APMEN TechTalks

Hi everyone and thanks for making it to our APMEN TechTalks webinar today.

We will start in the next couple of minutes to allow more people to join in.

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APMEN TechTalks

3 July 2020

ASIA PACIFIC LEADERS MALARIA ALLIANCE

Optimizing radical cure for vivax malaria: Informing policy and practice

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APMEN TechTalks

PRESENTERS

Radical cure for *P. vivax* elimination

Prof. Ric Price
Co-Chair, APMEN Vivax Working Group
Menzies School of Health Research, Australia

Challenges and experiences from Sri Lanka

Prof. Kamini Mendis
Professor Emeritus, University of Colombo
Independent consultant malariologist

Summary of APMEN VxWG's roundtable discussions

Dr. Kamala Thriemer
Coordinator, APMEN Vivax Working Group
Menzies School of Health Research, Australia

PANEL MEMBERS

Dr. Lek Dysoley
Deputy Director
National Center for Parasitology, Entomology and Malaria Control
Ministry of Health, Cambodia

Dr. Abdul Majeed
Advisor Malaria (Policy & Strategy)
Directorate of Malaria Control
Ministry of National Health Services, Regulation and Coordination, Pakistan

Dr. Rose Nani Binti Mudin
Head of Vector Borne Disease Sector
Ministry of Health, Malaysia

Moderated by Kamala Thriemer and Caroline Lynch

The webinar will be recorded and shared on APMEN social media platforms

Please send your questions to
apmenevents@apmen.org

Mechanics

- Audio/video of attendees will be disabled, but we encourage comments in the Chat box

- Format
  - Three 10-minute presentations

  - Panel discussion and Q&A (up to 50 mins)
    - You may type in your questions in the Q&A box
    - Name the speaker/s whom you wish to ask the question to
    - You can “upvote” a question by clicking the thumbs up

  - Additional poll questions

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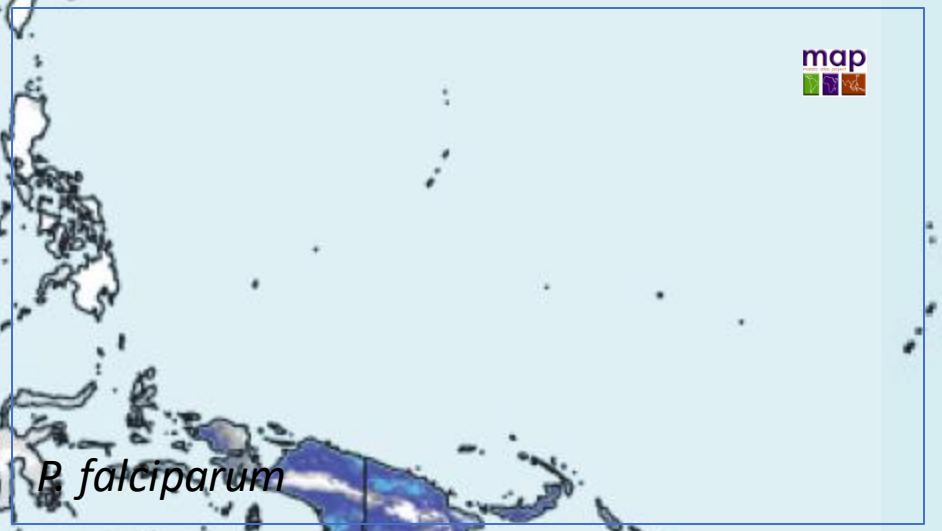
Radical Cure for *P. vivax* Elimination

Prof. Ric Price

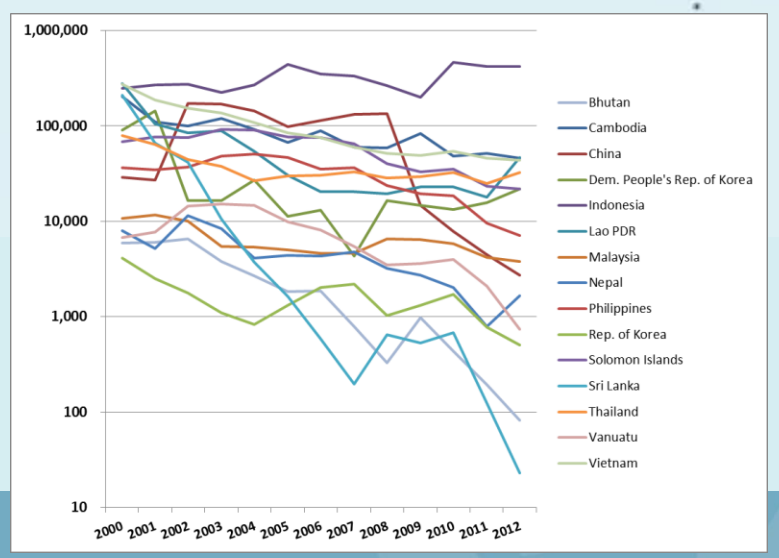
Menzies School of Health Research, Australia

Malaria in the Asia Pacific region



P. falciparum

P. vivax



Asia Pacific Malaria Elimination Network

2030 Target: 90% reduction; 35 countries eliminated; Asia Pacific - Free

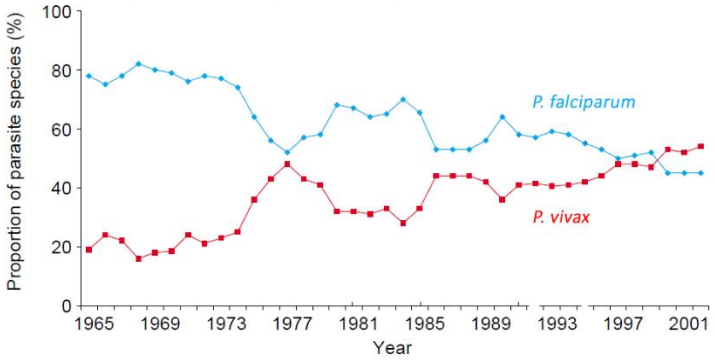
To generate evidence and share knowledge and best practices for countries in the Asia Pacific region to accelerate and maintain progress towards national and regional malaria elimination targets

21 Country Partners

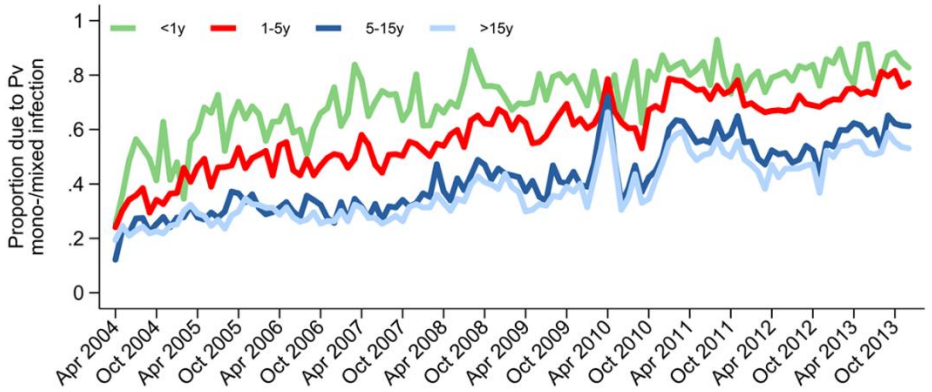
50 Partner Institutes

Rising proportion of malaria due to *P. vivax*

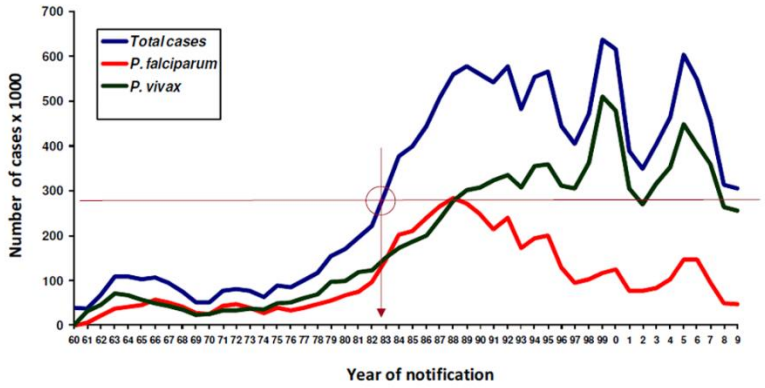
Thailand



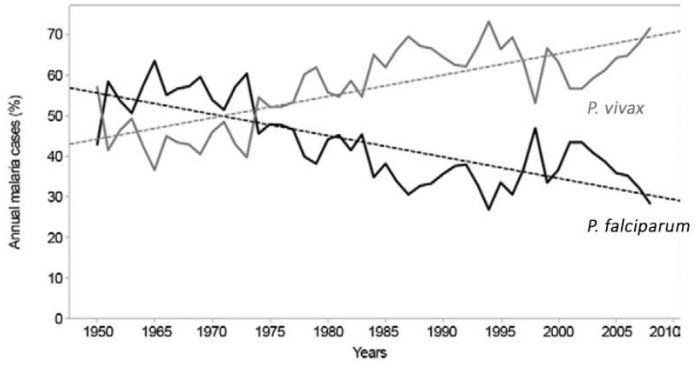
Papua, Indonesia



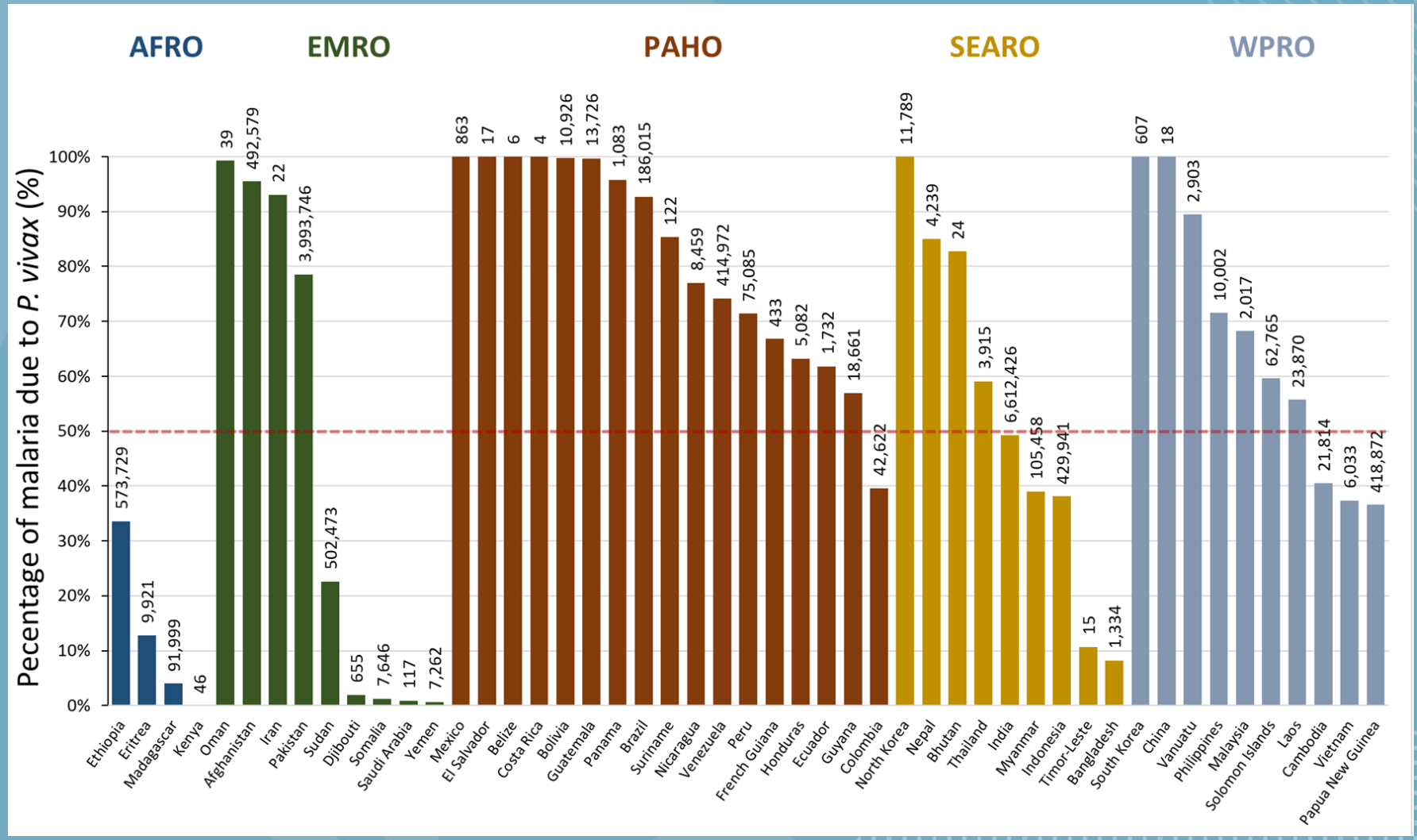
Brazil



Colombia



P. vivax becoming the dominant species of malaria in co-endemic countries



Price et al Trends in Parasitology 2020

Radical cure of *P. vivax*

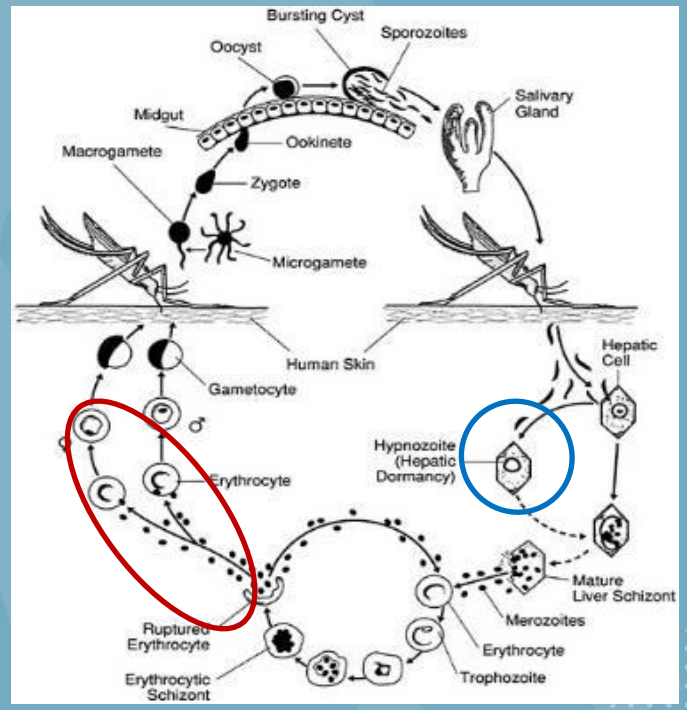
Schizontocidal Treatment

Chloroquine

DHA-piperaquine

Artemether-Lumefantrine

+



Hypnozonticidal Treatment

Primaquine

Tafenoquine

Primaquine dosing regimens

Pq efficacy is related to total dose administered

Primaquine	Total	Daily	Dose	
	mg/kg	mg/kg	mg	
Low Dose 14d	3.5	0.25	15 mg/d	Most countries
Low Dose 7d	3.5	0.5	30 mg/d	Brazil, China…
High Dose 14d	7.0	0.5	30 mg/d	?Chesson
Weekly	6.0	0.75	45mg	G6PD deficient

World Health Organization

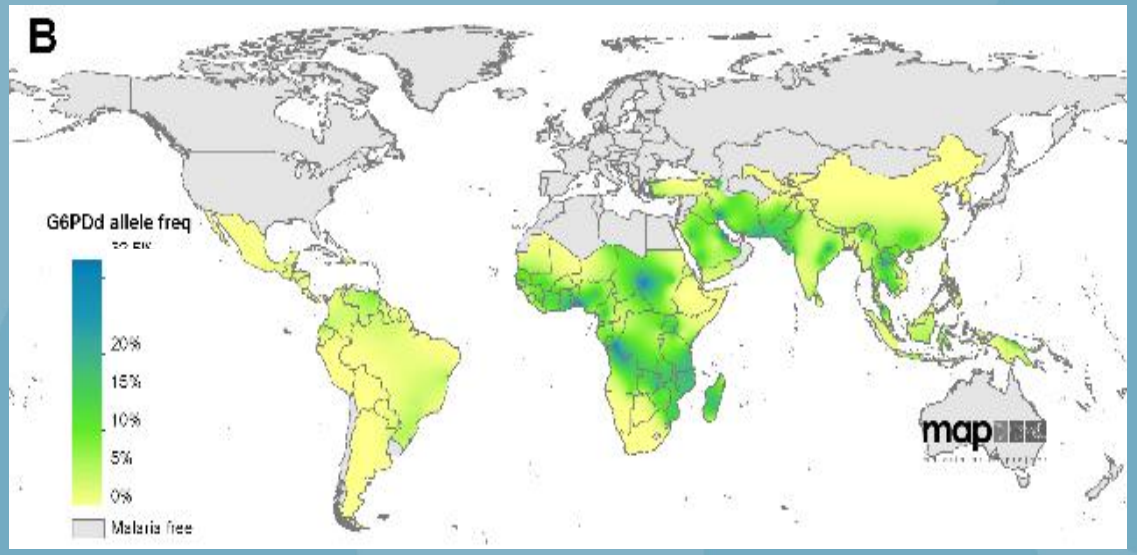
2015 Guidelines

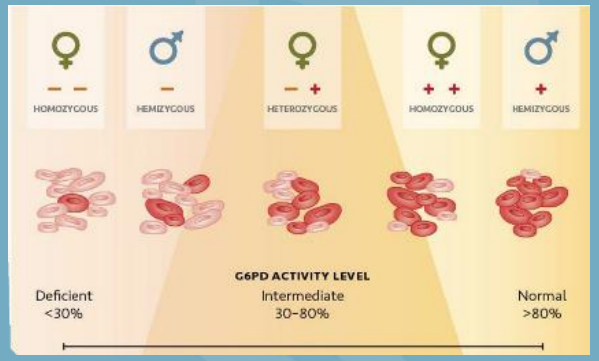
Good Practice: With G6PD deficiency testing

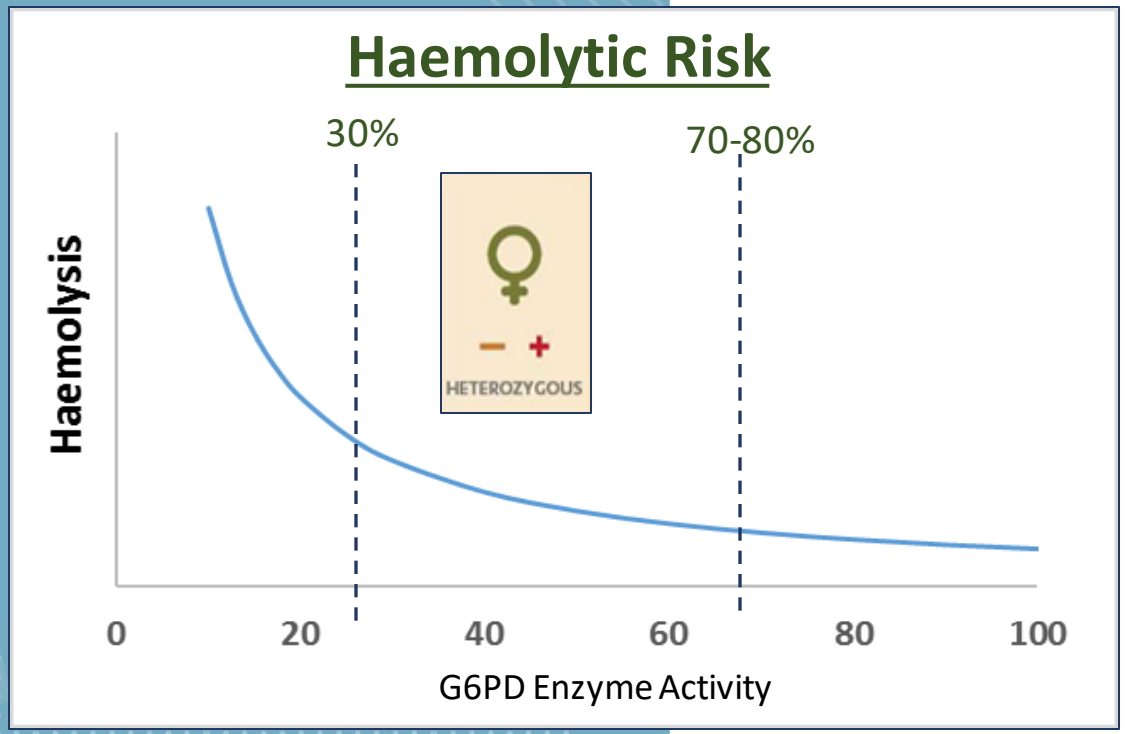
When G6PD status is unknown and G6PD testing is not available, a decision to prescribe primaquine must be based on an assessment of the risks and benefits of adding primaquine

Glucose 6 Phosphate Dehydrogenase

G6PDd distribution (1-25%)





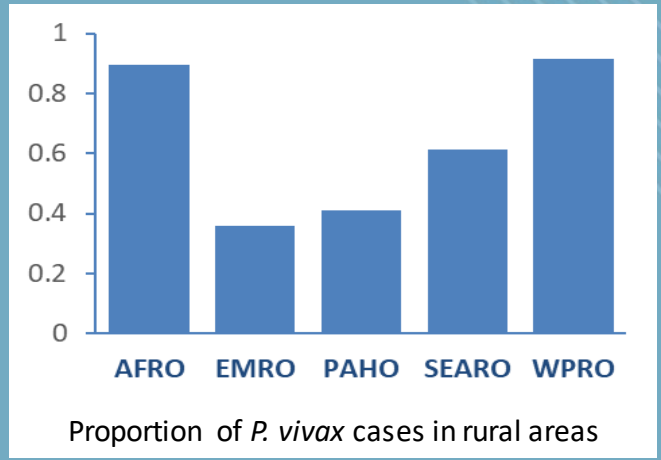


Challenges in delivering radical cure

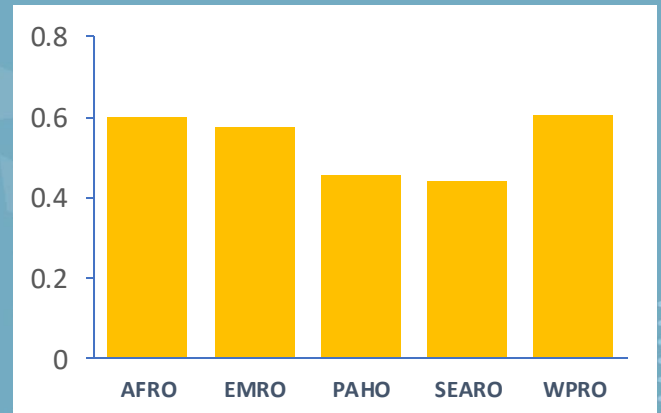
Greatest burden of P. vivax is in children and rural areas…

- Remote access and delivery
- Variable risk of relapse
- Poor adherence / effectiveness
- Variable G6PD deficiency
- Feasibility and cost of G6PD testing
- Supply chain
- Sustained financing
- …

➔ Heterogeneity of risks and benefits

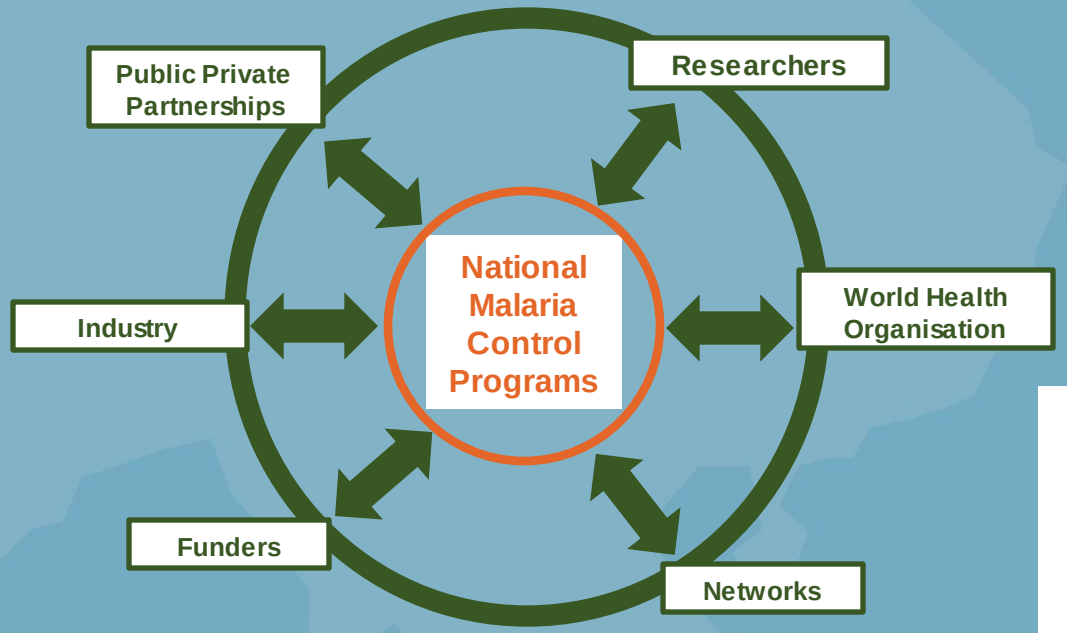


Proportion of *P. vivax* cases in rural areas

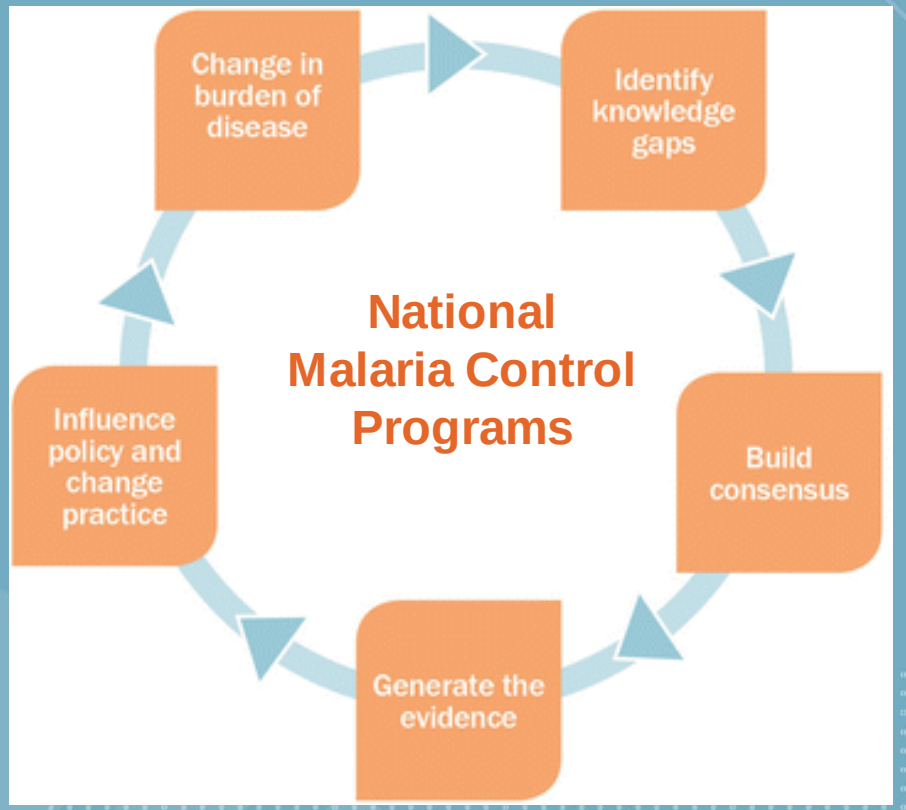


Proportion of *P. vivax* cases in **children**

APMEN Vivax Working Group



- Diagnosis
- Case Management
- Surveillance



The long and the short…

Adherence Issues

Tafenoquine
Single Dose

Primaquine…

High Dose	High Dose	Low Dose	Low Dose	Weekly
60mg x 7d	30mg x 14d	30mg x 7d	15mg x 14d	45mg x8

Need for G6PD Testing

New Tools and Strategies

Parasite Diagnostics

Better Pv RDTs
Ultrasensitive RDTs
RST
Autoscopes

FIND
Because diagnosis matters

G6PD Diagnostics

Qualitative Tests
Qualitative Tests

RDTs & biosensors

PATH

Treatment Regimens

Short Course Primaquine
Tafenoquine

MMV
Medicines for Malaria Venture

gsk
GlaxoSmithKline

Conclusions

- We can eliminate *P. vivax*, but if we are to meet the 2030 targets we will require novel tools and strategies

- There is no simple universal solution for safe and effective radical cure

- Marked heterogeneity of risks and benefits:

  ➔ integrated package of interventions tailored to the local context and socio political environment

Implementing radical cure for *P. vivax*

Successful country experiences & approaches

Prof. Kamini Mendis

University of Colombo, Sri Lanka

UNIVERSITY OF COLOMBO

Current recommendations to treat *P. vivax* and prevent relapses

Together with, or after schizonticidal treatment, **PQ for 14 days**, having excluded G6PD deficiency

Challenges:

- **Safety** – exclude G6PD deficiency
- **Adherence** – owing to the long duration of treatment

But… several countries have successfully implemented radical cure and even eliminated *P. vivax* – Sri Lanka, Timor-Leste, Bhutan

Whilst other countries are having difficulty in achieving coverage with G6PD testing and adherence to PQ treatment

Adherence to a 14 day regimen

- **Counseling** - there is evidence that when care is taken to explain the importance of the 14 day course of treatment and its associated risks, adherence can be as high as with DOTs.
- **Supervision**
- **Directly Observed Treatment** – in special situations.

Testing for G6PD status in clinical practice - issues

Point of care testing for G6PD

- **RDTs** - Several available, but none prequalified by WHO.
- **Cost** - not a major consideration, RDTs are affordable
- **Access** - Deployment at the most peripheral levels of the health system could be challenging e.g., performance and interpretation by village health workers

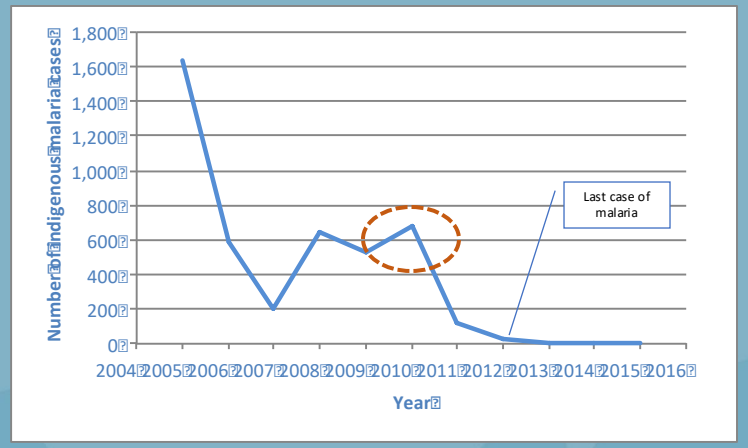
Is G6PD testing mandatory prior to anti-relapse PQ treatment ?

WHO recommendations:
When a patients G6PD status is unknown and when G6PD testing in not available, a decision to prescribe PQ must be based on an assessment of the risks and benefits of adding PQ

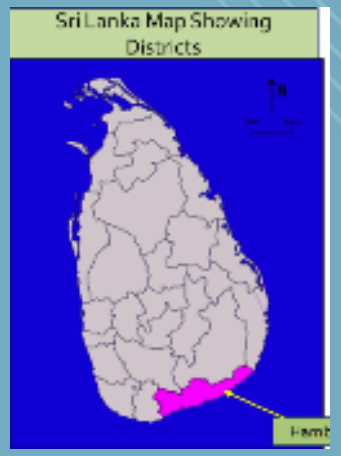
Country approaches to safe and effective PQ treatment

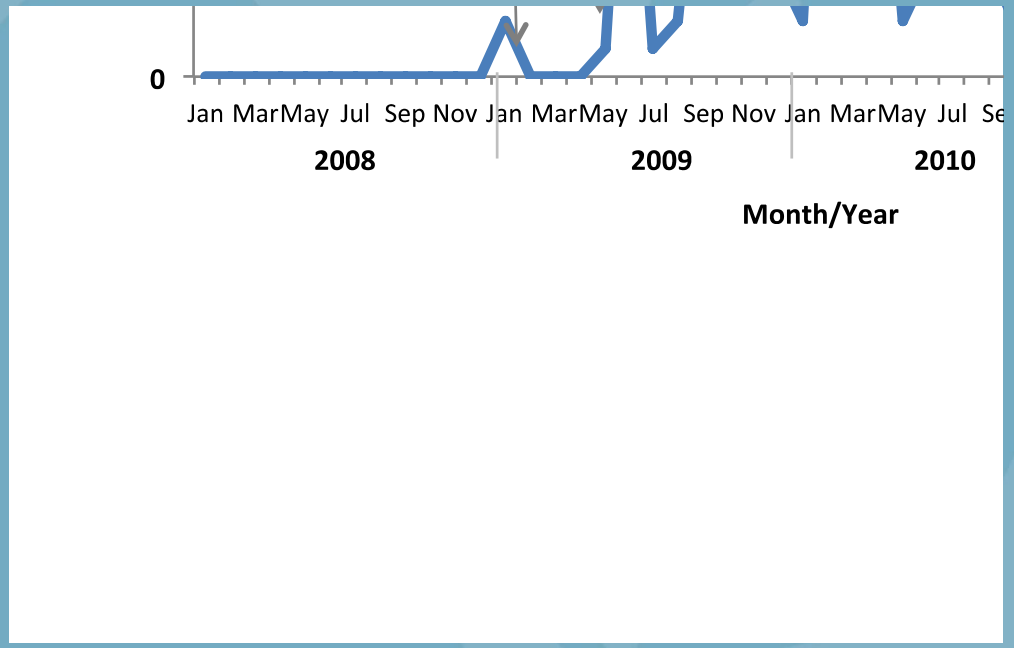
1. Assess the prevalence of G6PD deficiency in the country/area – the G6PD variant and extent.
2. Minimise the individual risk of haemolysis with 14 day treatment with PQ
   - Obtain past or family HISTORY of haemolysis in response to medication
   - COUNSELING the patient on:
     - ✓ The risk of haemolysis
     - ✓ How to recognize early signs of haemolysis
     - ✓ Stopping medication and seeking medical care immediately when there is evidence of haemolysis
3. If in a country/area/individual the risk is high or unknown, use **8-WEEK course of 0.75 mgs/kg per week of PQ** e.g. in foreign nationals in whom the G6PD status cannot be estimated.

A *P. vivax* outbreak during malaria elimination in Sri Lanka



maquine under observation





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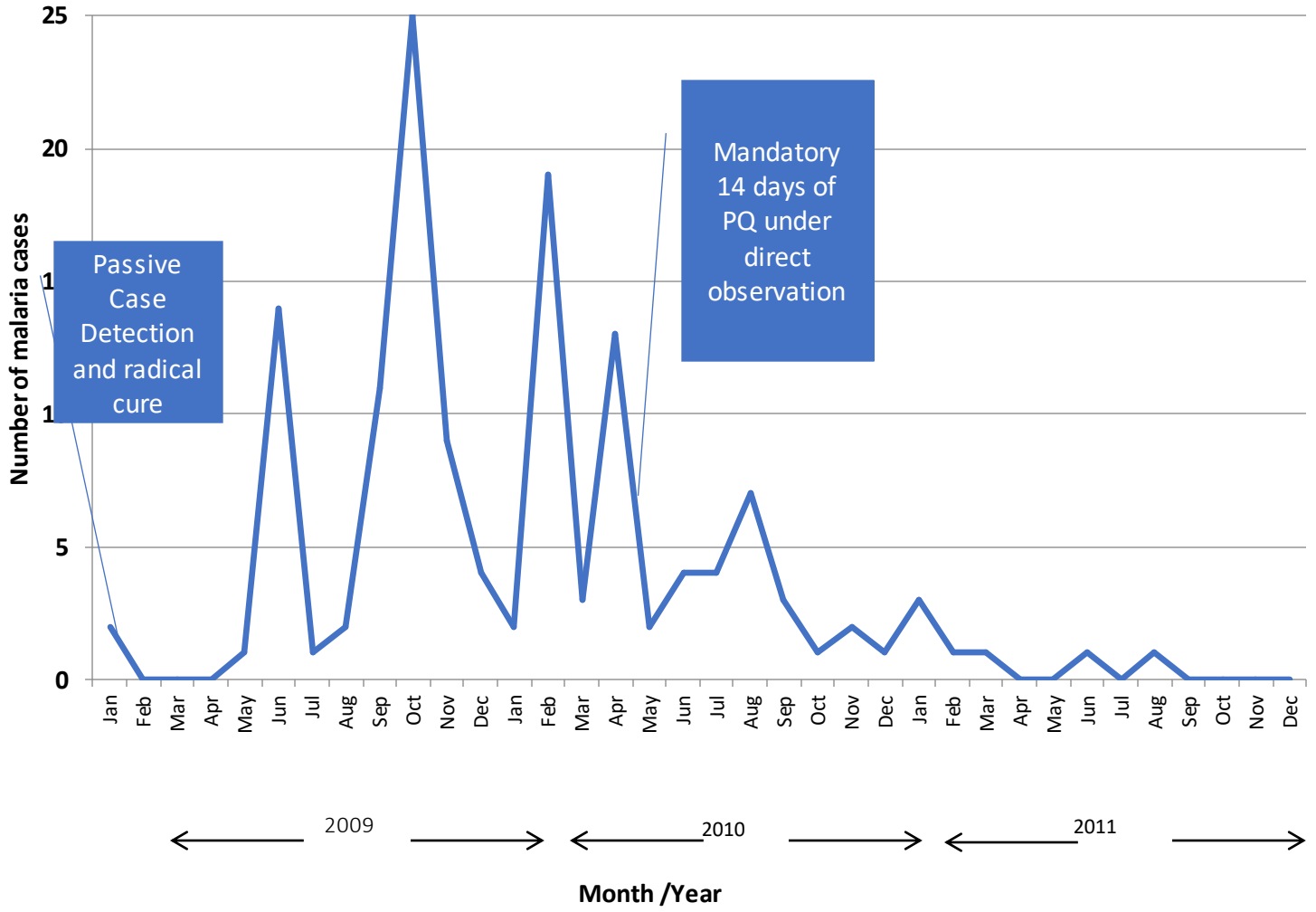
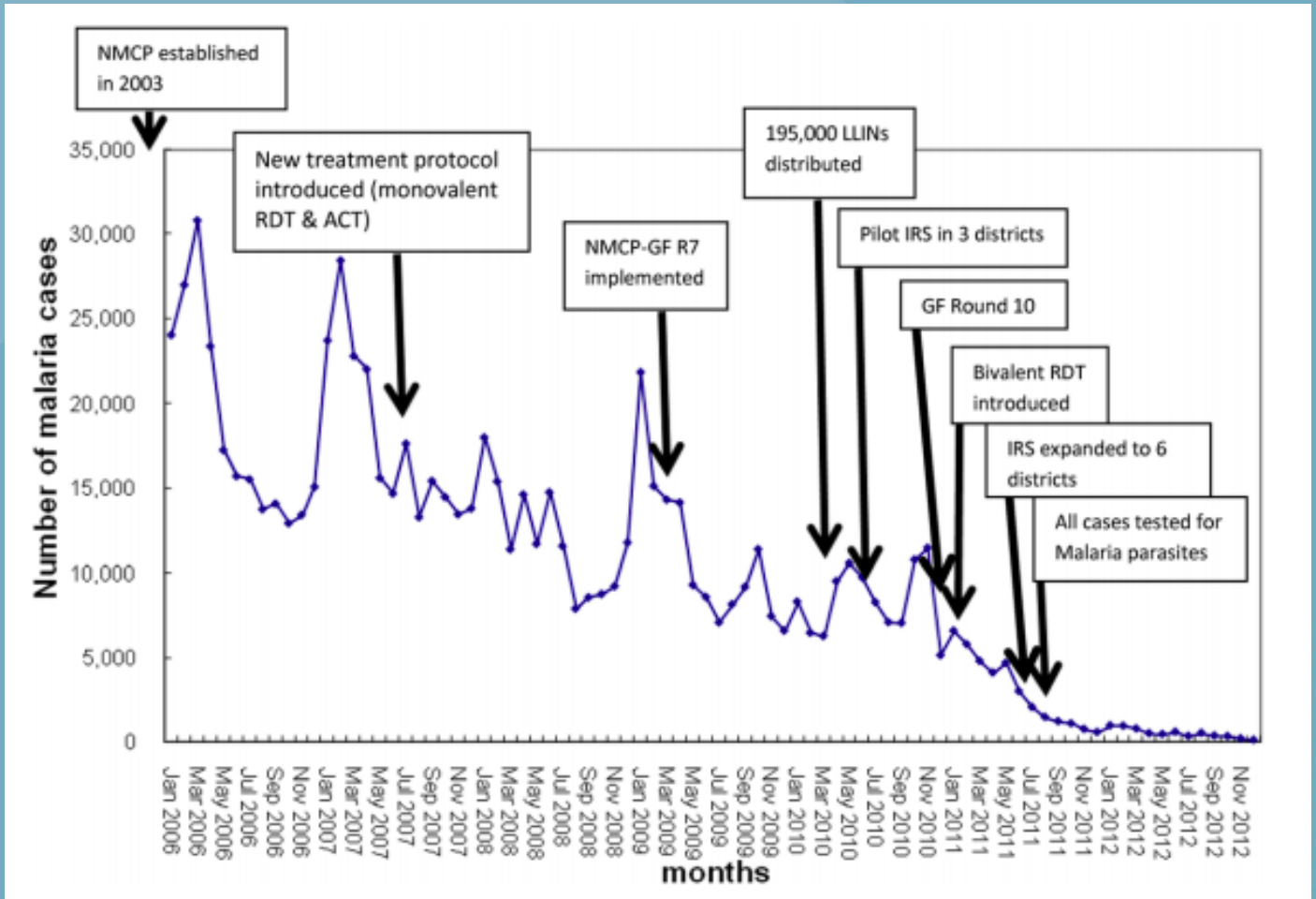
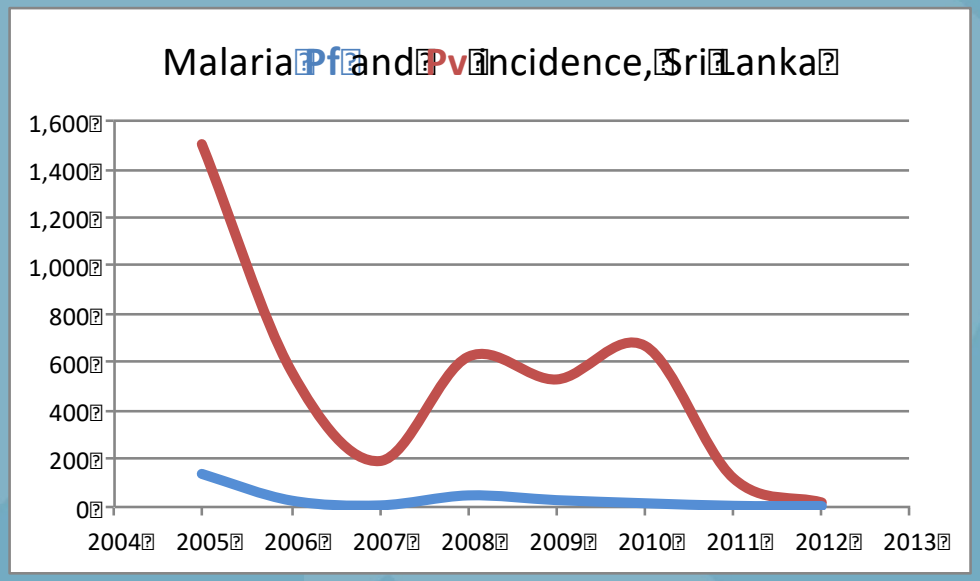


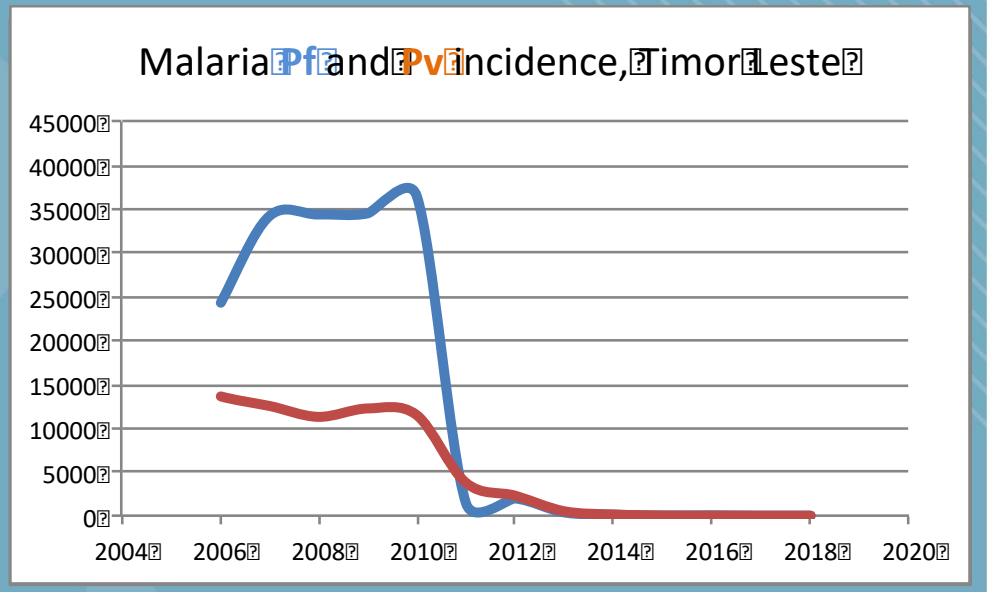
Malaria elimination from Timor-Leste

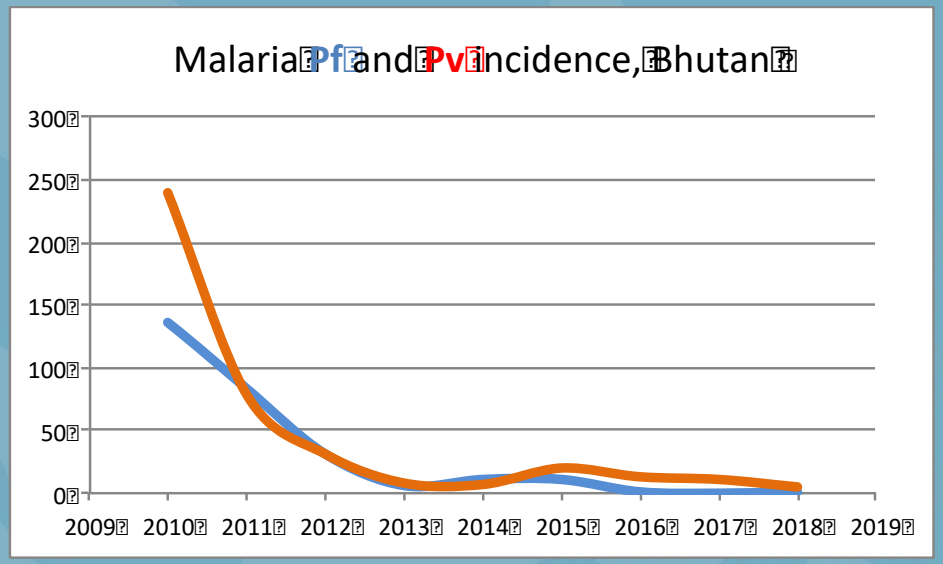


Yapabandara et al. Malaria Journal (2015) 14:109

P. vivax elimination is possible with current tools







Country practices on PQ treatment during prevention of re-establishment phase (POR) of malaria

In the POR phase:

- Few, mostly imported cases, therefore easier to deal with
- Some being foreign nationals, no idea of the G6PD status therefore, need for abundance of caution
- Greater need for G6PD testing even with imperfect point-of-care tests
- The need to prevent relapses is as great as during control or elimination
- All countries in the POR phase are now implementing 14 days of PQ after assessing the risk of haemolysis to the extent possible, while exercising caution.

NO RECENT REPORTS OF LIFE-THREATENING HAEMOLYTIC EVENTS FOLLOWING PQ TREATMENT IN COUNTRIES USING THIS APPROACH AND HAVE RECENTLY ELIMINATED MALARIA OR ARE IN THE POR PHASE

Concluding remarks

NO RECENT REPORTS OF LIFE-THREATENING HAEMOLYTIC EVENTS FOLLOWING PQ IN COUNTRIES USING THIS APPROACH AND THAT HAVE RECENTLY ELIMINATED MALARIA OR ARE IN THE POR PHASE

- Risk of life-threatening haemolysis with PQ in a G6PD deficient individual is real
- Every safeguard must be taken to prevent this
- Vital to assess and mitigate this if we are to eliminate vivax malaria

Summary of APMEN VxWG's Roundtable Discussions

Dr. Kamala Thriemer

Menzies School of Health Research, Australia

How can we bring new tools into policy and practice?

What are the remaining evidence gaps?

What is the policy pathway for the different options?

How can we develop roadmaps towards elimination?

How can we bring new tools into policy and practice?

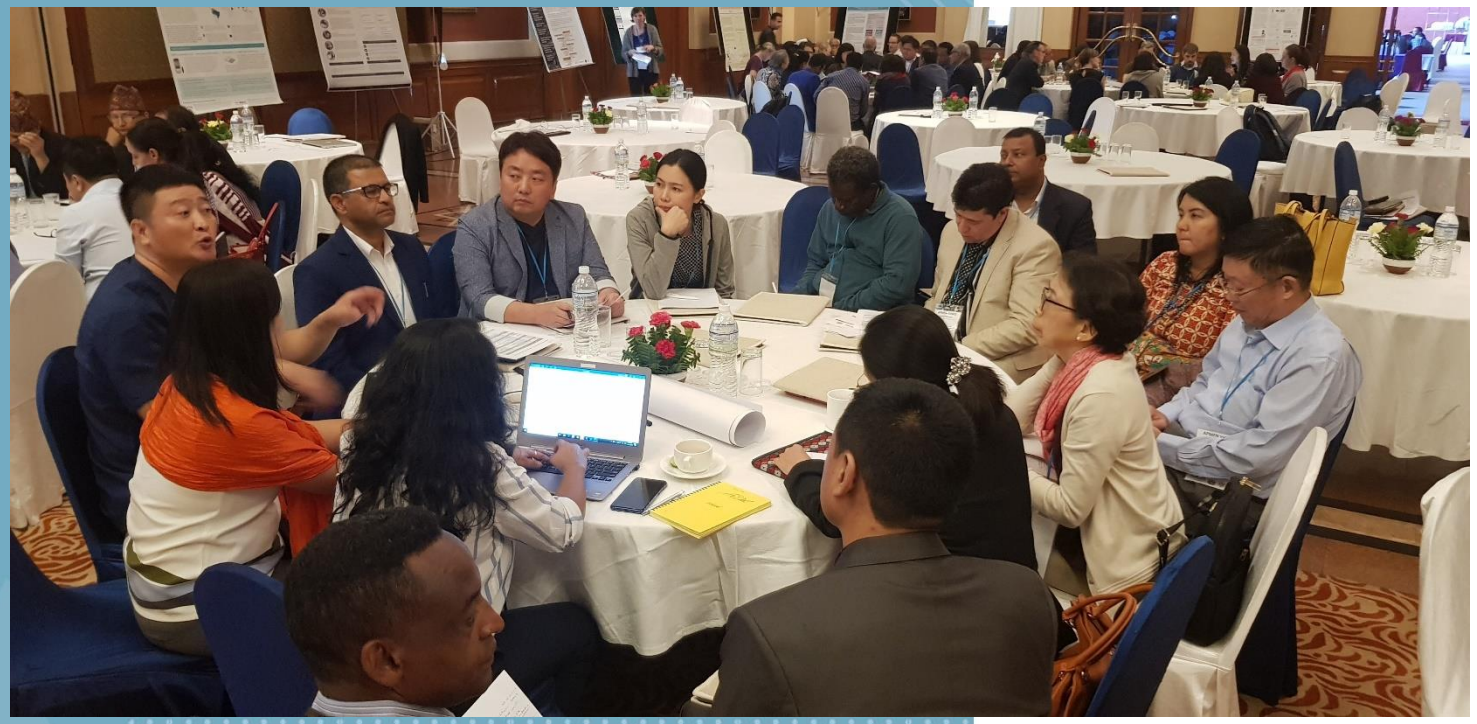
What are the remaining evidence gaps?

What is the policy pathway for the different options?

How can we develop roadmaps towards elimination?

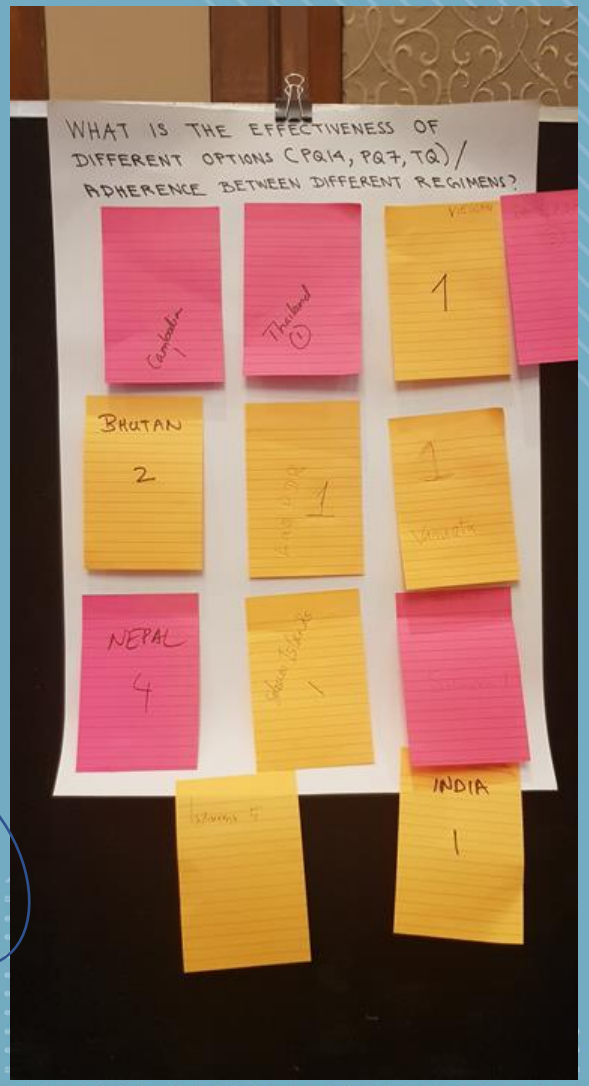
What are the remaining evidence gaps?

- Round table discussion during main meeting
- Separate tables for country partners & research partners
- Discussion about remaining evidence gaps
- 9 topics distilled from these discussion



What are the remaining evidence gaps?

- Robustness of new diagnostics
- How to improve adherence
- Effectiveness of current practice
- Cost-effectiveness of new tools
- Feasibility of new options (e.g. QA, supply chain etc.)
- G6Pd prevalence
- Vivax dynamics in country
- Effectiveness of new tools (≠efficacy)
- Safe delivery of new options



What are the remaining evidence gaps?

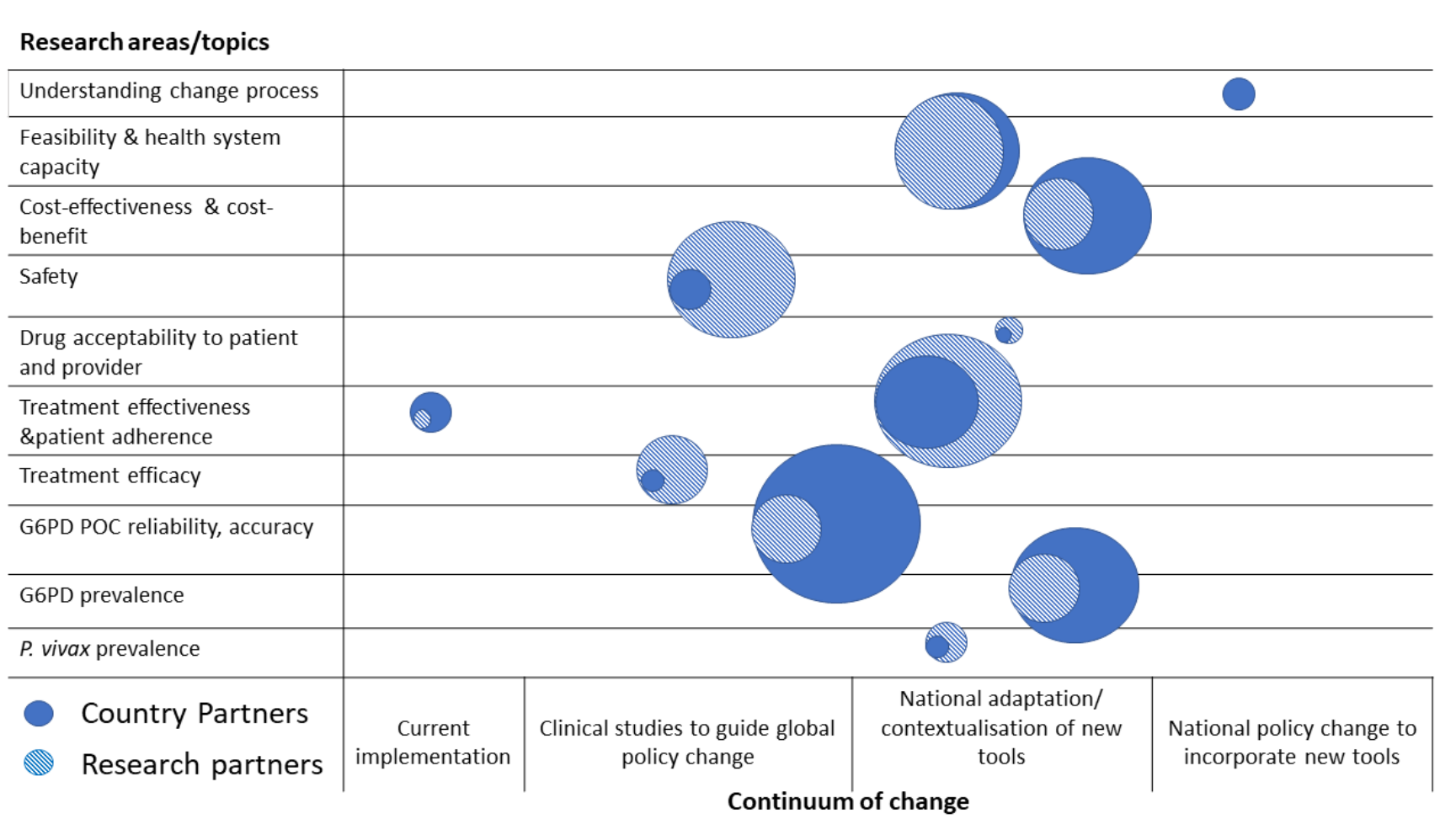
Question	Average Rank
What is the effectiveness of different options (PQ14, PQ7, TQ) and adherence between different regimens?	2.6
How well do new diagnostics work in the field (usability, robustness etc.)?	3.9
What is the best way to improve patients' adherence?	4.1
What is the cost effectiveness of different regimen options?	4.4
Feasibility of new interventions at different levels of health system (including supply chain capacity and quality assurance)?	4.4
What is the prevalence of G6PD deficiency in my country?	4.4
How can we ensure safe delivery of the different options?	4.9
How effective is the current practice?	5.3
What are the overall vivax dynamics in my country?	5.6

Addition interviews with three countries confirmed initial ranking

- Indonesia
- Cambodia
- Ethiopia

Ruwanpura, submitted

What are the remaining evidence gaps?



Ruwanpura, submitted

How can we bring new tools into policy and practice?

What are the remaining evidence gaps?

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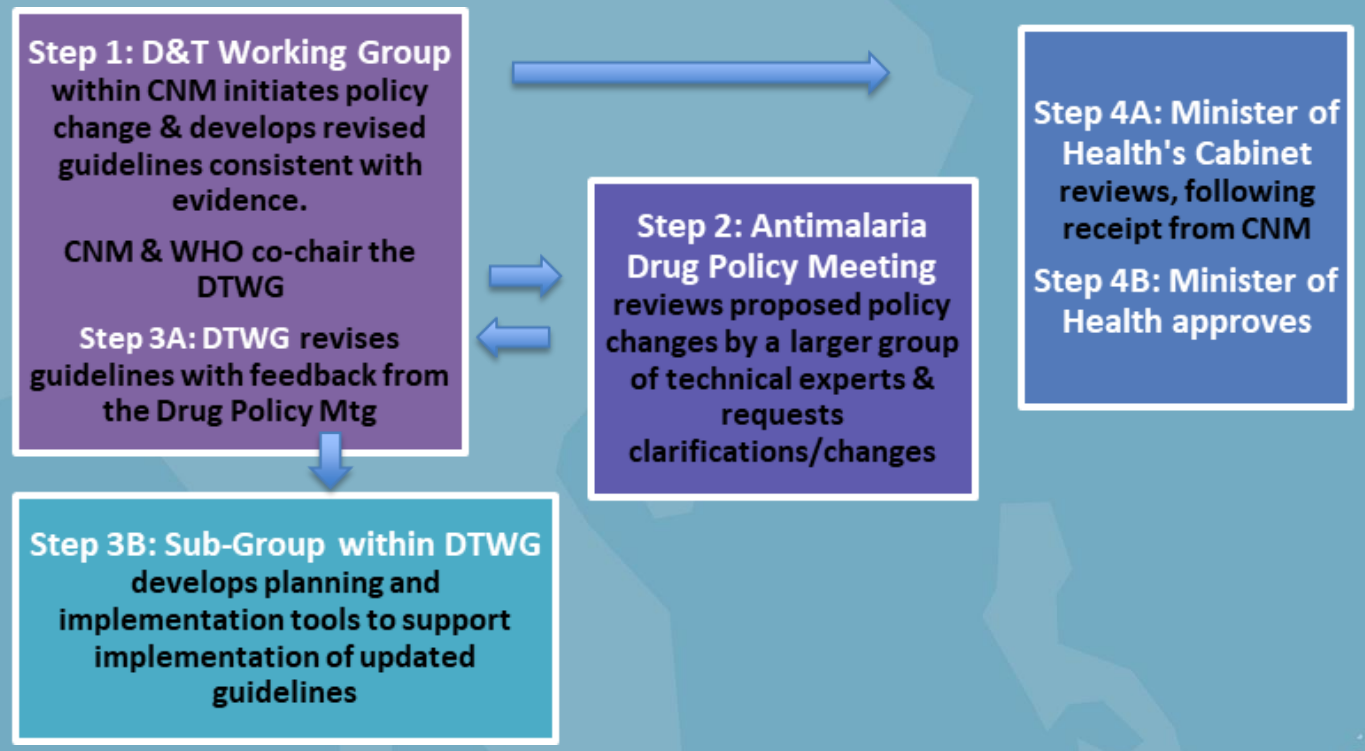
What is the policy pathway for the different options?

- Country partner workshop
- Additional Interviews with participants from 7 countries
- Additional Stakeholder interviews in those countries

What is the policy pathway for the different options?

Cambodia



Pakistan

Directorate of Malaria and other Vector Borne Diseases (DoMC) initiates, reviews and approves malaria guidelines.

What is the policy pathway for the different options?

- Large differences in the complexity of the pathways between countries
- NMCP plays critical role in initiating &influencing process
- Fluid process, not documented
- ToR for committees only available in few countries
- No consultation with Ministry of Finance
- Limited understanding of similar processes for other diseases

Interested to participate? Please get in touch!

How can we bring new tools into policy and practice?

What are the remaining evidence gaps?

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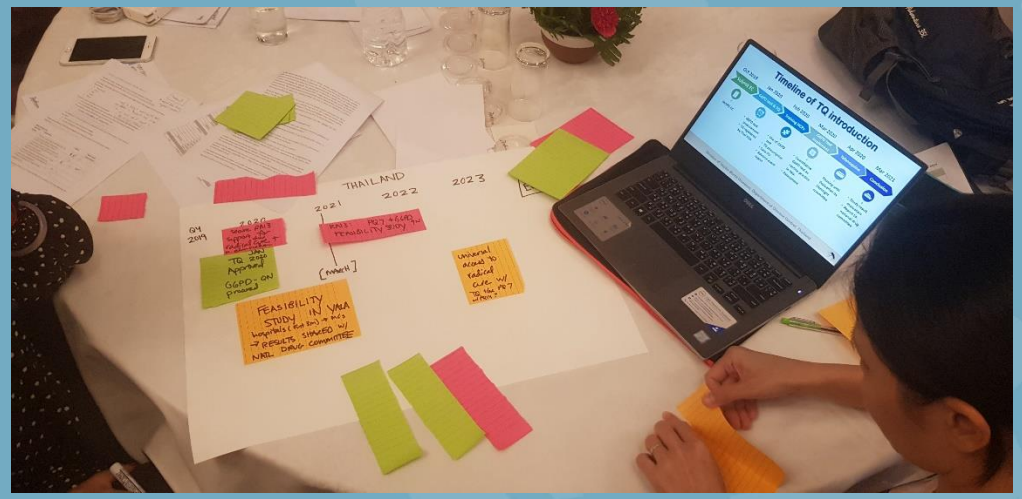

More in panel discussion

Acknowledgements

- NMCP Nepal - hosts of the 2019 VxWG annual meeting
- All facilitators, moderators & notetakers during meeting and workshop
- Varunika Ruwanpura & Josselyn Neukom for additional interviews
- All participants at the meeting & workshop and those who participated in the interviews

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Ministry of National Health Services, Regulation and Coordination, Pakistan

Dr. Rose Nani Binti Mudin
Head of Vector Borne Disease Sector
Ministry of Health, Malaysia

Moderated by Kamala Thriemer and Caroline Lynch

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