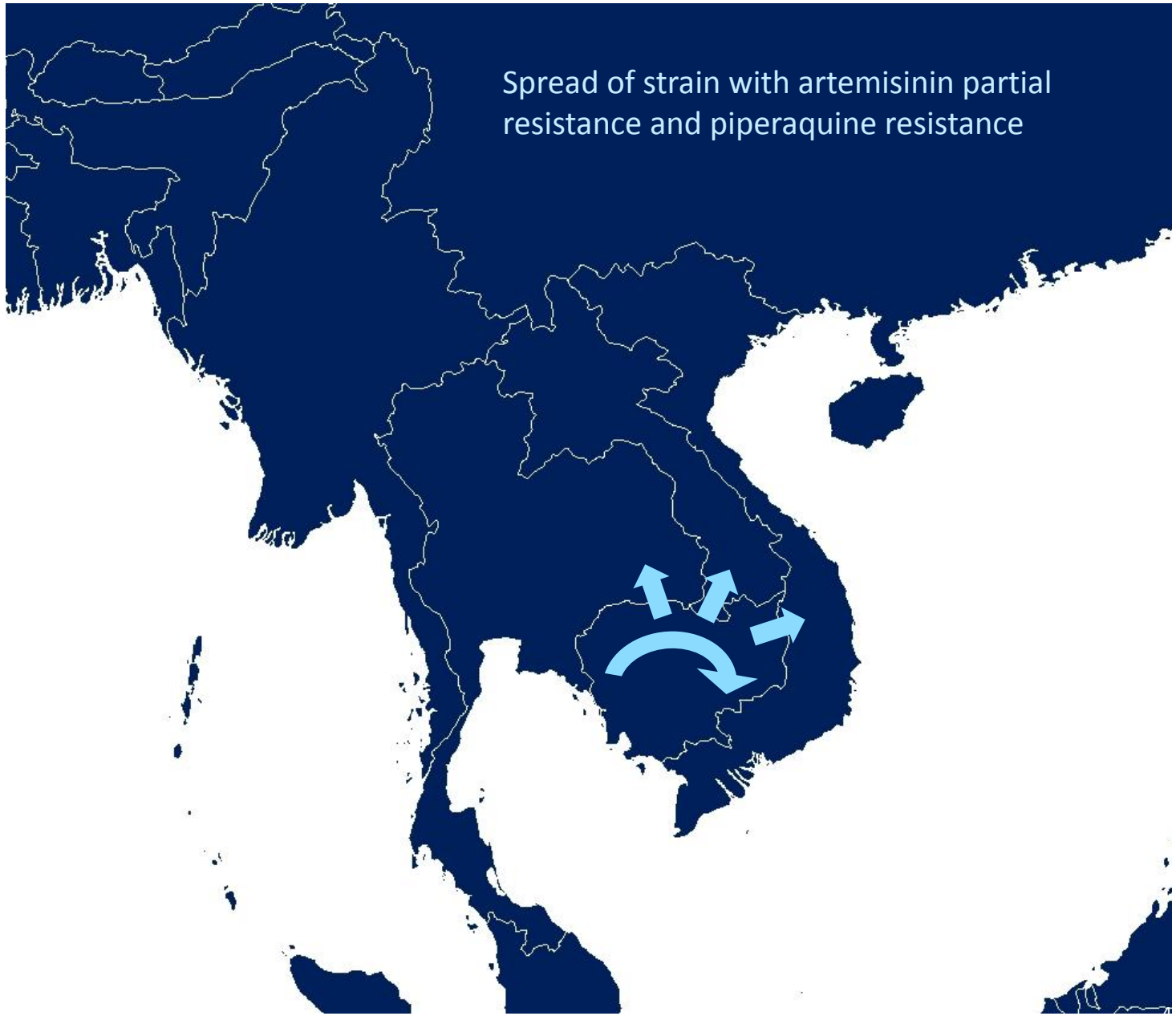
Risk of partner drug resistance

- In Southeast Asia, artemisinin partial resistance has not been seen to cause the emergence of partner drug resistance
- However, artemisinin partial resistance may have helped spread piperaquine resistance through a strain with artemisinin partial resistance and piperaquine resistance
- The spread of the resistant parasites across the region linked to massive drug pressure by DHA-piperaquine
- However, change in first-line treatment in Cambodia does appear to select against this strain



Imwong et al. 2017 Lancet Inf Dis.

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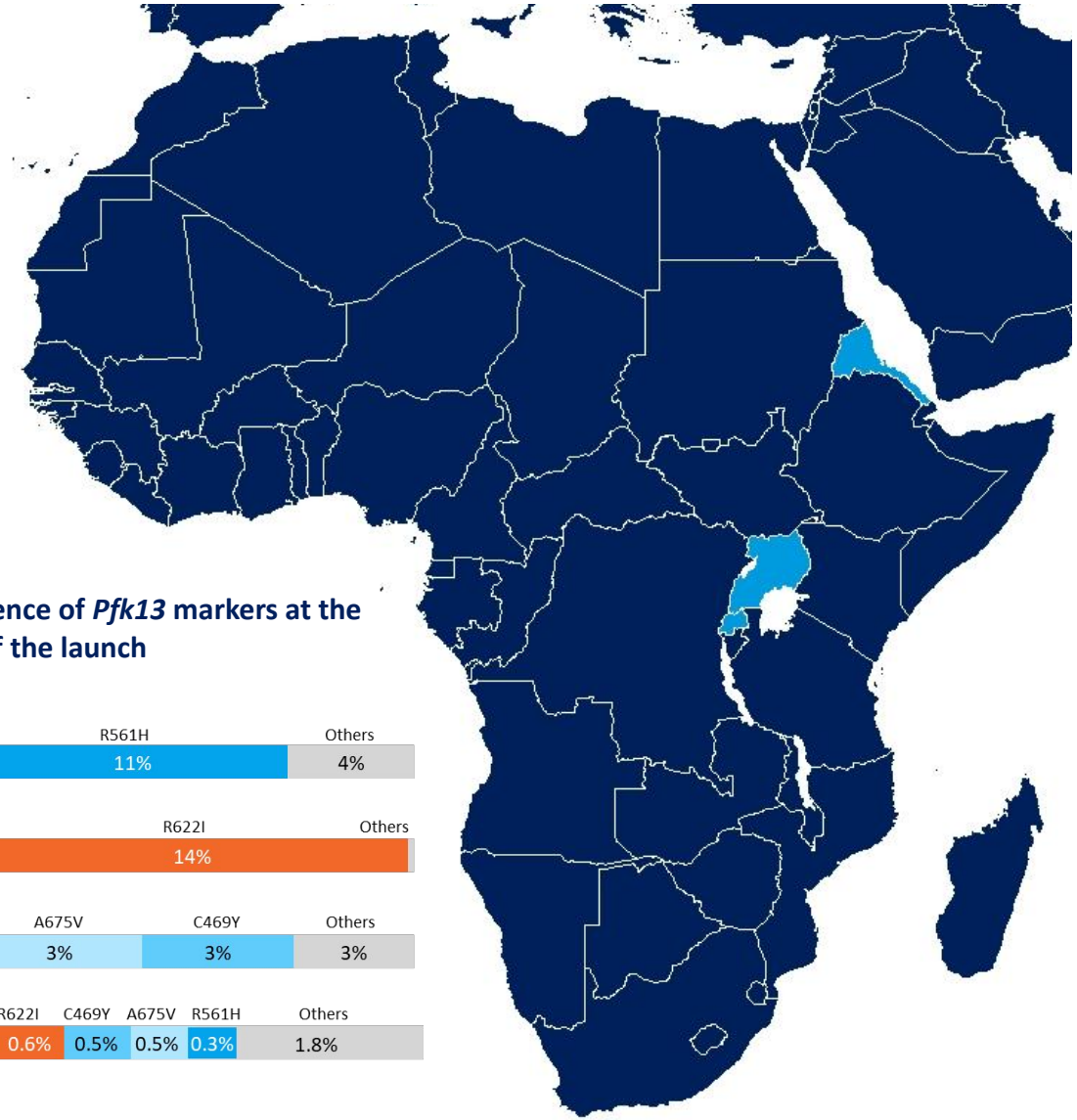
Background for the development of the Strategy of antimalarial drug resistance in Africa

- At the time of the launch of the Strategy, artemisinin partial resistance had been confirmed in three countries: Eritrea, Rwanda and Uganda.
- Since the launch of the Strategy, artemisinin partial resistance have also been confirmed in Tanzania in an area close to Rwanda
- High dependence of one ACT, artemether-lumefantrine
- Concerning gaps in the data available on efficacy and resistance



Prevalence of *Pfk13* markers at the time of the launch

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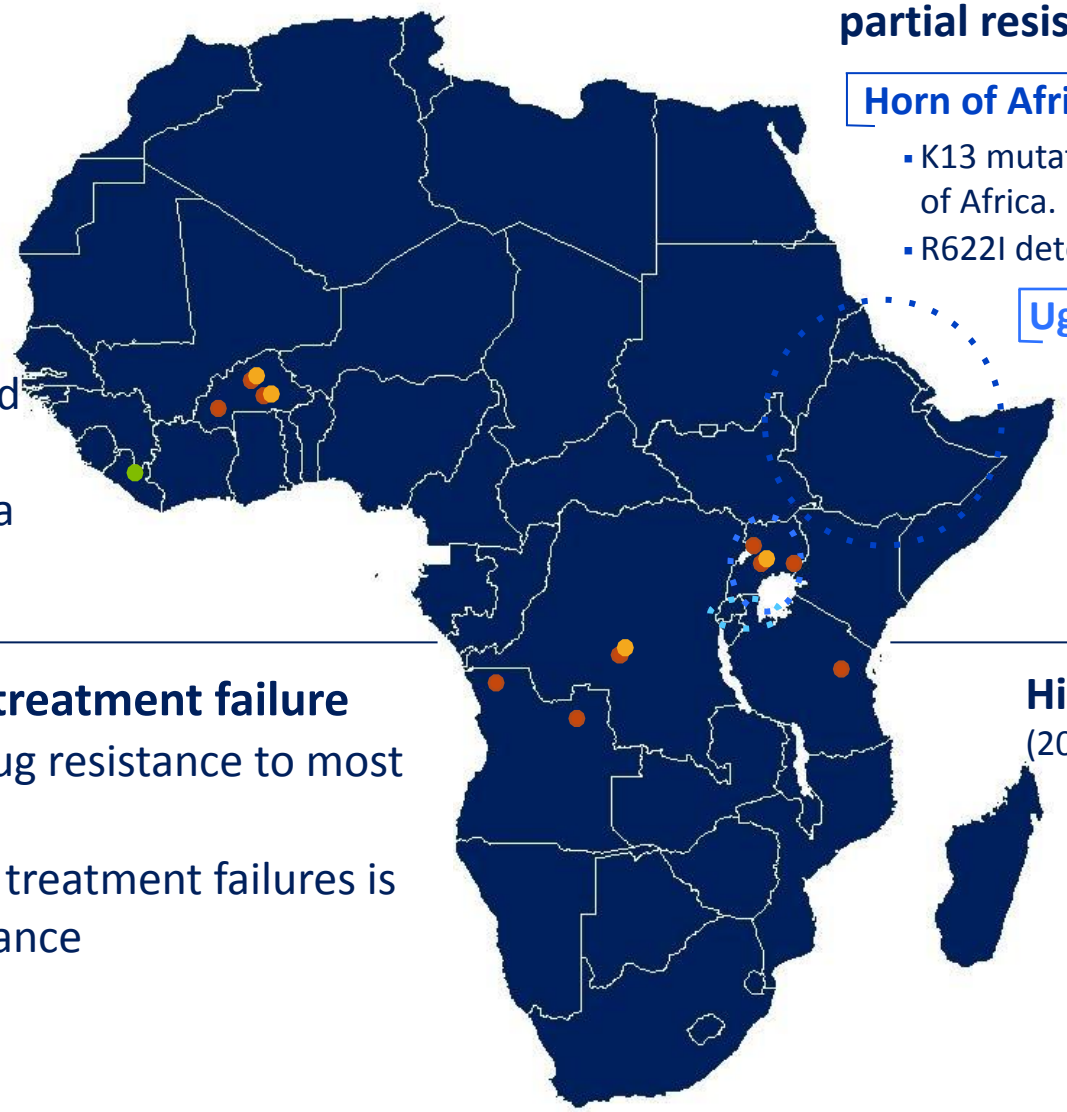
Antimalarial drug resistance in Africa

Artemisinin partial resistance in Africa

- Different mutations linked to artemisinin partial resistance has emerged and are spreading
- Delayed clearance associated with these mutations reported in 4 countries: Eritrea, Rwanda, Uganda and Tanzania



Three areas with distinct patterns of artemisinin partial resistance

Horn of Africa

- K13 mutation R622I detected in several countries in the Horn of Africa. Evidence of delayed parasite clearance in Eritrea
- R622I detected in parasites with *Pfhrp2/3* deletions

Uganda

- Delayed clearance identified. Different validated markers of artemisinin partial resistance detected

Rwanda & Tanzania

- Studies found delayed clearance and high prevalence of K13 mutation R561H

Scattered reports of high ACT treatment failure

- No confirmed ACT partner drug resistance to most used drugs
- Concerns that reports of high treatment failures is caused by partner drug resistance

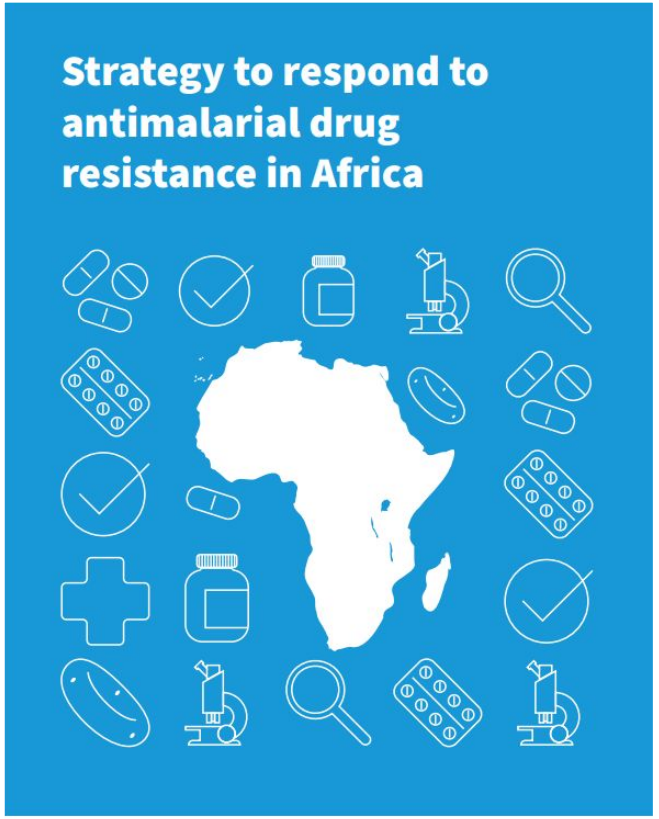
High failure rates in efficacy studies

(2015 -2023)

- Artemether-lumefantrine
- Artesunate-amodiaquine
- Dihydroartemisinin-piperaquine

Development of the Strategy for the Response to Antimalarial drug resistance in Africa

Launched in November 2022



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Development process

5 Working groups — **Working groups with 86 leading malaria experts**

74 Additional individual contribution — **Additional input from diversified panel of global and local stakeholders**

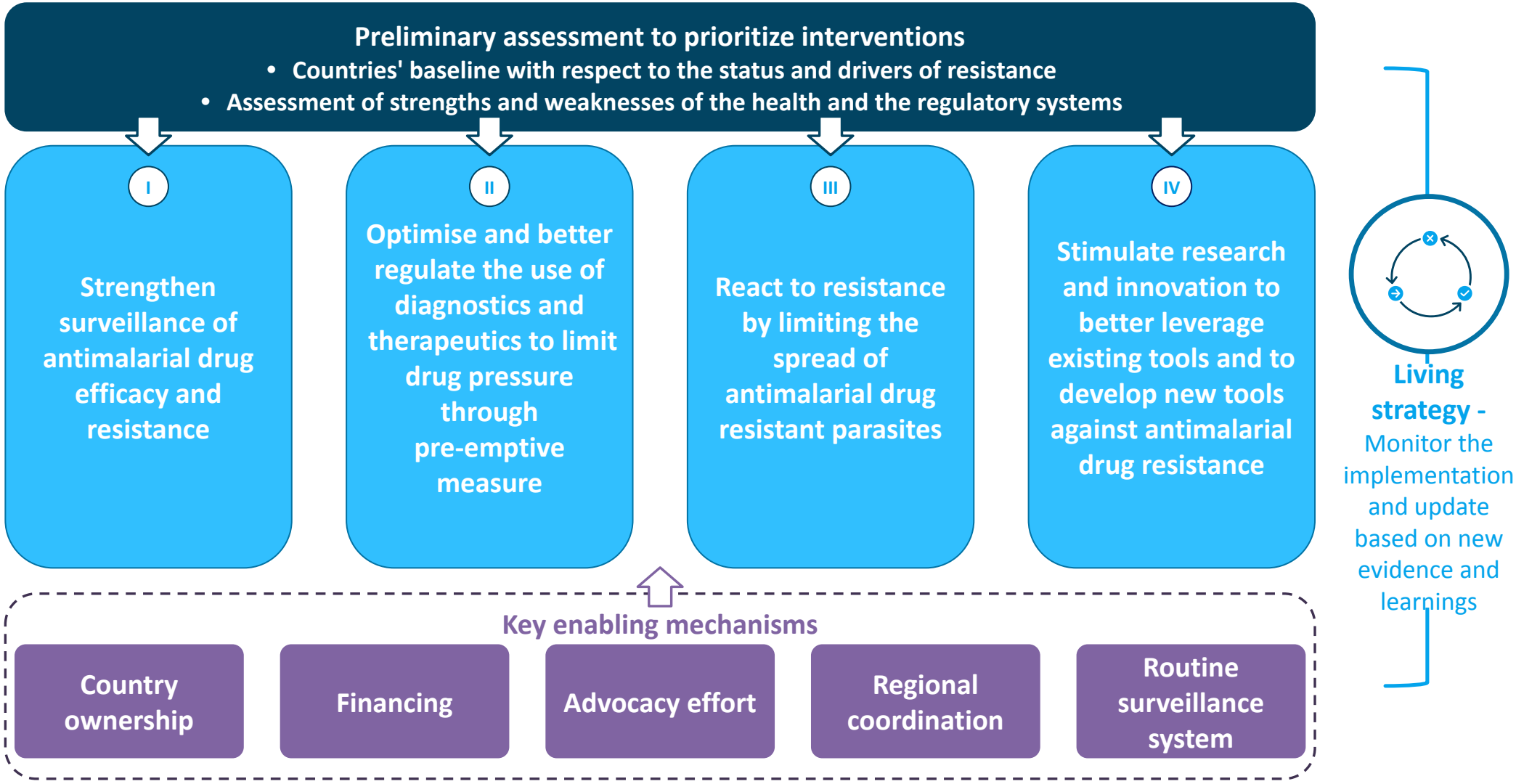
100+ Scientific papers reviewed — **Broad literature review to collect existing evidence**

2 Consultations — **Expert and public consultation**

- Strategy developed based on current understanding of drivers of resistance and the intervention needed to address these drivers.
- Strategy relies on better use of existing tools & development of new tools & strategies, with actions at global, regional and local level

Strategy to respond to antimalarial drug resistance in Africa

20 interventions across 4 pillars aiming to mitigate risks and respond to resistance



Strategy implementation | Selected WHO activities

- Collection and sharing of data in the **Malaria Threat Maps**

Malaria threat maps
https://www.who.int/teams/global-malaria-programme/surveillance/malaria-threats-map

Finished and published data

Planned and ongoing studies

- Planning to expand the current **external quality assurance (EQA) to include marker of antimalarial drug resistance** (current scheme offer an independent mean for laboratories to verify the quality of their nucleic acid amplification (NAA)-based malaria diagnostic methods)

- **WHO convened two meetings** in Kampala, Uganda in November:
  - **7 & 8 November:** A regional stakeholder meeting to align on intervention priorities to support countries responding to resistance
  - **9 & 10 November:** Meeting on surveillance of drug efficacy and resistance for countries in Eastern Africa and the Horn of Africa

Thank you

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