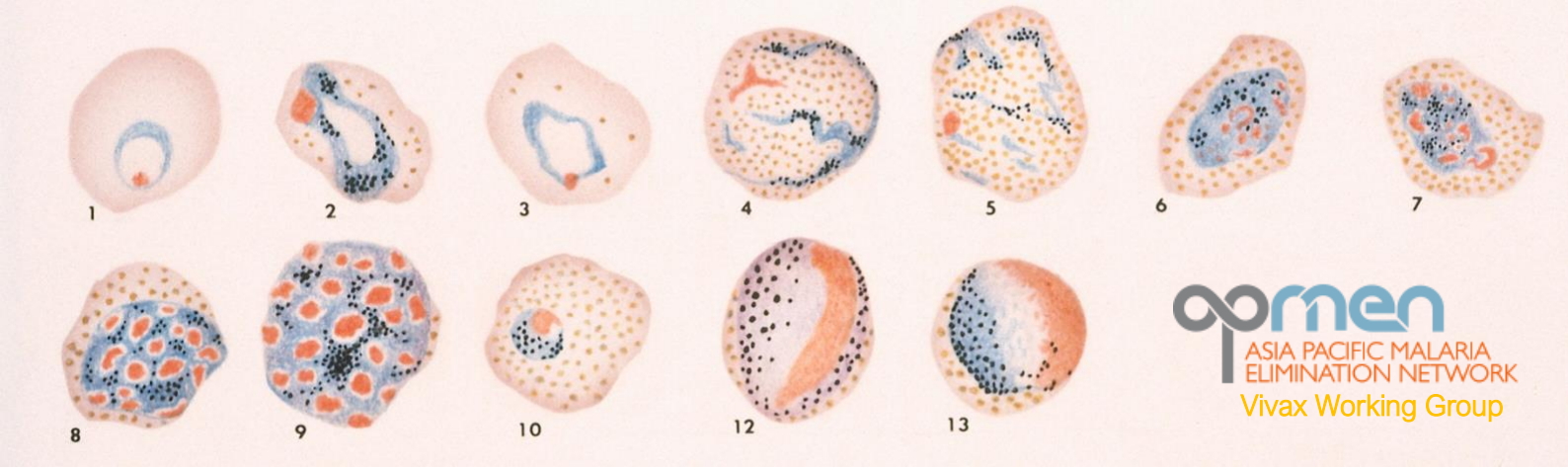

APMEN Vivax Working Group
Annual Meeting Report: August 9 – 11, 2021

Executive summary

The 2021 APMEN Vivax Working Group Annual Meeting was held online from 9-11th August 2021, with the theme **'From pipeline, to policy, to optimized implementation'**. The focus areas for the 3-day meeting were: optimizing radical cure – including an introduction to the development of an Options Assessment Toolkit with the National Malaria Programs; learning from history and early implementation; and "Show me the vivax" & access – exploring strategies to ensure access to optimized radical cure.

With 3.85 million estimated cases, the Asia Pacific Region has the world's largest vivax burden. The work of the APMEN Vivax Working Group is critical to this year's theme. To meet the 2030 elimination targets, novel tools and strategies alone will not be enough. Implementation and operational research, coupled with commitment to capacity building and context-tailored interventions will be essential. The Working Group is making a concerted effort to integrate gender equity and representation in all its work including through the annual meeting.

In all 154 participants took part from 18 countries[1]. This included 16 National Malaria Programs, 5 funding partners, 18 research partners and more than 13 implementing partners and civil society organizations who took part in discussions on strategies to increase access to vivax radical cure among remote, mobile, and hard-to-reach populations. Some groups also discussed access from a regional perspective.

> ***"THERE ARE ONLY NINE YEARS REMAINING TO ELIMINATE MALARIA IN THIS REGION AND IT IS IMPORTANT TO MOVE SWIFTLY TO MAKE SURE EVIDENCE IS USED."***
>
> **DR PRUDENCE HAMADE, MALARIA CONSORTIUM, APMEN VXWG, 2021**

The time to act is now. Time is becoming short for countries in the Asia Pacific region to achieve their malaria elimination targets of 2030. Yet, there are phenomenal opportunities, with more support and new tools coming online that could help countries to reach their targets.

New tools include new diagnostics such as higher sensitivity Rapid Diagnostic Tests and semi-quantitative G6PD tests. These tools have been approved by the Global Fund Expert Review Panel for Diagnostics (ERPD) meaning they can now be procured through Global Fund mechanisms.

The World Health Organization Global Malaria Programme (GMP) currently recommends either Artemisinin-based combination therapy (ACT) or chloroquine for *P. vivax* blood stage infection and a 14-day course of primaquine to prevent relapse[2]. WHO guidance further provides a 'good practice statement' that the G6PD status of patients should be used to guide administration of primaquine for preventing relapse[2]. The WHO GMP process for policy revision has been streamlined and improved to ensure that they anticipate products, develop recommendations, and optimize uptake in a timely, transparent, and

[1] Afghanistan, Bangladesh, Bhutan, Cambodia, Ethiopia, India, Indonesia, Lao PDR, Malaysia, Myanmar, Nepal, Pakistan, Philippines, Papua New Guinea, Solomon Islands, Sri Lanka, Thailand, and Vietnam.

[2] World Health Organization. WHO Guidelines for malaria, 13 July 2021. Geneva: World Health Organization; 2021.

predictable way to support National Program decision-making. *The timeline for revision of vivax treatment guidance is to be determined by the GMP.*

In 2019, most National Malaria Programs developed roadmaps to vivax elimination. A review of 2019 vivax roadmaps with national program partners found that *four countries are on track, while five countries have not made progress in line with their expectations having suffered delays related to COVID, the political situation or funding constraints.* Nevertheless, *most country programs were interested in, planning to, or already implementing testing or screening for G6PD activity.* Three countries in the region are currently implementing quantitative G6PD testing (Qn-G6PD). Two countries did not plan to incorporate Qn-G6PD testing, however, those same countries already implement national neo-natal G6PD screening programs. While most countries are not planning to change radical cure policy in the next two years, *one country is currently considering higher dose primaquine 7-day and three countries are considering a change to tafenoquine.*

"PRIMAQUINE IS NOT A BAR TO ELIMINATION…NOW IS NOT THE TIME TO WAIT FOR NEW TOOLS – IMPROVE CURRENT TOOLS WHILE NEW TOOLS ARE COMING ONLINE."

DR KAMINI MENDIS, INDEPENDENT CONSULTANT, APMEN VXWG, 2021

We can achieve higher coverage with current vivax radical cure tools - Currently, National Malaria Programs are focusing on the correct use of current WHO recommended radical cure for vivax and seeking to understand and improve patient adherence[3]. Many published studies show considerable variation on patient adherence to PQ-14, ranging from 44% up to 98%[4,5,6]. *Individual patient counselling and medical supervision[7] stand out for impact on patient adherence*. As the caseload declines, improving PQ adherence is important potentially through Directly Observed Treatment.

We need to be ready to incorporate new tools into health systems - new tools are coming online, with new higher sensitivity Rapid Diagnostic Tests for better detection of vivax malaria parasites and semi-quantitative G6PD tests having been approved by Global Fund Expert Review Panel for Diagnostics (ERPD). Studies on Primaquine 7-day higher-dose treatment are promising, and tafenoquine has been approved by regulators, and launched, in the United States (2018) and Australia (2019). It has also been registered in Brazil (2019), Thailand (2019) and Peru (2020). Registration[8] of tafenoquine in Myanmar, the Philippines and Vietnam is expected in 2022.

Several operational and implementation research studies are underway including feasibility of using Qn-G6PD at different levels of the health system. Several partners are investigating the reliability of semi-

[3] World Health Organization. Adherence to long-term therapies: evidence for action. World Health Organization; 2003.
[4] Cheoymang A, Ruenweerayut R, Muhamad P, Rungsihirunrat K, Na-Bangchang K. Patients' adherence and clinical effectiveness of a 14-day course of primaquine when given with a 3-day chloroquine in patients with Plasmodium vivax at the Thai–Myanmar border. Acta Tropica. 2015;152:151-156. doi:10.1016/j.actatropica.2015.08.008
[5] Rosa E, Shafira ID, Oktaria D, Arifianto A. Adherence to Plasmodium vivax malaria treatment in Hanura Public Health Center, Pesawaran District of Indonesia. Research Square. 2020. doi:10.21203/rs.2.21806/v1
[6] Saravu K, Tellapragada C, Kulavalli S, et al. A pilot randomized controlled trial to compare the effectiveness of two 14-day primaquine regimens for the radical cure of vivax malaria in South India. Malaria Journal. 2018;17:321. doi:10.1186/s12936-018-2472-5
[7] Fuangchan A, Dhippayom T, Kongkaew C. Intervention to promote patients' adherence to antimalarial medication: a systematic review. Am J Trop Med Hyg. 2014;90:11-19. doi:10.4269/ajtmh.12-0598
[8] To note, registration of a medicine does not mean that it can be used within the health system, either the public or private sector, until it is formally launched. For many countries, launch will only be possible after National Malaria Programs approve the use of the drug in their health system.

quantitative G6PD tests (e.g. Institute Pasteur Cambodia, AFRIMS – Cambodia, Menzies and PATH) and feasibility of G6PD testing at lower levels of the health system (e.g. iccdr,b, FIND and PATH). Multi-country studies to determine the feasibility of using new shorter treatments including primaquine higher dose 7-day and/or single-dose tafenoquine, with semi-quantitative G6PD tests at different levels of the health system are ongoing in Brazil and planned for Thailand, Ethiopia, India, Indonesia, Papua New Guinea, and Peru (PAVE). Ongoing or planned studies are being identified and mapped through vivaxmalaria.org and the Malaria Eradication Scientific Alliance (MESA).

One approach to accelerating optimal vivax radical cure is *to proactively identify modifications needed in the health system to accommodate any future policy changes, and to identify bottlenecks to efficient policy change and implementation that have been encountered in the past or that may be encountered.* To do this, the Partnership for Vivax Elimination (PAVE) have developed a framework that identifies risks and assumptions that could impede progress towards vivax elimination. *This framework allows National Programs and partners to systematically identify and rank actions, either operational research or implementation activities, required to prepare for policy change* and move quickly to implementation to achieve their 2030 targets.

Streamlined policy processes can help achieve elimination targets by speeding up the adoption of new tools and treatment options. Policy change can take up to three years in some Asia Pacific countries (Ruwanpura et al, 2021). By identifying and addressing the causes of lengthy policy change processes, future delays can potentially be mitigated when introducing new tools. Most countries rely on WHO recommendations to trigger their national policy change processes. *To assist NMPs in adopting WHO revised guidance once it is available, the APMEN VxWG, Menzies and PAVE will work with national programs to develop an Options Assessment Toolkit (OAT).*

Where G6PD testing is being used, vivax radical cure has been strengthened, but there are improvements to be made to increase test proficiency. *Ease-of-use of the semi-quantitative G6PD test is an issue,* especially in remote areas where health workers lack proper training and background. When deploying G6PD tests, NMPs need to target tools based on vivax incidence, the type and level of health facilities, the training level of health staff and quality of available testing equipment. *High quality training and supervision is important for effective use of semi-quantitative G6PD tests*, when developing training, consider targeted trainees; group organization; theoretical and practical training including step-by-step procedures, results interpretation, assessments including evaluation and competency testing, and continuous monitoring. *NMPs and partners can also make use of online tools such as* those available on the *P. vivax* information hub *and the G6PD Operational Research Community of Practice (GORCoP).*

Community is central – but getting current or new tools to where they are needed is a huge challenge. Partners use several strategies to *increase access to vivax radical cure* including community case management, community referral, border post screening and touchpoints for forest goers, surges in health worker capacity during seasonal increases in transmission, mobile clinics, partner engagement at community level, and neonatal G6PD screening.

Access relies on community engagement and involvement – however, many programs stop short of enabling volunteers to provide case management services. There is sometimes tension between what programs can legally request volunteers to do within a health system, and the ideal for increasing access at community levels. Where community volunteers *could* be asked to test and treat patients, there is often

reticence among National Programs to place testing and treatment tools in the hands of non-clinical personnel. As a result, most programs work with volunteers to *increase access by identifying and referring patients upwards in the health system and post-treatment for follow-up* to ensure adherence to treatment.

"THERE IS A NEED FOR CSOS AND PARTNERS TO PLACE MORE FOCUS ON THE 'SOFT SIDE' I.E. INTEGRATION OF SERVICES, RECOGNISING VOLUNTEER SYSTEMS AND ASSESSING IMPLEMENTATION IN ADDITION TO THE HARD SCIENCE SUCH AS TQ AND NEW TECHNOLOGIES."

PROFESSOR MAXINE WHITTAKER, CSO REPRESENTATIVE, APMEN VXWG 2021

NMPs and partners face *key challenges including strategies to increase patient adherence, access and referral, testing and treatment by non-clinical health workers, availability of vivax radical cure tools where patients present for care, control of malaria at border areas and conflict and insecurity.*

Innovative options to increase access included diagnostic network optimisation - (DNO) a potentially cost-effective approach to deploying diagnostics to the places where they can achieve highest impact for least cost. At higher levels, *multisectoral approaches have been employed by some programs to increase access.* While malaria is often dealt with by malaria programs, participants highlighted that *malaria control and elimination needs to be a multisectoral and community approach as malaria control work requires a lot of components* (e.g. logistics). A multisectoral approach can achieve more than an approach that focuses exclusively on health.

"MULTISECTORAL COMMITMENT IS ESSENTIAL WHICH NEEDS STRONG EFFORTS AND COORDINATION."

MR LEO MAKITA, DIRECTOR, NATIONAL MALARIA PROGRAMME, PAPUA NEW GUINEA, APMEN VXWG, 2021

ACTION POINTS & PLAN

Through discussions and country requests, the **APMEN VxWG identified the following action points** to incorporate into their workplan over the coming 12 months:

Action points	Status	Lead organization
Knowledge collation & dissemination		
Develop HS-RDT brief to provide NMPs with more information on new tools emerging	PAVE currently developing an evidence brief on HS-RDT for dissemination to NMPs	PATH & PAVE
Develop evidence brief on proven strategies to increase patient adherence	APMEN VxWG currently developing evidence brief proven interventions to increase patients adherence	APMEN VxWG
Identify and map any ongoing or planned operational research on HS-RDTs	Incorporated into APMEN VxWG workplan	PAVE & APMEN VxWG
Develop evidence brief on access strategies for remote and mobile populations	Systematic review protocol being developed for 2022	Menzies school of Health Research
Undertake TechTalks on treatment adherence, access and referral to share strategies and approaches proven to increase patient adherence that could be integrated into program activities.	Incorporated into APMEN VxWG workplan. Techtalk on adherence planned for Q1, 2022	APMEN VxWG
Provide more information to NMPs and partners on ongoing and planned feasibility studies investigating the use of 8-Aminoquinolines and G6PD testing at different levels of the health system		PAVE & APMEN VxWG
Implementation and Operational Research		
Ensure alignment between vivaxmalaria.org OR/IR database and the MESA database	Incorporated into APMEN VxWG plan	MMV
Support partners to secure funding and undertake IR and OR to answer any operational questions required to be addressed to support policy change	Incorporated into APMEN VxWG plan	APLMA/APMEN
Further identifying program priorities		

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Contact NMPs and stakeholders across the region to undertaking prioritisation exercise.	• Country prioritisation is underway with all National Programs and CSOs in the Greater Mekong Subregion • Prioritisation meetings are planned for 5-7 additional countries in the Asia Pacific in Nov/Dec 2021 • In-depth prioritisation planned with Pakistan DMC – December 2021 and PNG NMP Q1, 2022. • Prioritisation ranking meetings to be held with regional researchers Q4 2021 – Q1 2022	PAVE & APMEN VxWG
Streamlining policy processes		
Document policy processes across countries in the Asia Pacific where programs want to change policy in the next 2-3 years.	• Currently planned in countries in which in-depth prioritisation is undertaken • Underway and near completion across Greater Mekong Subregion	PAVE & APMEN VxWG
Determine previous causes of delays and help national programs determine how they can mitigate those delays in the future.	• Currently planned in countries in which in-depth prioritisation is undertaken • Underway and near completion across Greater Mekong Subregion	PAVE & APMEN VxWG
Identify 2-3 country National Programs that may be interested in developing the OAT with Menzies, APMEN and MMV.	• Recruitment for OAT scenario developed underway • OAT liaison with National Malaria Programs identified – NMPs will be contacted Q4 2021 to determine interest in being involved in OAT process	Menzies & APMEN VxWG
Implementation		
Make generic training materials on treatment and G6PD testing available to National Malaria Programs	• Generic training materials are in draft form and available on request • Once finalised, training materials will be uploaded to vivaxmalaria.org	PAVE, FIND, Menzies and any partners involved in training on new tools

	• Reaching out to partners who are working on operational research or implementation of new tools to collate training materials • Training materials on G6PD training are also available at PATH's GORCoP site. Please contact GORCoP@path.org for more details on materials and how to join and learn from the G6PD Operational Research Community of Practice	
Document partner strategies for improving access of vivax radical cure to remote and mobile populations	• Posters on access strategies presented at Annual WG meeting are available: Poster 1 - Afghanistan, poster 2 - Malaysia, poster 3 - Thailand, poster 4 - Cambodia, poster 5 - Myanmar	National Programs and CSO representatives
	Advocacy	
Advocate to research and financing partners to support OR on the use of HS-RDTs	• Included in APMEN VxWG plan	APMEN VxWG
Support dissemination of WHO-GMP timelines for policy guidance once available.		NMPs, APMEN VxWG and PAVE

Contents

Acronyms

ACT	Artemisinin Combination Therapy
APLMA	Asia Pacific Leaders Malaria Alliance
APMEN	Asia Pacific Malaria Elimination Network
ARMPC	Advocacy and Resource Mobilization Partnership Committee
ASEAN	Association of Southeast Asian Nations
BCC	Behavior Change Communication
BMGF	Bill and Melinda Gates Foundation
CBMM	Community-based Malaria Management
CDC	Center for Disease Control
CNM	National Center for Parasitology, Entomology and Malaria Control
CHW	Community Health Worker
COVID	Coronavirus Disease
CSO	Civil Society Organization
CQ	Chloroquine
DHS	Demographic Health Survey
DOT	Directly Observed Therapy
DNO	Diagnostic Network Optimization
DVBD	Division of Vector Borne Diseases
FDA	Food and Drug Administration
FIND	Foundation for Innovative New Diagnostics
GDG	Guideline Development Group
GIS	Geographic Information System
GORCoP	G6PD Operational Research Community of Practice
GMP	Global Malaria Program
GMS	Greater Mekong Sub-region
GPS	Global Positioning Satellite
GTS	Global Technical Strategy
HCP	Health Care Providers
HF	Health Facility
HIV	Human Immunodeficiency Virus
HRP2	Histidine-rich Protein2
HTA	Health Technical Assessment
IR	Implementation Research
LDH	Lactate Dehydrogenase
LLIN	Long Lasting Insecticide Nets
MC	Malaria Consortium
MDA	Mass Drug Administration
MOH	Ministry of Health
MMC	Myanmar Medical Council
MMP	Mobile Migrant Population
MMV	Medicines for Malaria Venture
MMW	Mobile Malaria Workers
MP	Malaria Post
NGO	Non-Governmental Organization
NMLCP	National Malaria and Leishmaniasis Control Program
NMP	National Malaria Program
NSP	National Strategic Plan

OAT	Options Assessment Toolkit
OR	Operational Research
PATH	Program for Appropriate Technology in Health
PAVE	Partnership for Vivax Elimination
PCR	Polymerase Chain Reaction
PDR	People's Democratic Republic
Pf	Plasmodium Falciparum
PEPFAR	President's Emergency Plan for AIDS Relief
PICO	Population, Intervention, Comparison, Outcomes
PNG	Papua New Guinea
POC	Point of Care
PQ	Primaquine or Pre-qualified
Pv	Plasmodium Vivax
PVPI	Pharmacovigilance Program India
RAM	Rotarians Against Malaria
RBM	Roll Back Malaria
rfMDA	Reactive Focus Mass Drug Administration
RDT	Rapid Diagnostic Test
SDG	Sustainable Development Goals
SOP	Standard Operating Procedure
SRC	Safe Radical Cure
TB	Tuberculosis
TBD	To be determined
TGA	Therapeutic Goods Administration
TQ	Tafenoquine
UCSF	University of California at San Francisco
USAID	United States Agency for International Development
UNU	United Nations University
VHW	Village Health Worker
VHV	Village Health Volunteer
VMW	Village Malaria Workers
VxWG	Vivax Working Group
WHO	World Health Organization
WWARN	Worldwide Antimalarial Resistance Network

Acknowledgements

- NMP partners for engagement and participation in meeting
- All presenters
- Advisory council
- Writing team
- APMEN
- MMV, PATH

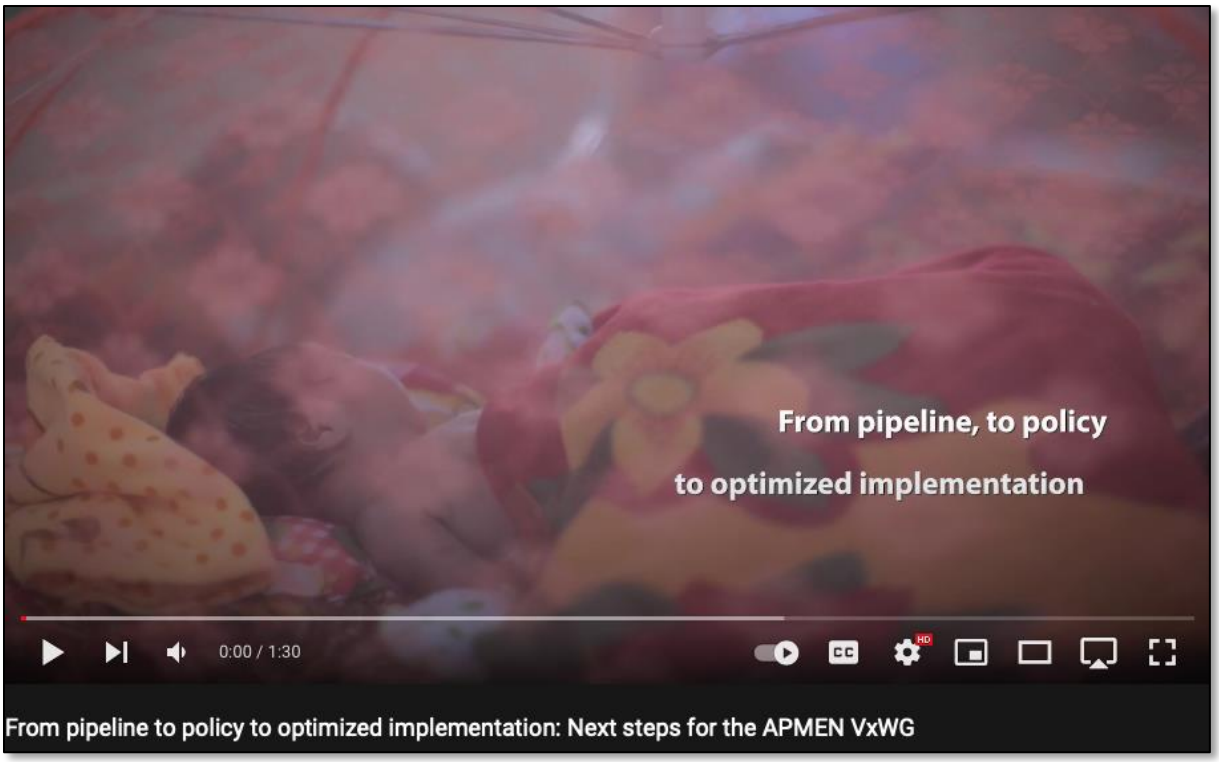
Opening and Introduction

Meeting overview

The 2021 APMEN Vivax Working Group (VxWG) Annual Meeting was held online from 9-11 August 2021, with the theme **'From pipeline, to policy, and to optimized implementation'**. The focus areas for the 3-day meeting were:

- Optimizing radical cure – including an introduction to the development of an Options Assessment Toolkit with the National Malaria Programs;
- Learning from history and early implementation;
- "Show me the vivax" & access – exploring strategies to ensure access to optimized radical cure.

Dr Sarthak Das and **Dr Karma Lhazeen** gave the opening remarks. **Dr Caroline Lynch** provided the agenda overview and then welcomed all the participants, and wished all for successful deliberations and better understanding of vivax in the region and globally, with the goal of eliminating malaria by 2030. The following video on the APMEN Vivax Working Group was shown to participants.



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Gender and Regional Representation

As a guiding principle, the APMEN VxWG wants to ensure gender equity and regional representation in its governance and activities.

- With Dr Karma Lhazeen as the Chair, Dr Caroline Lynch as the Co-chair, and Dr Manash Shrestha as the Technical coordinator, the VxWG has a 2:1 ratio for both female: male and Asia-Pacific (AP): Non-AP representation.
- For governance, the VxWG's advisory council, composed of four members at the present, has a 1:1 ratio for both female: male and Asia-Pacific (AP): Non-AP representation.

In the APMEN VxWG annual meeting 2021, the gender and representation metrics for the key people involved were:

Key People	Total	Female: Male ratio	AP: Non-AP ratio
Session chairs	7	4:3	5:2
Speakers/Presenters	19	10:9	14:5
Facilitators	13	8:5	10:3

Day 1: From pipeline to policy

Session One - Overview and objectives: Out of the pipeline

Chair: Dr Kamala Thriemer, Associate Professor, Menzies School of Health Research, Charles Darwin University

Session objectives:

- To provide an update on all new developments concerning Vivax malaria.

1.1. Outcomes, considerations and action points

Diagnostics

- New Higher sensitivity diagnostics are becoming available for vivax malaria. These will allow greater detection of infection for febrile/suspected patients
- The RapiGen Biocredit Pf/Pv is Global Fund ERPD approved and can be procured through Global Fund grants.
- The SD Biosensor is a semi-quantitative G6PD test that can discern between deficient, intermediates and normal G6PD enzyme activity in individuals.
- The SD Biosensor is ERPD approved and can be procured through Global Fund grants.

Treatment

- Primaquine (PQ) is the current mainstay for radical cure with shorter treatment options coming onstream – these are Primaquine 7 day at higher doses (1mg/kg) and Tafenoquine single-dose (with Chloroquine only).
- The biggest challenge with PQ is compliance, with healthcare workers concerned about drug safety while patients not adhering to the full treatment course when they feel better.
- Compared to primaquine, tafenoquine requires higher G6PD activity and thus, G6PD testing is mandatory for use of TQ, especially to differentiate whether patients have deficient, intermediate, or normal (>70%) enzyme activity.
- In-vitro and in-vivo is ongoing and planned to investigate potential synergistic and antagonistic effects on different blood-stage treatments with TQ and CQ, with the results expected by the end of 2021.
- Two paediatric 8-AQ formulations are under development for infants older than 6 months: Dispersible PQ 2.5mg and 5mg tablets and, Dispersible sweetened TQ 50mg tablets for infants with 5-35kg weight range.

WHO global guidance and policy change

- For uncomplicated malaria caused by vivax, ovale and malariae, these can be treated with ACT or CQ if susceptibility is maintained.

- Standard recommendation in all transmission settings for preventing relapses is PQ14 except for pregnant women, infants under 6 months, women breastfeeding infants under 6 months and women breastfeeding older infants with unknown G6PD deficiency status.
- In cases of people with G6PD deficiency, a weekly schedule of primaquine can be given but the feasibility of conducting point-of-care G6PD testing is difficult in most countries.
- When G6PD status is unknown and testing unavailable, prescribing PQ must be based on an assessment of the risks and benefits of adding PQ depending on the situation, G6PD deficiency prevalence as well as relapse risk.
- The pathway has been designed to deliver timely, high-quality recommendations for malaria endemic countries and the processes are transparent, consistent, efficient, and predictable.
- The timeline for revision of vivax treatment guidance is to be determined.

Poll results showed that NMPs and partners were most interested in receiving more information on:

- Higher-sensitivity diagnostics
- Primaquine 7-day and Tafenoquine treatments
- WHO policy processes and timelines
- Quantitative G6PD tests

APMEN VxWG Action points

- With PATH, develop an evidence brief on higher sensitivity Rapid Diagnostic Tests for dissemination to NMPs
- Develop and disseminate evidence briefs on Primaquine 7-day treatment and tafenoquine
- Identify and map any ongoing or planned operational research on HS-RDTs
- Advocate to research and financing partners to support OR on the use of HS-RDTs
- Advocate for clearer timelines from WHO on potential vivax treatment guideline revisions

1.2. Higher sensitivity Vivax diagnostics and G6PD tests

Dr Gonzalo Domingo, Head, Diagnostics, PATH-Seattle

Challenges with diagnosing vivax malaria

- Key challenge with vivax malaria is that when people develop symptoms as it presents in the blood stage, there is very low parasite density.
- The available diagnostic tests are the least sensitive, with RDTs performing worse than microscopy at the point-of-care.
- Liver-stage hypnozoites of *P. vivax* are very difficult to detect as they are not circulating in the blood.
- However, there are new serological assays being developed to determine recent exposure to vivax malaria and thus have a high chance of having hypnozoites.

The mechanisms of diagnosing blood-stage malaria

- RDTs diagnose the presence of malaria parasite proteins or antigens and in the case of Vivax malaria, detects **lactate dehydrogenase** (LDH).
- However, *P. vivax* produces **very little LDH per parasite** compared to HRP2 for *P. falciparum*. Thus, RDTs that work well for *P. falciparum* need to work better to accurately diagnose *P. vivax* but currently available RDTs have poor detection for LDH and do not work well for vivax.
- LDH and antigen concentration can now be quite accurately measured using tests developed by CDC (Q-Plex Human Malaria Array (5-Plex)).

New diagnostic tests

- New tests are also coming out, such as RapiGen (South Korea) that has an order of magnitude improvement in LDH detection at lower concentrations than current WHO-prequalified Pv RDTs.
- Modelled data on potential clinical performance based on analytical sensitivity, estimate that the new RDT could detect nearly 22% of asymptomatic cases compared to current detection rates of 4%, and 94.7% of infections among febrile patients compared to the current 91.2%.
- RDTs with improved detection are becoming available over the next few years and could potentially improve case management by identifying lower density infections.

Other technologies are also coming online, such as for Hemozoin detection (Hemex/Gazelle) which is at least equivalent to microscopy and better than mRDTs. There is a promise of serology to detect hypnozoites parasites that will improve access to a broader set of vivax infected individuals.

Diagnostics to measure G6PD activity

- Current clinical and laboratory tests for G6PD deficiency are either quantitative and involve measuring enzyme activity with one instrument and haemoglobin with another, or the qualitative fluorescent spot test.
- Both tests are fairly complex and have inherent temperature control to measure enzymatic activity, presenting major barriers to access.
- A few years back, Access Bio introduced a point-of-care qualitative G6PD test that met many operational characteristics desired for a G6PD deficiency test. It is similar to a RDT in terms of complexity and with minimum sample preparation but does not correct for temperature and could not accurately differentiate females with intermediate G6PD activity from those with normal activity, posing a limitation for TQ.
- There were also some limitations in results interpretations due to changes in the hue, the difficulty to make a qualitative test that worked over a broad temperature range, the lack of a control line and did not provide any controls. Access Bio and Humasis are now producing new tests with controls though both require clinical evaluation but nonetheless are progressing to address limitations.
- In contrast, quantitative and semi-quantitative Point of Care (POC) tests are a bit more involved. Although they require an instrument, they accurately diagnose female G6PD activity, which is crucial in informing treatment with Tafenoquine.
- G6PD deficiency diagnosis also provides equity in terms of diagnosing females to the same standard as males.

- These POC tests also correct for temperature, making them more accurate over the whole range of operating temperatures for malaria clinics. However, they are not as simple as qualitative tests as they have some sample preparation requirements and require instruments.
- The most advanced in terms of clinical evaluation and the only test with Global Fund ERPD approval is SD Biosensor's STANDARD Test, a semi-quantitative test with thresholds on the label aligned with WHO PQ classification that can be used to diagnose G6PD male and female deficiency, alongside intermediate female as well as normal cases.

Shelf life, box size and stability of G6PD tests

- Clinical performance data from Brazil indicates that the SDB Qn-G6PD test meets performance purposes under clinical studies. Interpretation and instrument requirements are challenges, but the tests provide accuracy and the initial shelf life of 12 months is being extended to 18 months.
- Manufacturers are exploring smaller unit numbers per kit to account for the short shelf life as well as alternate platforms.
- A very robust pipeline of products is coming through which could operate across different platforms that may help address the stability issue. Partners are also working on training to improve ease of interpretation.

In summary, there are POC tests available designed to meet the needs of the malaria community with adequate performance, complexity and workflow but are not perfect. The new generation of tests need more qualification in clinical studies, are constrained by operating temperature and no control lines, but are being addressed. The quantitative tests require instrumentation that inherently constrains access and the shelf life is being improved but nowhere near that of RDTs.

There are a couple of products such as RapiGen Biocredit RDT with lower LDH detection limit. There is no clinical data, with the available data derived in laboratories and superimposed on clinical data. This represents an opportunity to conduct clinical studies to evaluate the performance in intended settings. For the POC G6PD deficiency test, there are extensive clinical studies for analytical performance of these products that are going to be published soon. There is an opportunity to conduct operational studies to assess their use under programmatic circumstances.

These products are commercially available, there is an **exciting opportunity to understand what happens when combining the detection of more vivax cases and which proportion receives radical cure**.

1.3. WHO Current Guidance for Treatment of Malaria and Process for Policy Change

Dr Neena Valecha, Regional Malaria Advisor, World Health Organisation - South East Asia Regional Office

Preventive chemotherapies and case management for all aspects of malaria were laid out as per WHO's Current Guidance. Here we highlight vivax-related treatment.

(Please refer to video for the remainder of the presentation notes regarding WHO Guidance for IPTp, IPTi and SMC.)

Vivax treatment as per WHO Guidelines

- For uncomplicated malaria caused by vivax, ovale and malariae, these can be treated with ACT or CQ if susceptibility is maintained.
- Standard recommendation in all transmission settings for preventing relapses is PQ14 except for pregnant women, infants under 6 months, women breastfeeding infants under 6 months and women breastfeeding older infants with unknown G6PD deficiency status.
- In cases of people with G6PD deficiency, a weekly schedule of primaquine can be given but the feasibility of conducting point-of-care G6PD testing is difficult in most countries.
- When G6PD status is unknown and testing unavailable, prescribing PQ must be based on an assessment of the risks and benefits of adding PQ depending on the situation, G6PD deficiency prevalence as well as relapse risk.

WHO guidelines and the process for policy change.

- Guidelines address an area of uncertainty and unmet needs.
- The WHO and partners have recently been moving away from "one-size-fits-all" approaches to malaria control, instead recommending data-driven actions and strategies tailored to local settings.
- The development process is ensured to be explicit and transparent, draws from multidisciplinary expertise and perspectives, and aims to minimize the risk of bias while balancing potential benefits and harm. Publicly available evidence is used and the recommendations are made such that they can be adapted to the local context.
- The WHO Global Malaria Program (GMP) held online consultations in 2019 to identify new topics needing recommendations and gather suggestions for updating existing recommendations. Existing recommendations for malaria control were reviewed by GMP staff and an external consultant in January 2020.
- Standard WHO guideline development processes include forming guideline-specific steering groups and individual guideline development groups (GDGs) for each technical area (chemoprevention, vector control, elimination, treatment, diagnosis, vivax, and anemia).
- Furthermore, an editorial working group of seven malaria experts ensures consistency, comprehensiveness and coherence of consolidated guidelines across different intervention areas, with each GDG including some members of this editorial group.
- As of February 2021, all current recommendations can be found in the WHO Guidelines for malaria available online. The document includes links to evidence underpinning each recommendation and has a feedback tab to help identify recommendations requiring updates or clarification. Current recommendations will continue to be reviewed and updates will display the date of the most recent version.

The WHO policy pathway

1) Anticipating products or strategies likely to be key in future efforts for malaria control and elimination. This involves defining unmet malaria-related public health needs alongside preferred product characteristics of malaria products and strategies that could address these needs, and supporting the

research and development (R&D) effort. Afterwards, the pipeline is scanned for new products to determine whether there is sufficient evidence to support a WHO recommendation. (*This step provides transparency and predictability, and helps shape the R&D space for new products*);

2) Develop recommendations on what to do and what malaria control products to use based on best available evidence. This step entails developing recommendations for new tools and strategies through the WHO's guideline development process, ensuring that recommendations around the use of a specific product is developed in parallel with its prequalification assessment, and then issuing WHO recommendations and related prequalification listings. (*The WHO prequalification process ensures that diagnostics, medicines and other disease control products meet global standards of quality, safety and efficacy*); and

3) Optimize uptake of recommendations by improving the way they are shared and updated such as through an online platform for dissemination. This step includes ensuring that recommendations are easily accessible for all stakeholders, supporting the adoption of recommendations and monitoring their uptake and impact, and finally identifying the potential need for new or improved recommendations through effective feedback loops.

- The pathway has been designed to deliver timely, high-quality recommendations for malaria endemic countries and the processes are transparent, consistent, efficient and predictable.
- Lessons from frontline workers and implementers feed into the overall process at all stages to improve the policy pathway.
- The current timeline for when recommendations are expected to be updated and published in the WHO Guidelines for vivax treatment are to be determined.

1.4. *P. vivax* Radical Cure Treatments – Today and on the Horizon, Opportunities and Challenges

Dr Penny Grewal, Senior Technical Consultant, Medicines for Malaria Venture

Currently available radical cure treatment regimens for vivax malaria

- Primaquine (PQ) is the current mainstay for radical cure.
- A high-dose PQ course (1 mg/kg) is under WHO ERG review, which will also guide whether mandatory G6PD testing will or will not be required with a higher dose of PQ.

Primaquine

- The biggest challenge with PQ is compliance, with healthcare workers concerned about drug safety while patients not adhering to the full treatment course when they feel better.
- The biggest liability is the G6PD issue. There is a perceived feeling of safety with PQ because the treatment can be interrupted, though there may be a need for G6PD testing before high dose PQ and definitely before TQ.

Treatment expected to be made available soon

- Single dose radical cure Tafenoquine (TQ) is available for patients aged over 16 years.

- TQ is contraindicated for pregnant women, people who have less than 70% G6PD enzyme activity or unknown G6PD activity.
- Compared to primaquine, tafenoquine requires higher G6PD activity.
- G6PD testing is mandatory for use of TQ, especially to differentiate whether patients have deficient, intermediate, or normal (>70%) enzyme activity.
- Currently, TQ can only be used with CQ blood-stage treatment. Tafenoquine's limitation is the need to be given at Day 1 and 2 of Chloroquine dose, due to how the drug was administered during clinical trials.
- Modelling work is planned to establish wider dosing windows for CQ and TQ. There is also no data to support TQ use with any ACT.
- Work is still pending on a pharmacokinetic analysis on the blood sample due to the COVID-19 pandemic. Furthermore, there are in-vitro and in-vivo work planned to investigate potential synergistic and antagonistic effects on different blood-stage treatments with TQ and CQ, with the results expected by the end of 2021.
- Two paediatric 8-AQ formulations are under development for infants older than 6 months:
    - Dispersible PQ 2.5mg and 5mg tablets and,
    - Dispersible sweetened TQ 50mg tablets for infants with 5-35kg weight range.
- WWARN is doing a meta-analysis on safety and efficacy for paediatric PQ, with WHO prequalification anticipated in 2023.
- The sweetened TQ is being developed in a blister pack with two tablets on one side and one on the other to allow a proposed dose variation by weight band and will be provided in a 30-tablet pack to enable countries to put together the appropriate dosage. This is currently under review by AU-TGA and will be submitted to endemic countries from 2022 onwards.

G6PD tests

- New and reliable tests are coming online but it requires changing patient flow and revised treatment algorithms and cost implications.
- There is also potential for using G6PD patient cards for male patients for subsequent relapses and challenges associated with G6PD intermediate patients.

Risk management for Tafenoquine

- Two activities are planned for additional risk management for TQ - mandatory G6PD testing, and training of healthcare providers on G6PD, testing, signs of acute hemolytic anemia, and safety reporting.
- From a pharmacovigilance perspective, TQ is available in the US while the CDC is conducting a study. There has been no report of adverse incidents and one report of lack of efficacy when given with artemisinin family.
- The Thai FDA has been working with the WHO 3S program and has developed good guidance on roles, responsibilities and detailed descriptions of adverse events and profiling, with a stimulated report planned after approval.
- Brazil is also planning for a feasibility study to follow up patients on Day 7 and 14 using a digital app, and for patients to return for assessment.

Dr Grewal concluded by saying that there is a lot of ongoing and planned work to see how to get those drugs safely and effectively to the affected communities.

1.5. Out of the pipeline - Question and Answer session with participants

Q1. There was talk about the tailored new treatment guidelines, to be non-prescriptive, and to have a global guideline that can be adapted to the local context. Can you talk a little bit more about how this works out in reality and what is the mechanism behind that or support that?

A: Respondent - Dr Neena Valecha, Malaria Regional Advisory WHO-SEARO

- Taking the example of vivax malaria treatment using primaquine, a good practice is to do a G6PD test and before prescribing primaquine for 14 days. But G6PD testing is not readily available in the community setting where treatment is given. It is not possible to be prescriptive as primaquine is not given without the G6PD test, and safety concerns need to be addressed.
- There was a study done in collaboration with MMV, to address the safety issues with close monitoring of patients by providing G6PD cards, telling them about the side effects and what to look for by the community health workers. This may not be ideal but the treatment can be given with close monitoring.
- Some countries are still reluctant to use combination therapy even with the recommendation to use combination therapy for drug resistance or treatment failure (of more than 90%). Support is given on how to monitor the efficacy and proper use of the current treatment guideline.
- Therefore, even when the ideal guidance is given, countries are not able to do it or sometimes they want to use a product that they have, then technical guidance is provided based on the requirement of the particular country, region or area or even at subnational level.

Q2. There was a mention of a new product on testing. Can you explain more about the comparison of CareStart SD Biosensor and new tests such as Humasis and other new products? Also, the cost of SD Biosensor and if the cost is prohibitive in terms of implementation?

A: Respondent - Dr Gonzalo Domingo, Head Diagnostics, PATH

- On the Humasis and new CareStart tests, there is not enough clinical data but laboratory tests indicate that they perform just as well and there are improvements over the previous CareStart tests. It will be interesting to see how they perform in point-of-care and clinical settings but there are no studies as yet.
- SD Biosensor is committed to have the cost of USD 300-350 per instrument for malaria-endemic countries, and USD 3.50 per disposable. As with RDTs, the price may vary based on distributors and the method of procurement.
- Without competition, this is significantly more expensive than current RDTs. On the other hand, the cost may be justified as many countries are approaching elimination phase.

Q3. For clarification on the RDTs, the cancelled RDTs are no longer available through the Global Fund mechanism or in general?

A: Respondent - Dr Gonzalo Domingo:

- CareStart RDTs are no longer available through the Global Fund but Access Bio is still working to address quality issues under the WHO prequalification scheme.
- However, neither the RapiGen RDT and SD biosensor are WHO pre-qualified and this is still a step required to be addressed.

Q4. What are other platforms that might improve stability? Can you explain about those and where they are in the pipeline?

A: Respondent - Dr Gonzalo Domingo:

- In contrast to malaria RDTs that are on the same platform, there are a series of G6PD tests being used with different ways of measuring enzyme activity (such as different substrates and additional enzymes).
- It will take around 18 months before market entry but there are also more products that can be anticipated beyond the SD Biosensor, which will also affect the pricing.

Q5. When is the expected timeline for the conclusion of ASEAN 3 countries review of Tafenoquine?

A: Respondent - Dr Penny Grewal:

- It should be done at the end of the year (2021).
- Reflecting on all of the new tools which were only pipe dreams during the first APMEN VxWG meeting, it is a very exciting time for Vivax as we actually have new tools, and it's very incredible. We have always been talking about how we are going to overcome the G6PD problem and Gonzalo showed exciting tools. The whole compliance issue we have with PQ, we have single dose TQ. For the first time, we can actually say, "Yes we have got something in vivax and we can actually get going". I am just very excited about that.

Q6. What is the timeline of the pre-qualification of the G6PD test and what will be the recommendation for the countries to start to use these G6PD tests at the point of care before WHO prequalification?

A: Respondent - Dr Neena Valecha:

- This is expected at the end of the year around September or October 2021.

Q7. What is the expected timeline for Vivax recommendation and the three-stage process that you described with some examples?

A: Respondent - Dr Neena Valecha:

- This has been recently started and there is a training of PICO questions, with guideline development group meetings, external reviews and evidence review group. From a recent observation, it has taken about 6 to 8 months. It depends on the topics and many other issues.

1.6. Poll results - 'What tools would you like to have more information about after today's session on new tools?'

The following are the ranked results for the poll question "What are the most interested tools or information in learning more about after today's session?". A total of 87 participants responded to choose a maximum of five options out of ten.

Rank	Option	Votes	% response
1.	**Higher sensitivity Rapid Diagnostic Tests for vivax**	**49**	**56%**
2.	**Primaquine 7-day**	**41**	**47%**
3.	**Tafenoquine**	**36**	**41%**
4.	**WHO Policy Timelines and Processes**	**29**	**33%**
5.	**Quantitative G6PD test**	**28**	**32%**
6.	Pediatric primaquine	24	28%
7.	Qualitative G6PD test	19	22%
8.	Hemozoin detection	16	18%
9.	SeroTAT	14	16%
10.	Fluorescent Spot Test	11	13%

Session Two: Policy Change Process and Design

Chair: Dr Prudence Hamade, Malaria Consortium, UK

The objectives of the session were to:

- identify the progress of changes of thinking on radical cure since the last APMEN Working Group meeting held in Kathmandu 2 years ago; and
- share and highlight best practices around the theme of evidence, policy and access.

2.1. Outcomes, action points, comments and points to consider

- There are only nine years remaining to eliminate malaria in this region and it is important to move swiftly to make sure that this evidence is used.
- An online platform that collates all available Implementation and Operational Research studies on vivax is available at vivaxmalaria.org. The purpose of the database is to allow decision-makers and other researchers identify ongoing studies, determine where there may be gaps in research and avoid duplication of effort.
- The database can also serve as a hub to connect researchers, national malaria programs, policy makers and implementers to discuss research plans and activities in the region.

Action points

- Ensure alignment between the MESA elimination database and the vivaxmalaria.org website database.

2.2. Vivax-related Operational and Implementation Research in the Asia Pacific

Dr Bipin Adhikari, Mahidol Oxford Tropical Medicine Research Unit (MORU), Thailand

Overview of Operational Research

- Operational Research (OR) is a subset of implementation science that studies methods to promote the uptake of research findings into routine healthcare in clinical, organisational, or policy contexts.
- It is also action research where researchers, policymakers and health workers collaborate to identify and develop solutions to problems around the implementation chain, and deal with implementation findings of the program.
- It has three main roles: (1) structuring an implementation problem and the characteristics of implementation; (2) prospective evaluation of an intervention; and (3) strategically reconfiguration of services based on feedback.

Vivax Malaria Database

- A collection of scientific information and evidence around vivax malaria can be found at <**vivaxmalaria.org**> which is easily accessible to policy makers and stakeholders.
- The data can be used for evidence-informed decisions, policy making, and implementation. It can also help researchers, national malaria programs, policy makers and implementers to come together, make connections, discuss or plan research, learn from past research and share information about ongoing research in the region.
- An easily navigable "search" function shows the breakdown of studies in the database, such as those being prepared, ongoing and completed, what type of research are deposited, and by country.

2.3. Question and answer with participants

Q: Does database also feeds into https://mesamalaria.org/mesa-track which is a living database that captures research projects and institutions' portfolios in malaria elimination and eradication.

A: Respondent - Dr Caroline Lynch

- Dr Rosalind Howes has kindly alerted us to that database and thinks that vivax has a different focus in concentrating more on OR and IR, but will keep an eye on the MESA database to ensure relevant studies are captured. There is also a need to work on the reverse vivax MESA for collection of in-depth information.

2.4. Groupwork – National Malaria Program and vivax roadmaps

Facilitator: Dr Phyoe Yarzar, PATH – Myanmar

The NMP group work focused on NMPs' 2019 roadmaps and achievements to date. The session was intended to help identify areas where the programs have questions or needed further support to achieve

and optimize the use of radical cure, highlight best practices on early implementation of G6PD analyzers and accessing remote populations, and to enable programs and partners to learn from each other's plans and thoughts on vivax elimination.

The NMP group work session was intended to:

1. Determine progress made in the Vivax roadmaps since 2019; and
2. Identify areas where NMPs have questions and need further support.

2.4.1. Outcomes, considerations and action points

Key points and outcomes

- Timelines are quite short, and it is important to have WHO recommendations
- **Progress since Oct 2019:** Of the countries reporting through the groupwork, four are on track with relative to their roadmap set out in Oct 2019, the remaining 5 countries are in the same position having suffered delays related to COVID, political situation or funding constraints.
- **Changes in diagnostic tools:** The majority of country programs were interested in, planning to or already implementing testing or screening for G6PD activity. Three countries are implementing quantitative G6PD currently. Thailand recently obtained WHO prequalification for quantitative G6PD test. Lao PDR is able to expand G6PD testing to health center level and able to identify intermediate females and Cambodia was able to move from qualitative to quantitative G6PD test but no prequalification obtained yet from WHO. Malaysia is screening all newborns with qualitative G6PD tests and quantitative G6PD tests are available in all hospitals. Philippines also has newborn screening G6PD tests but not all the patients will know their status.
- **Changes to treatment:** While most countries are not planning to change radical cure policy in the next two years, one country is considering PQ7 and three countries are considering a change to TQ.

Requested support from National Programs

- Financial and technical support for operations research especially pilot study on G6PD tests,
- Support to develop strategies to improve treatment compliance,
- Training materials for using G6PD tests,
- Technical support to identify access strategies to reach remote patients
- Procurement and supply chain support,
- Guidance from WHO on the safety and use of tafenoquine

Per country action points available in Annex two

2.4.2. National Malaria Program Groupwork

The group work discussion was based on the following questions:

- How would you describe the status of activities on vivax now relative to the roadmap you developed in 2019? Has your program approach changed since 2019?
- Does your program want to consider any diagnostic changes in the coming 2 years? Yes/No/Don't know, if yes, what are you considering?

- Do you want to consider any treatment change options in the next 2 years? Yes/No/Don't know If yes, what are you considering?
- Is there anything that you would like to understand or know about how to improve current treatment of vivax in terms of its use or its delivery?

Nine NMP program teams took part in groupwork discussions. Table 1 below provides outcomes of discussions that took place during NMP groupwork around the four questions provided above.

Commonalities between countries

TABLE 1: PER COUNTRY OUTCOMES OF GROUPWORK DISCUSSIONS ON VIVAX ROADMAPS

Country	Status of 2019 Roadmap	Diagnostic changes in coming 2 years	Treatment changes in next 2 years	Improvement needed or any comments
Afghanistan	No change but malaria has decreased from 2020, due to COVID lockdown, security challenge and case management. Treatment regime is 8 days PQ and 3 days CQ	No G6PD testing but trying to identify budget for rolling out the G6PD testing. Interested in the HSRDT but concerned on false positive RDT issues.	No change and the current regime is low cost and still effective.	Operational research on G6PD deficiency prevalence was conducted once, more than ten years ago, but due to recent population growth as well as Afghanistan's ethnic diversity, updated information is required.
Bhutan	Delayed due to COVID-19 pandemic.	G6PD testing is now included in the guidelines, and in the process of procuring G6PD tests with GF budget	Implementation of treatment strategy for PQ14 is ongoing. National Strategy and Treatment Guidelines are already updated.	Tafenoquine is still not WHO pre-qualified and looking for guidance from WHO for Tafenoquine as treatment regime.
Cambodia	On track.	Able to move from qualitative to quantitative G6PD test.	Tafenoquine is not yet approved by MOH. Still under evaluation. Planning to implement PQ short course 7days by 2022.	Still looking for a more evidence for Biosensor
Lao PDR	On track. The new malaria strategy for 2021 to 2025 has been developed.	G6PD testing has been extended to the health centers and high burden areas.	Considering to include Tafenoquine in the future.	Will do pilot study first to know the risk and make sure that Tafenoquine can be used safely.
Malaysia	On track but updating treatment guidelines is slow due to COVID pandemic.	For diagnostics, qualitative G6PD tests are currently being done for all newborns. Quantitative G6PD test is available in all hospitals in Malaysia. There is no urgency	Will consider using Tafenoquine if the safety data of combination treatment of ACT and Tafenoquine is available and when Tafenoquine is registered in Malaysia.	Need safety data on combination treatment with ACT and Tafenoquine. Pharmacovigilance system is also well-established. If using Tafenoquine it will be incorporated in the existing system.

Country	Status of 2019 Roadmap	Diagnostic changes in coming 2 years	Treatment changes in next 2 years	Improvement needed or any comments
		for point of care quantitative G6PD testing except for outbreaks of vivax malaria which is quite a slim chance.	Fast tracking on use of Tafenoquine can be done through administrative circular. No changes needed to current treatment. Access to hospitals is also available for indigenous populations.	
Myanmar	Not much different from 2019. Still using primary 14 days for the radical cure. No new changes because of the current political situation	G6PD deficiency prevalence is approximately 10-13% in country but hard to fully quantify as each ethnic group has a different deficiency level. NSP for 2021-2025 includes G6PD testing – the plan for the future. But this is dependent on GF funding and the evolving political situation.	There is no plan to change treatment options in the next 2 years. PATH approached NMP regarding introducing TQ but because of the current political situation, no follow-on contact could be established.	*P. vivax* is around 80% of all malaria in Myanmar. It is difficult to determine If the cases are relapse and need strategies about vivax treatment and control.
Philippines	No change, same as in 2018	There is no change and keeping the microscopy and RDTs. New-born screening of G6PD has already taken place.	No changes for treatment guideline in the next 2 years.	Would want to have more data on compliance for the 14-day treatment on *P. vivax* and strategies on treatment accessibility for patients living in most isolated areas.
Solomon Islands	Delayed due to funding constraints	G6PD Qualitative test was discontinued by Global Fund, Quantitative tests, such as SD Biosensor are not in the immediate plan.	Low dose PQ for 14 days was the main regimen. No immediate changes in treatment guidelines.	Improvement needed for procurement and supply chain and to overcome health workers' hesitancy to prescribe primaquine for lack of POC G6PD test.
Thailand	The National treatment guidelines have already been updated ahead of schedule.	Already started to procure quantitative G6PD tests.	Tafenoquine approval and pre-qualification were already done.	A joint feasibility study with UCSF to assess community-level provision of PQ14 and G6PD quantitative testing is ongoing, with UCSF having recruited the

Country	Status of 2019 Roadmap	Diagnostic changes in coming 2 years	Treatment changes in next 2 years	Improvement needed or any comments
				participants. A feasibility study on PQ7 and G6PD at all levels of the health system.

Presentation from National Malaria Program breakout groups

General overview

- Most of the activities in Thailand and Lao DPR are ongoing. A lot of activities were successful and have been completed in the past few years. Except the activities related to Tafenoquine may still be pending in both countries. For Thailand even though the research protocol had been approved by the ethical committee, the research could not be conducted due to COVID-19 situation in Thailand.
- In Bhutan, Tafenoquine and G6PD testing are still in the process and waiting for WHO prequalification for G6PD testing. Bhutan has updated the guideline incorporating G6PD as one of the requirements for treatment of *P. vivax*. Bhutan being a mountainous country, it is considering introducing Tafenoquine as a treatment regime for the *P. vivax.*
- Afghanistan is the same as other countries. The big challenge Afghanistan faces is insecurity with COVID-19. Limited budget for a new grant is another challenge. Case management for vivax malaria is chloroquine and 8 weeks regime by primaquine. G6PD testing is not available.
- Laos updated the guideline for G6PD quantitative testing and developed a second line policy for falciparum and vivax that is artesunate plus mefloquine and artesunate plus piperaquine. Regarding primaquine, it is the same as last year with 14 days treatment depending on the G6PD testing results. There was a discussion on the need for the quantitative G6PD test if tafenoquine is considered in the future. Laos has planned for national study/operational research for future consideration of Tafenoquine treatment.

2.4.3. Question, answers & comments with and from participants

Comments from chair: Dr Prudence commented that Tafenoquine comes with some reservations, including the need for accurate testing of G6PD deficiency. Countries like China and Sri Lanka have managed to eliminate malaria as well as Malaysia without the introduction of the drug.

Q: Has Thailand found that TQ is needed or would different dosage regimes be sufficient to achieve elimination in the next 9 years?

A: Dr Prayuth – DVBD, Thailand: Thailand is hoping to have more choices for the national program to manage vivax malaria. That is why Tafenoquine was introduced this year, but the study could not be completed due to COVID-19 situation. Thailand has been using primaquine for more than 30 years already. If other choices are available to manage vivax and accelerate malaria elimination in some populations, it will be good for the national program.

Comment – Dr Prudence Hamade. The timeline is quite short, and it is important to have WHO recommendations. It is known that Tafenoquine is not recommended in children under 16 years. G6PD deficiency testing is still required to use primaquine. Ideally, a different regime other than primaquine with a cheaper option should be available and affordable especially in remote areas where community health workers deliver the treatment.

Comment - Professor Maxine Whittaker. Understanding what is needed to reach the elimination date of 2030 considering the time it takes for OR and for policy changes - is important. It may need some parallel OR activities - but need also to utilize to maximum effectiveness the tools at hand - as some countries in the region have already done. The parallel research activities help in the endgame but may not be the main game.

2.5. Poster Session – overview and discussions

The objectives of the partner poster session were to highlight and share experiences of:

- Early implementation of G6PD analysers; and
- Accessing remote populations with Vivax treatment.

Poster 1.

Access to malaria diagnostics and treatment in rural remote areas in Kanchanaburi, Thailand: The poster discussed the implementation challenges of mobile and migrant populations in Kanchanaburi province across the border with Myanmar. The project deploys trained community health workers to provide service delivery and monitoring using reach, test and treat strategy based at malaria posts.

Facilitator: Warisala Chatuchinda

Q1. What kind of G6PD test is used in these areas?

A: Not all patients are tested for G6PD, only those in the pilot study are tested for G6PD.

Q2. As the radical treatment for P. vivax is 14 days, how do you ensure the compliance of these patients who are mobile and migrant populations?

A: We use community health volunteers to follow up daily with them. But it is difficult for those who are in remote areas and during the rainy season.

Q3. In view of malaria elimination, how do you plan for case identification and foci investigation etc?

A: It is difficult with mobile and migrant populations for both compliance and follow-up. There is a need cross border collaboration for cross border migrants as well as cross province collaboration for internal migrants and in-country partnership to reach the goal of malaria elimination.

Q4. Do all the suspected malaria cases go to government facilities when you refer? Also un-documented migrants?

A: No, patients go to government hospital for malaria as they can access services from malaria posts, undocumented migrants can also access service there but they need to be followed up by CHV but there are also language barriers.

Q5. How do you manage the migrant patients for compliance according to 1-3-7 strategy?

We used an online malaria platform for the staff to follow up every week. The success rate for follow up is 60% to 70%. We could not check blood again for around35% which we need to improve.

Q6. Any specific strategy for logistics for community health volunteers in malaria posts?

A: We build the capacity of the CHV and improve their knowledge. But there are language barriers.

Poster 2.

Malaria Elimination in Eastern Myanmar: Saw Win Tun, SMRU, Thailand

The poster discussed on malaria elimination by providing radical primaquine treatment with G6PD testing. G6PD testing is feasible and doable in remote settings by using quality training and by closely engaging with the local communities.

Facilitator: Sonia Cheung

Q1. Do you engage volunteers to do the G6PD test?

We engaged with the community leaders and stakeholders before we implement the activities. We trained the village health workers for the G6PD testing.

Q2. It is a very good approach to extend the G6PD coverage through volunteers at the community level. Any challenges with asking volunteers to do the G6PD test? For example, the test kits will need regeneration and need a high capacity of volunteers to do the test.

Our program started in 2014 and in our project the volunteers are well experienced as they have been living in the area with vivax malaria for a long time. The key challenge is the remoteness and difficult access to the malaria posts.

Q3. Could you comment on the quality of the training and what level of training is needed to perform the test reliably and also on the needs of refreshers' training?

A refresher training for Biosensor and G6PD test kits was provided especially to identify intermediate women which is challenging for us. We are planning for more refreshers training but restriction imposed by COVID pandemic.

Q4. How do you ensure the quality of malaria post workers?

We did a proper quality training (4 days training with theory and practice), and we monitor with field supervisor monthly and zonal coordinator quarterly to make sure that they are able to do the testing.

Poster 3.

From evidence to nationwide policy – the rollout of *P. vivax* Radical cure with G6PD testing in Cambodia: Bunmeng Chhun, CHAI, Cambodia

The poster discussed on the rollout of *P. vivax* radical cure with G6PD testing in Cambodia. Diagnostic tool has changed from qualitative RDTs which were only eligible for males to quantitative devices for both males and females. Better treatment coverage was seen with this change.

Q1. Do you know what factors limit access to the G6PD test? Was it distance/time/cost to the G6PD testing facilities?

Factors affecting the access of the patients to the G6PD tests are less likely to be due to costs as the tests were provided free of charge. Distance and transportation may be key challenges as the patients detected by village malaria workers (VMW) needed to be referred to the health facilities (HFs) that have trained HCW and equipped with G6PD test and Pv radical cure services that are normally more than 5km away from the villages.

Q2. The compliance level of 14-day PQ treatment was very high; what were the main drivers for this?

The high level of compliance observed to the PQ14 may be due to two things: counselling from HFs prior to providing treatment and follow-up by HF staff or VMW in the villages on day 3, 7 and 14. VMW followed up in person while the HF staff used phone calls.

Q3. Do you have a strategy approach in dealing with sub-microscopic malaria?

Microscopy utilization is mostly at provincial and referral hospitals; and currently most health centers use RDT.

Q4. Have you encountered any limitation with the max 30c of storage requirement for the G6PD test?

Storage for G6PD tests is not an issue for program implementation as the national program has already procured and distributed a small fridge to each HF to keep the G6PDs test within the required temperature.

Q5. Do you think the in-person adherence follow-up by VMW is sustainable?

The in-person adherence follow-up by VMW is sustainable for the 14-day treatment. However, expanding the role of VMWs beyond adherence to follow-up on side effect/drug adverse events will be quite challenging as they are volunteers and their knowledge is limited to detect side effects of the treatment.

Poster 4.

Improving access to malaria diagnosis and treatment services at high-risk provinces of Afghanistan through Community Based Management of Malaria (CBMM). Dr Saboor Yousafzai, Healthnet TPO, Afghanistan

The poster discussed on challenges of delivering malaria treatment and testing services to remote high-risk provinces including nomadic people, by trained community health workers. Challenges include inadequate human and financial resources, poor infrastructure and low health seeking behaviors.

Facilitator: Yucheng Tsai

Q1. Was there any available follow up for Primaquine dosing following P vivax diagnosis?

Vivax malaria treatment is with PQ as per protocol and used by health facilities and follow up is conducted with community health workers

Q2. How was CHW case reporting managed. Paper or digital platform?

Malaria case reporting by CHW is tally sheets and case register and the reporting is still paper-based and reported to the Ministry of Public Health, then the data are entered into the central database

Poster 5.

Malaria elimination programme in Malaysia: Reaching the unreachable - Dr Tam Jenn Zheung, Ministry of Health, Malaysia

The poster discussed on reaching the remote population in Malaysia through government public services and community-led approaches. Lessons learned for good service coverage are (1) strong integration between government, communities, and private sector, and (2) establishing malaria posts which are more cost effective and sustainable.

Facilitator: Vilayphone Phongchantha

Q1. How does Malaysia address the community volunteers' cost?

The volunteers are usually the members of the villages. There is no operation cost, no incentive required for community volunteers as they are willing to work for their own communities.

Q2. Malaysia established the static malaria post which is very cost effective. Is there any research on economic analysis?

Yes, costing and analysis was conducted but not readily available because it was done by a different section.

Q3. Can you explain about the process of surveillance and outbreak management in unreachable areas?

For malaria surveillance, the sub-sector officer collects the information and data and reports to the head office in the urban areas. The sub sector officers screen the malaria cases and regularly report the cases. They are also given targets to achieve and need justification for not reaching the targets

Day Two - Overview & objectives: To policy and towards optimized implementation

Session Three: Priorities and Options Assessment

Session Chair: Dr Prayuth Sudathip, Department of Disease Control, Ministry of Health Thailand

The objective of the session is to understand the priorities in eliminating malaria in the Asia Pacific region.

3.1. Outcomes and Action points: Introduction to a prioritization framework for vivax elimination in the Asia Pacific Region

Dr Caroline Lynch, Regional Adviser, Medicines for Malaria Venture

- There is a need for a systematic framework to prioritise actions to accelerate vivax elimination for countries to meet their 2030 elimination targets
- We make many assumptions about what will happen through our activities, this framework identifies those assumptions and allows stakeholders to rank how important addressing them are to eliminating malaria.

Action points

- Contact NMPs and stakeholders across the region to undertaking prioritisation exercise.

What are we doing to prioritise vivax activities?

- To achieve the 2030 vivax malaria elimination goal, it is important to ensure patients have access to optimized case management, which can be by improving the current set of tools, or by integrating new tools to the treatment algorithm in the WHO Guidelines.
- To realize this, it is important that health workers have the capacity to provide optimal case management. This in turn is based on identifying mechanisms to improve the use of current tools or to revise policies to incorporate new ones.

How are we capturing key priorities?

- Using a Theory of Change approach, key assumptions and grey areas between the inputs, outputs, outcomes and impact that are not acknowledged but expected to be in place for implementation, have been identified.
- It is important to identify where this “magic of implementation” is expected to happen in the vivax elimination pathway to properly identify potential risks to the activities and expected impact.
- Based on the group work on day one, some risk areas included assumptions of timely procurement processes and health workers having capacity for the tools available.

- These assumptions have been converted into questions which are ranked by stakeholders to identify knowledge gaps, common priorities and gaps across the region, or between countries at different stages of malaria elimination.
- NMPs across the Asia-Pacific, as well as researchers, Civil Society Organisations, and other key stakeholders will be requested to rank their priorities, or add additional risks they feel are important for national programs to address.

What is the output of this work?

- The expected output will be a list of questions most important to NMPs and partners to address to achieve vivax elimination, to identify knowledge or information gaps, and to identify commonalities between regions and sub-regions, and divergences between stakeholders.

Next Steps

- APMEN VxWG will contact NMPs and key partners over the coming months to add key assumptions that may be missing. The information will then be made accessible to address key questions through the APMEN VxWG where possible, and also to collate evidence, address knowledge gaps, and amplify for advocacy.

3.2. Poll Results – priority questions for new tools

Most of the respondents rated 'very important' to understand the adherence to treatment, reliability of quantitative G6PD point-of-care tests, efficacy and safety of Tafenoquine, value and acceptability of new tools, and perceptions of affordability of these new tools.

TABLE 2: POLL RESULTS IN RESPONSE TO THE QUESTION 'WHAT NEW TOOLS ARE IMPORTANT FOR YOU TO HAVE MORE INFORMATION ABOUT?'

	How important to understand the following to achieve vivax elimination? (n=75)	Not important	Slightly Important	Important	Fairly Important	Very important	Don't know
1.	Whether health service providers at different levels of the health system can **adhere to treatment protocols** that include new radical cure tools?	15%	7%	1%	**16%**	**61%**	0
2.	**How reliable are quantitative G6PD** point-of-care tests under real-life conditions?	12%	11%	23%	**23%**	**27%**	5%
3.	The **efficacy and safety of Tafenoquine** with different ACT blood-stage treatments?	9%	12%	23%	**24%**	**27%**	5%
4.	Whether **Health workers and patients value and accept new Vivax radical cure tools**?	12%	12%	16%	**24%**	**33%**	3%
5.	NMP and financing partners **perceptions of affordability** of new tools?	8%	8%	17%	**25%**	**33%**	8%

Session Four: Policy and Options

Session Chair: Dr Neena Valecha, WHO Malaria Regional Advisor – SEARO

The objective of the session is to understand the policy changing process in regional countries, and to introduce the Options assessment toolkit.

4.1. Outcomes, considerations and action points

Key points and outcomes

- Streamlined policy processes can help achieve elimination targets by speeding up the adoption of new tools and treatment options.
- Timelines for policy change at country level can vary between 3 months and 3 years.
- Identifying causes of lengthier policy change processes can also help reduce future delays when introducing new tools.
- Most countries depended on WHO recommendation, thus there will be a tighter deadline for implementation of revised vivax recommendations once those are available.
- APMEN, the Menzies School of Health Research, and the Medicines for Malaria Venture (MMV) are jointly developing an Options Assessment Toolkit to assist NMPs in assessing their options for radical cure tools. The OAT will also consider the factors feeding into making policy change.
- Different factors are involved in policy change, and are not limited to the malaria burden, vivax epidemiology or countries' elimination stage, and considers health systems and training capacities, political and economic factors and the ability or willingness to adapt to new changes.

Action points

- Document policy processes across countries in the Asia Pacific where programs want to change policy in the next 2-3 years.
- Determine previous causes of delays and help national programs determine how they can mitigate those delays in the future.
- Identify 2-3 country National Programs that may be interested in developing the OAT with Menzies, APMEN and MMV.

4.2. Opening the black box of policy

Ms Varunika Ruwanpura, Menzies school of Health Research

Methods

- Research was undertaken in seven Asia-Pacific countries to better understand how national malaria policy-making processes currently work, and to identify aspects that can be streamlined and improved to speed up the processes.

- The seven countries had diverse socio-economic statuses, population size and funding sources for malaria. The malaria policy processes were mainly garnered from proxy documentation, such as terms of references for technical working groups.

Findings

- Ideally, the health policy formulation process should be more transparent, timely and evidence-based, and keep in view the context, the types of actors, and processes involved in each step.
- A regular review of the policy making process, (e.g. on a six-monthly or annual basis), can help improve the policy formulation process.
- Standard health ministry processes for policy change were unclear from the perspectives of national malaria programs. This highlights the need for most policy formulation processes to have more clarity and specificity.
- Historically, the time between availability of evidence and achieving policy change takes 7-10 years, meaning the new tools may only be available for implementation after 2030. Streamlined policy processes can help achieve elimination targets by speeding up the adoption of new tools and treatment options.
- One key difference among the study countries was that the timeline for changing malaria policy varied from three months to three years.
- Better documented, clearer and more transparent malaria policy processes can potentially improve and speed up the policy process.
- Setting up a standard policy process within the Ministry of Health framework can give NMPs access to clearer guidelines for policy decision making.

Most countries depended on WHO recommendation, thus there will be a tighter deadline for implementation of revised vivax recommendations once those are available.

Conclusions

- Identifying causes of lengthier policy change processes can also help reduce future delays when introducing new tools.

4.3. How to decide between all options for vivax radical cure

Dr Manash Shrestha, Technical coordinator, APMEN Vivax Working Group

What is an Options Assessment Toolkit?

- APMEN, the Menzies School of Health Research, and the Medicines for Malaria Venture (MMV) are jointly developing an Options Assessment Toolkit (OAT) to assist NMPs in assessing their options for radical cure tools. The OAT will also consider the factors feeding into making policy change.
- Different factors are involved in policy change, and are not limited to the malaria burden, vivax epidemiology or countries' elimination stage, and considers health systems and training capacities, and the ability to adapt to new changes.
- The objectives are to determine which radical cure tool combinations are available, create epidemiological and contextual scenarios that are reflective of vivax endemic countries in the Asia

Pacific to identify the optimal set of radical cure tools that can be used in each scenario, to determine specifications of tools required for the different scenarios, develop the OAT in consultation with experts using an adapted Delphi-process and based on available literature, and to test and apply the OAT among the Asia Pacific NMPs preferably by the next APMEN meeting.

Why develop an Options Assessment Toolkit?

- The toolkit will help tailor and adapt WHO guidelines to the local context, help prime the systems to incorporate new tools coming onstream over a short period, increase the influence of evidence in policy adoption, identify non-technical factors, and proactively develop the tools to align with WHO normative guidance.

What is the timeline for toolkit development?

- The toolkit is currently in pre-development, with finalization planned for May-July 2022. Pre-development involves recruiting key people, reviewing toolkit development methods, identifying variables and protocol submission to Menzies ethics committee.
- The development stage will include detailed literature review, determining the measurability and priority of initial variables with NMPs, develop 4-5 scenarios, and consult regional experts to match the combinations of tools with the scenarios.
- The testing phase will trial the combinations' feasibility, a matrix to guide NMPs systematically assess the options, costing the funding requirements for each tool, and determining remaining policy uncertainties will be done.
- In the finalization stage, there will be a step-by-step framework, a landscape template, and a weighing tool for NMPs to assign weightage to variables, and a matrix with validated criteria and options. The toolkit is planned for piloting at the 2022 APMEN meeting.

Next steps

Using a comprehensive participatory approach, the toolkit development will include consultations with the NMPs in 2-3 countries, the recently formed APMEN Vivax Working Group Advisory Council, regional and global experts, and methodologists/people experienced in toolkit development.

4.4. Questions, answers, comments and points to consider

Q1. How to decrease the policy change timeline and what were the reasons for the delay?

A: The research was mainly exploratory and descriptive, and did not cover the reasons for delays in the policy pathway, which is planned for future research. On how this can be done quicker, it is quite different to compare the reasons across different policy processes, as policy has to be interpreted and changed with the country's context and difficulties. The national authorities know best on how to speed up the process, and the mapping is meant to show that better documenting the processes can be an approach.

Q2. Forty participants from NMPs were contacted but only seven were interviewed. Was there hesitation or information not available for such a participation rate in the study?

Seventeen NMPs were at the meeting, and seven came back on further request. There were mixed reasons – especially time availability and interests. The researchers also did not push much to get a big group due to the volume of work involved.

Q3. Will you be concentrating on the same countries, or will the study expand to cover other countries?

A: Latin America will be very interesting to study, as it is very different from the Asia Pacific region. This is something worth looking into. Under the **PAVE** Initiative, MMV and PATH are doing policy mapping in Latin America to identify policy pathways and bottlenecks to reduce delays.

Q4. How is the effort to develop the OAT going to recruit key people and identify those who have relevant expertise?

A: There will be a call for applications to hire a consultant, a scenario developer, and this is likely to be a post-doctoral position at the Menzies school. There will be a detailed post coming out on this in a short while.

Q5. Will the OAT development timeline coincide with the Global Fund application round?

A: The APMEN VxWG is waiting for the WHO's recommendations, and will try to make the timelines align as much as possible with the Global Fund application. Having an idea of all the timelines will be good to fit in the OAT development timeline.

Q6. Whenever any tool is to be used, there are other considerations beside its effectiveness, such as political issues, heterogeneity, lack of a uniform policy and cost implications. How is the OAT development process taking those into consideration?

A: There are many different factors beyond health that feed into health policy making. However, it is difficult to measure non-technical components such as political will and commitment. These can perhaps be assessed qualitatively through statements of policymakers, or tangibly if there are plans in place or available funding. However, this does not reflect the strength or efficacy of commitment, and a composite indicator may be a way forward.

Q7. Is there any specific mechanism what will better focus the attention of senior political leaders?

A: APMEN VxWG will try to engage APLMA on the matter, and already has close collaboration. There work will be tied-in and APLMA will be a key member of the OAT development effort.

Session Five: G6PD Testing and Patient Adherence

Session Chair: Dr Lek Dysoley, Deputy Director, National Center for Parasitology, Entomology and Malaria Control (CNM), Cambodia

The objective of the session is to share experience on improving current practice, based on findings in Sri Lanka, Bangladesh, Lao PDR and Thailand.

5.1. Outcomes, considerations and action points

Primaquine, adherence and elimination

- Primaquine is not a bar to elimination, but elimination – countries should work on improving adherence and coverage. Now is not the time to wait for new tools – improve current tools while new tools are coming online.
- Elimination will be made much easier, especially with vivax, if there was a safer and more effective tool than PQ14.
- Efficacy of any tool tends to deteriorate with implementation level due to various factors – this is the case for PQ14, the WHO-recommended therapy for vivax radical cure.
- Many published studies show considerable variation on patient adherence to PQ14, ranging from 44% up to 98%.
- Individual patient counselling and medical supervision stand out for impact on patient adherence
- As the caseload declines, improving PQ adherence is important and necessary through supervision, improved treatment and DOTs.
- A strong community health workforce is necessary for malaria elimination.

G6PD testing

- Where G6PD testing is being used, vivax radical cure has been strengthened since the arrival, but there is a lot more to be done to improve test proficiency. Ease-of-use is an issue, especially in remote areas where health workers lack proper training and background.
- When deploying G6PD tests, NMPs will need to consider their priority areas based on vivax incidence, the type and level of health facilities, the quality of health staff and available testing equipment
- Proper training is important for effective use of quantitative G6PD tests, and points to consider include targeted trainees; group organization; theoretical and practical training including step-by-step procedures, results interpretation, assessments including evaluation and competency testing, and continuous monitoring.
- NMPs can also utilize online tools such as PAVE and the G6PD Operational Research Community of Practice (GORCoP).

5.2. Patient adherence to P. vivax radical cure

Dr Kamini Mendis, Independent consultant, Sri Lanka

Primaquine and adherence

- PQ14, is the WHO recommended therapy, has very high efficacy to prevent relapses but real-world effectiveness may be much lower due to poor adherence. Efficacy of any tool tends to deteriorate with implementation level due to various factors.
- Many published studies show considerable variation on patient adherence to PQ14, ranging from 44% up to 98%. The effect has ranged from no effect on relapses when unsupervised, to being equally effective when both supervised and unsupervised. Such variation is due to the conditions under which the medicines were dispensed to the patients. In some studies, the patient was given detailed instructions whereas others gave the medicines without any instructions.
- When individual patient counselling was done well, the outcomes as measured by either adherence or relapse rates have been reasonably good.
- Several interventions such as improved packaging, individual patient counselling, visual media, a combination of visual media and verbal instructions, community education training for healthcare workers, supervision, SMS and DOTs, convenient drug regimens and better drug formulations have been associated with increased adherence. Individual patient counselling and medical supervision stood out for impact.

Sri Lanka's elimination experience.

- In the early part of the elimination effort, the country relied on vector control combined with early diagnosis and treatment at wide coverage, which were powerful and effective tools. Sri Lanka did not place much emphasis on improving PQ14 adherence as it could not spare manpower due to the heavy malaria burden.
- But as case numbers declined after 2005, things changed with vivax becoming the main form of malaria. There was an outbreak of vivax malaria in army camps in the context of the Sri Lankan civil war, with soldiers bringing back malaria to their hometowns across the country. The reason for the increase was due to a large increase of the vectors in the river flowing near the army camps. The outbreak was brought under complete control through many methods, including widespread larviciding of the aforementioned river alongside advocacy to the soldiers.
- The soldiers were initially treated with 3-day chloroquine and were allowed to go home on leave with PQ14 with counselling. However, there was a policy change, where infected soldiers were kept in the barracks for 14 days and PQ was given as DOTs. From this point onwards, all infected persons were given PQ as DOTs.
- The shift towards giving PQ14 as DOTs to all infected persons was one of the important factors in Sri Lanka's elimination approach.
- When the caseload is low, improving adherence to PQ is important and necessary through supervision, improved treatment and DOTs. In the elimination phase, the emphasis is on individual cases and detailed case investigations, hospitalization for every case, and supervised PQ treatment and DOTs is feasible with negligible additional cost. Most importantly, a strong community health workforce is necessary for malaria elimination.

> ***"Adherence to primaquine has not been a bar to malaria elimination up to this point."***
>
> **Dr Kamini Mendis**

5.3. Implementing Point-of-Care G6PD tests – early experiences from Bangladesh, Cambodia, Lao PDR and Thailand

Dr Chansuda Wongsrichanalai, Independent consultant, Thailand

When deploying G6PD tests, NMPs will need to consider their priority areas based on vivax incidence, the type and level of health facilities, the quality of health staff and available testing equipment.

- Further down the endemic area, as some facilities are remote and poor, deployment will need to be considered on a case-by-case basis. At the village malaria worker level, the current quantitative G6PD test is not recommended.
- There is a constraint of access, as at the hospital level, there are few malaria cases. Therefore, it is easier to conduct the tests whereas there are much more malaria patients at remote facilities where testing is difficult.
- Proper training is important for effective use of the quantitative G6PD tests, and points to consider include: targeted trainees; group organization; theoretical and practical training including step-by-step procedures; results interpretation; assessments including evaluation and competency testing; and continuous monitoring through supervisory visits.
- The ratio of trainer to trainee is also important, with the sessions in Cambodia and Lao PDR having three to five participants to one analyzer during the practice, though a better ratio may be needed for participants requiring additional attention.
- There are some concerns from the study on real world implementation which indicate the possible need for refresher training.
- Commodity expiry is also an issue, due to both the shelf-life of the test strips and reagents as well as the fixed grouping of 1 code chip that cannot be are under discussion with the manufacturer in collaboration with PATH.
- Radical cure has been strengthened since the arrival of quantitative G6PD testing, but there is a lot more to be done to improve test proficiency. Ease-of-use is an issue, especially in remote areas where health workers lack proper training and background.
- Regional collaboration among NMPs is needed to accelerate expansion of use, and to utilize online tools such as **PAVE** and G6PD Operational Research Community of Practice (GORCoP).

5.4. Question, answers & comments with and from participants

Q1. At what point or caseload is it feasible for countries to implement to ensure a high level of coverage?

A: There is no fixed threshold to decide when it is feasible for individual countries to ensure a high level of coverage. It depends on the country and its health system's capacity. Countries will judge when it is possible to do detailed counselling due to the caseloads and capacity, and will shift approaches as such.

Q2. Given the challenges posed by the COVID-19 pandemic, what is the feasibility of implementing DOTs in terms of both financing and the burden on the health worker?

A: When the caseload is high, it is a huge burden and it is not possible to do DOTs. But as countries progress towards the end stages of elimination, it is absolutely necessary to prevent relapse. Countries should not

start bothering about DOTs until they reach a low level of cases when it becomes relevant and possible. Before that, they should use vector control, early diagnosis and treatment at wide coverage to bring down the caseload. Then the health workers will have more time to do DOTS, supervised treatment and patient counselling. As clinics will no longer have many patients, they can spare the time and resources to do DOTs.

Q3. Is there any place for regimen like PQ7 and Tafenoquine given in that context?

A: There is potential for improving the situation. Primaquine is not a bar to elimination but elimination will be made much easier, especially with vivax, if there was a safer and more effective tool than PQ14. There is a need for a better tool. TQ, if it can be delivered safely, will improve the situation. And if the evidence is available, PQ7 will halve the problem, as it goes from 14 days to 7 days. But countries do not need to wait until then. Countries in GMS and elsewhere have already done very well to bring down the malaria burden. But now is not the time to wait for something. If a new tool comes, countries will have to adopt it soon.

Q4. Do you know of any modification in the Quantitative G6PD procedure that has been made in the field and how it might affect the test result?

A: For example, the test device is supposed to be inserted into the analyzer before collecting finger-prick blood. Some want to modify this step by collecting blood specimen first, mix blood with the buffer and set aside, then inserting the test device into the analyzer. This is not right as the blood-buffer mixture needs to be transferred to the sample hole of the test device in the analyzer immediately. Enzyme reaction begins right away when we mix blood with buffer. If we wait, the analyzer may not measure G6PD enzyme activity at the optimal reaction time.

Q5. If tafenoquine can only be given to those with over 70 % G6DP activity, what can be done for those with activity between 30% and 70%? This would mean prescribing different drug regimens which complicates the activity and not just the use of the diagnostic tool.

A: Tafenoquine is prescribed to those with >=70% G6PD enzyme activity. Those with intermediate G6PD activity should be given primaquine for radical cure according to the local treatment guideline. Tafenoquine does not 'replace' primaquine. Treatment regimens will become more complicated. But if, for example, 5% of those tested for G6PD are found to have under 70% activity, then 95% of them can take the single dose tafenoquine DOT before leaving the clinic and we do not have to worry about their adherence to daily primaquine x14 days.

Responding to Comments on training

Comments:

"*Trainings are challenging during COVID-19 pandemic. Please consider seriously.*"

"*Virtual training is the most common during (the) pandemic*."

"Even with the virtual one, it's still challenging for the practical assessment."

Virtual training for quantitative G6PD testing does not seem practical and measuring its effectiveness is difficult. NMPs need to consult among local experts how to handle the situation based on the local context

and COVID-19 situation. If there are local trainers available, and Qn-G6PD test has already been introduced to the area, it might be possible to continue with occasional re-fresher training of the local trainers by trainers from the central level via videoconference. But training a whole new group virtually is indeed a challenge.

Day 3: Towards Optimized Implementation

Session Six: Show me the 'vivax' – access strategies

Session Chair: Mr Leo Makita, Department of Health, PNG

The objective of the session is to discuss access issues and strategies on reaching vivax patients, and on engaging other sectors.

6.1. Approaches to achieve access: Outcomes, considerations and action points

- Diagnostics are often unavailable, inaccessible and underutilised even when there is capacity.
- Diagnostic Network Optimization (DNO) is a potentially cost-effective approach to deploying diagnostics to the places where they can achieve highest impact for least cost.
- By optimizing the testing network, more patient samples are projected to be tested and more patients are getting diagnosed and to achieve operational efficiency.
- FIND is working with one Ministry of Health to pilot the system for G6PD test and if successful, it will be made more broadly available so that NMP partners can implement it directly with country data.

Multisectoral approaches

- Up until now, malaria has been dealt with by programs but it needs to be a multisectoral and community approach as malaria control work requires a lot of components (e.g. logistics) and therefore having a multisectoral approach one can achieve a lot more rather than just focusing on health.
- Multisectoral commitment is essential which needs strong efforts and coordination.
- In PNG, the trilateral project brings together government departments in Papua New Guinea for the first time, including the Department of Health, Foreign Affairs, National Department of Health, Central Public Health Laboratory, Institute of Medical Research, School of Medicine, and the Provincial Health Authorities. Similarly, the project, brings together different governmental departments in China and Australia.
- Key focal populations can be targeted through multisectoral activities including; high risk populations and communities; groups with risky professions such as the military and mining; and remote farming communities. There is also an opportunity to work through nutrition and school programs to ensure high malaria coverage among children, pregnant women and migratory populations.
- In sub-Saharan Africa, the Advocacy & Resource Mobilisation Partner Committee (ARMPC) have recently developed and released guidance on multisectoral engagement.

Working with remote populations

- Work with local people who have the local knowledge, local culture and the local language as they are seen as the driving forces amongst their peers and the proximity to the health center.

- For forest-going populations, Mobile Malaria Workers (MMWs) can cover treatment of 3-7-14 day follow-up and can shed light on how to increase treatment through community dialogues.

APMEN VxWG Action points

- Work closely with CSO partners to understand their work on mapping policies and processes for community level access
- Collate, or advocate to partners to collate, evidence and develop evidence briefs on proven interventions to increase access for remote populations, patient adherence and referral completion.
- Document best practices identified by NMPs and partners as increasing access at community level
- Provide briefs to partners on Higher Sensitivity Rapid Diagnostic Tests for Pf/Pv and G6PD tests
- Provide more information to NMPs and partners on ongoing and planned feasibility studies investigating the use of 8AQs and G6PD testing at different levels of the health system
- APLMA action points: To identify and facilitate the establishment of multisectoral national taskforces, to support CSO advocacy for case management at community levels and facilitate cross-border discussions and research collaboration.

6.2. Diagnostic Network Optimization – Informing the roll out of G6PD testing

Dr Rosalind Howes, FIND

Diagnostics are critical to the healthcare systems and accurate diagnosis ensures the right care for patients, informs surveillance which is a key role in global health security. However, diagnostics are unavailable, inaccessible, and underutilized even when there is capacity.

- To achieve impact, testing must be accessible to the patients who need it, identifying gaps in the health system (i.e. where to position diagnostic capacity geographically within the region).
- The more availability of testing sites, the better the coverage but at a higher cost. So diagnostic network planning is based on manual methods and expert consensus with advantages but it can lead to limited objectivity with respect to some of the trade-offs.
- There has been a move towards a more analytics-based approach namely Diagnostic Network Optimization (DNO). The demand for testing with local capacity to improve access is seen to be the most cost-effective approach.
- In the Philippines, DNO analysis is performed for TB testing capacity across the country. The key issues are: 1) how to improve the usage of existing GeneXpert testing network; and 2) how to increase testing coverage. In western Kenya, the DNO scenario aims to scale up testing coverage and increase demand by accessing missing cases.
- The DNO analysis helps to identify the diagnostic gaps and fill these gaps either by improving sample referral networks associated with each site, or by recommending additional new GeneXpert devices.
- By optimizing the testing network, more patient samples are projected to be tested and more patients are getting diagnosed and to achieve operational efficiency.

- As there was a strong need for making these DNO analysis more widely available, FIND partnered with LLamasoft to develop OptiDx which is a bespoke DNO software funded by Gate Foundation and USAID, which will be made freely available for Ministry of Health teams.
- The relevance to vivax and quantitative G6PD testing is that DNO framework is highly flexible to accommodate countries with different constraints (e.g. low vivax case numbers lead to a lower demand for G6PD testing and therefore there is a risk of wasting tests) with either Primaquine or Tafenoquine (e.g. mobile migrant population on motorbikes).
- The DNO model can define utilization and cost effectiveness scenarios and to make a comparison for a more optimal strategy to help to understand the feasibility of introducing G6PD testing and to anticipate the broader system requirements in advance of policy changes bringing in new radical cure tools and to budget for future procurement requirements.

Next steps: FIND is working with one Ministry of Health to pilot the system for G6PD test and if successful, it will be made more broadly available so that NMP partners can implement it directly with country data.

6.3. Lightening talks

6.3.1. Integrated Activities to Detect and Prevent Malaria Disease

Dr Isaac Quaye, RBM Multisectoral Working Group

In most cases in Africa, there is passive or active case detection for febrile patients presented at the clinic or during outreach activities of the community health workers. And data on incidence can be accessed in active MIS or DHS studies of the national malaria control program, to scale up case detection, treatment, and prevention towards the goal of elimination phase in Africa and southern Africa.

The incidence of malaria is largely heterogeneous and it is important to understand geospatial transmission. In most cases in Africa, cases are detected passively/active-passively through community health workers and health facilities or actively in surveys or following outbreaks.

- Africa is focused on *P. falciparum* as a main agent, however, as *P. vivax* is becoming a problem, the Pan African P. vivax and Ovale Society has been able to work on drawing people's attention to the African continent to be able to achieve the Sustainable Development Goals or the Global Technical Strategy (GTS) goals, for malaria elimination.
- There are key focal populations targeted with multisectoral activities include; 1) high risk populations and communities; groups with risky professions such as the military and mining; the remote farming communities for example, Japan's engagement to increase rice production. Opportunities are also explored to assist with malaria prevention and implement key nutrition interventions for vulnerable populations (e.g. among school children, and pregnant women, and migratory populations) in Africa.
- The recommended path for countries includes: 1) advocacy for multisectoral activities and then implementation of the ARMPC guide which was recently released; 2) involvement of the End Malaria Councils to be able to engage in leadership, financing and tools for their activities; and, 3) access to RBM website for guidelines which outlines specific malaria activities in a multisectoral approach.

6.3.2. Expanding Mobile Malaria Services to Hard-to-Reach communities in Northern Cambodia

Mr Lieven Vernaeve, Malaria Consortium, Cambodia

The goal of the project is to ensure that malaria services are expanded and are available to the remote areas including mobile and migrant populations and forest goers in remote northern Cambodia which borders Laos, Thailand and Vietnam.

- As most of the malaria cases are situated in the forest areas with small family plantations, mobile malaria services are provided to these hard-to-reach communities by training local MMWs who are supported by MC staff to increase early detection and treatment. There are 85 mobile malaria workers working in 6 provinces along the border areas.
- Some work in malaria posts which are open seven days a week with two 2 mobile malaria workers in place at exits and entries of forests or forested areas where testing, health education, and distribution of bednets can be carried out.
- Other mobile malaria workers conduct monthly outreach activities at selected places where there are plantation workers in the forest and stay overnight if required. Co-track alert investigations are conducted for *P. falciparum* or mixed cases.
- During the first six months of 2021, MMWs with the local communities were able to carry out more than 28,000 RDT tests and although the positivity rate is relatively low for Pf and mixed cases, there are more Pv cases. As Cambodia is in the elimination phase, the country is focusing more on vivax cases.
- The main message is to work with local people who have the local knowledge, local culture and the local language as they are seen as the driving forces amongst their peers and the proximity to the health center.
- MMWs can also cover treatment of 3-7-14 day follow-up and can shed light on how to increase treatment in community dialogues.
- Distance is a challenge for MMWs as they need to go far to conduct the 14-day treatment for radical cure.

Suggestions include: 1) the possibility of deploying mobile nurses to go to the hotspots for G6PD; and 2) train MMWs to perform G6PD testing in those specific hotspots.

6.3.3. Australia, China and Papua New Guinea trilateral collaboration on Malaria and Health Security

Mr Leo Makita, National Malaria and Vector Control Program, Ministry of Health, PNG

The trilateral collaboration partnership that was developed with Australia, China and PNG where Australia provides the funding, China provides support and PNG is the beneficiary.

- The project is founded on a partnership model consisting of a three-tiered governance structure with representation from all countries at each level (i.e. high-level government, technical directors and a project management unit).
- The project brought together relevant government departments in Papua New Guinea for the first time, including the Department of Health, Foreign Affairs, National Department of Health, Central

Public Health Laboratory, Institute of Medical Research, School of Medicine, and the Provincial Health Authorities.

- In China, the partners include the Ministry of Commerce, the National Health Commission, and the National Institute of Parasitic Diseases.
- In Australia, partners include the Department of Foreign Affairs and Trade, Burnett Institute, the Australian Defence for malaria and Infectious Disease Institute.
- This partnership model is seen as a successful model for a multisectoral approach to malaria elimination.

6.4. Questions, answers, comments and points to consider

Q1. What data would you need to go to country programs? Is there data that you must have or other data that's not necessary that would strengthen the model? When are studies needed on geospatial location and testing sites?

For accessibility networks, (i.e. how long it would take from A to B), that data is all inbuilt into the model and is already using existing data sources. The countries would need to define information regarding specific testing sites, where vivax cases are being reported from, possible sites for implementing G6PD tests, and the number of cases. The Ministries of Health would have good databases on where the facilities are across the countries. Optimization models could easily be included and the GPS coordinates for those health facilities. One of the assumptions is that the burden would be stable over time. Case monitoring by the Ministries of Health (e.g. from previous 3 years) to do risk mapping assuming that risk is fairly stable over time would be important. Other data would include the cost of implementation but it should be all data that is routinely available.

Q2. The data for health facilities may (or may not be) available, however, community sites geolocalization may be more difficult to obtain. Are you collaborating with other initiatives that may be mapping activities for other purposes (i.e. other disease programs, vector control, phone networks etc.)?

MoH has had the health facility data. In cases where it is not available, health facility GPS data can be obtained from various online sources - the Malaria Atlas Project have previously collated these for example, whilst acknowledging that community posts will be harder to map. This may require working with local teams (MoH/district level/NGOs) to help to map these out. This is a potential challenge ahead.

Q3. How does high-level partnership increase access to vivax patients at community level – either directly or indirectly?

A: This project is directly involved in the issues of vivax since there are collaborators working on the issue of G6PD testing, short course vivax treatment, 14 to 7 days to form policy which is a direct benefit of this vivax partnership.

Q4. How do the teams build trust with communities and how long does it take?

MC makes a point to choose community members, i.e. local people selected by the community and the process does not take long. The most important step is the introduction of the project and the introduction of staff supporting the mobile malaria workers. However, the selection is also based on local knowledge, local language skills which is seen as a step closer to the health center as well as the communities to jointly identify the potential mobile malaria workers. In this way, trust is built up quickly.

Q5. Do migrant patterns shift regularly and how do you plan for this?

Planning is difficult but what needs to be done is to do close monitoring. In order to support MMWs, there are monthly meetings, together with a strong monitoring system, and the networks in the communities. The community or the networks are the most important source of information in order to keep up with the movement of people. These occupational movements (legal or illegal) are changing fast due to the season, or the increased number of rangers trying to protect the forests. Therefore, it is important to keep the same mobile malaria workers but areas can be adjusted for screening to take place. An outbreak of malaria in a completely different location has implications for reporting in the MIS system and for coordination with the National Malaria Program.

Q6. Can you describe how the community dialogues are being used to increase uptake as radical treatment as recommended by Dr Kamini Mendis?

Community dialogues are in its first phase and the initial steps are being supported by MC staff. In the second phase, MC staff will train community volunteers regarding the advantages and disadvantages of regular testing for *P. vivax and* the risks and possible solution to radical cure. Discussions are guided by the community facilitators but they leave it up to the community to come up with the solutions. It is a different approach than being directive about radical cure and the approach taken through the community volunteers. Most of the communities have resources to find their own solutions.

Q7. Can you share about compensation mechanisms and any challenges with sustainability?

Mobile and village malaria workers receive some compensation (e.g. USD 5 a day plus transport cost and meeting attendance), which is aligned with the national program compensation rates. On sustainability, MMWs working in plantations in big companies get integrated into the broader national malaria program at a time of project closure, is seen as a good approach for sustainability. On the other hand, MC is making a lot of investment in closely monitoring the MMWs, who are well trained by the health center staff and this investment could be reduced if it gets integrated into a national program without proper financial support. Therefore, it is important to decide on when and where to use this methodology for the country with well-defined goals and objectives. MC's work along the border areas (e.g. 10 km area) tied to specific objectives is due to considerations for the distance and accessibility to the health centers (50km or more). Sustainability should be questioned if the objective is met in the targeted area.

Q8. What do our NMCP colleagues think about the feasibility of a multisectoral End Malaria Council to facilitate progress towards elimination?

In general, malaria has been dealt with by programs but it needs to be a multisectoral approach and even a community approach as malaria control work requires a lot of components (e.g. logistics) and therefore having a multisectoral approach one can achieve a lot more rather than just focusing on health. Dr Hamida Hamid also noted that feasibility multisectoral 'end malaria' council or forum is a good idea but multisectoral commitment is essential which needs strong efforts and coordination.

Session Seven - Groupwork: Strategies to increase access to radical cure amongst remote populations

Chair: Dr Hamida Hamid, Ministry of Public Health, Afghanistan

Facilitator: Yucheng Tsai, Clinton Health Access Initiative

At the start of the session, Dr Hamida highlighted that improving security, addressing geographic barriers to access, and strategies are needed to increase radical cure access in remote populations.

The objective of the session was to identify and learn about current strategies to increase access to vivax diagnostics and treatment.

Participants were divided into groups and asked to discuss five topics:

- Strategies to increase access to vivax case management among remote, mobile or hard-to-reach populations;
- Approaches to increase coverage of vivax case management;
- Innovative strategies or research on access;
- Ways to improve access to vivax diagnosis, treatment and care among most at risk communities;
- Ways to leverage multisectoral collaborations to increase access.

Transcripts of the discussions were coded and out of those discussions six key themes emerged that broadly aligned with the discussion topics, these were; target populations, key challenges, country strategies to increase access, country needs and planned research/innovation.

7.1. Outcomes, considerations and action points

"There is a need for CSO and partners to place more focus on the 'soft side' i.e. integration of services, recognising volunteer systems and assessing implementation in addition to the hard science such as TQ and new technologies." Professor Maxine Whittaker

- Access strategies must include community level health workers. However, there is sometimes tension between what programs can legally do within a health system, and the ideal for increasing access at community levels.
- Remote and mobile populations need to be disentangled to identify internal migrants among mobile groups

- Partners use several strategies to increase access to vivax radical cure including; community case management, community referral, border post screening and touchpoints for forest goers, surges in health worker capacity during seasonal increases in transmission, mobile clinics, partner engagement, neonatal G6PD screening, modified elimination strategies and multisectoral collaboration.
- NMPs and partners face key challenges including strategies to increase patient adherence, access and referral, testing and treatment by non-clinical health workers, availability of vivax radical cure tools where patients present for care, control of malaria at border areas, and conflict and insecurity.
- Partners expressed the need for more information, evidence collation and operational research on the feasibility of using 8-AQs and quantitative testing at different levels of the health system.

Action points

- Document partner strategies for improving access of vivax radical cure to remote and mobile populations.
- Collate and develop evidence briefs on access strategies to remote and mobile populations.

7.2. Country discussions on access strategies and key challenges

In all, 13 countries[9] took part in discussions about strategies to increase access to vivax radical cure among remote, mobile and hard-to-reach populations. Some groups also discussed access from a regional perspective.

There was consensus that **access strategies must include community level health workers** and/or peripheral facilities in coordination with community workers. Some participants expressed the need for community level case management, whereas others suggested that peripheral health facilities be trained in testing and treating with community health workers trained for patient follow-up. Mobile outreach, through mobile nurses trained for hotspot areas (e.g. forests) was also a strategy used in a couple of countries. Small clinics, based at community level, were used in Malaysia, but halted after it was found the strategy was not cost-effective.

7.3. Key populations

Remote, mobile or hard-to-reach population the groups discussed in relation to access to vivax radical cure. For some participants this included military populations. It was highlighted that there needs to be a clear distinction between types of migrant groups with emphasis on the need to understand internal migration routes to target circular or seasonal domestic migrants moving between high and low transmission areas.

[9] Afghanistan, Bhutan, Cambodia, Ethiopia, India, Indonesia, Malaysia, Myanmar, Nepal, Pakistan, Papua New Guinea, Thailand and Vietnam.

7.4. Country strategies to increase access among remote, mobile or hard-to-reach populations

Community case management - Several countries utilise Community Based Malaria Management where volunteers test and treat patients with malaria. In some cases, diagnosis of patients is double-checked by higher level facilities before community level treatment.

Community referral - Most countries draw on community health workers to refer patients to the formal health system. This approach is not specific to vivax malaria, but involves identifying patients and either actively bringing them to the next level of the health system using an incentive for community workers (e.g. India), or requesting them to refer upwards.

Border post screening – These are used in higher burden areas along border posts and are staffed by village residents who provide testing and treatment services for malaria. However, they are not able to address adherence. Challenges for these border posts and some of the unique aspects of vivax and strategies could be strengthened.

Touch points - In Cambodia a strong network of Volunteer Malaria Workers identify patients at 'touchpoints' – places near forested areas where mobile migrants and forest goers would go to buy food and goods before entering the forests - and connect patients with health centers for provision of services including a G6PD test. Patients with multiple vivax relapses have sought advice from village malaria workers and subsequently health facilities to which they are referred.

Seasonal capacity surge - In Ethiopia, malaria transmission peaks between September and December. During this period, Regional Health Bureaus are supported with temporary health workers and clinics to provide malaria services in endemic states. The program aims specifically to address malaria among hard-to-reach communities and the workload during that period is shared by public health officers. This allows the program to be more targeted in time with resources.

Mobile clinics Have been used in Malaysia to test and treat but were determined to be cost ineffective as travel time of one week outweighed the treatment time of 2-3 days. Setting up small clinics was a more cost-effective option.

Blood surveys in rural areas In India, blood surveys were undertaken 2-3 times a year to identify any malaria patients.

Neonatal G6PD screening Several countries in the region already have neonatal G6PD screening programs the results of which they could use to guide radical cure treatment. Mothers are provided with the vaccination record and G6PD records for their children.

Community and implementing partner engagement at village and national levels was highlighted as a key factor to access remote populations. In Cambodia, for example, engagement meetings are held monthly with malaria partners to identify how to ensure access to remote populations.

Multisectoral strategies Partnerships with *private sector* business owners has been an access strategy in Malaysia where plantation owners have provided physical facilities and capital for malaria treatment activities. In other countries for engagement with the military, *Ministries of Defence* often have their own treatment guidance and engagement including border patrol police ensuring there is some alignment with the national malaria strategy. The *Ministry of Education* in several countries is important to implementing

a school-based malaria elimination strategy including Behaviour Change Communication and proactive case detection among school-going children in endemic areas.

Elimination Strategies

- **Modified 1-3-7 strategy –** in remote areas of Nepal once malaria is notified, the case is notified and investigated concurrently with the foci investigation.
- **Active case detection -** Cambodia is moving from passive to active case detection, which has a role in both Pf and Pv, with weekly house-to-house visits in endemic areas. It has moved from VMWs to mobile malaria teams to reach MMPs.

7.5. Key challenges to ensuring access to vivax radical cure

- Adherence, and especially adherence among highly mobile populations remains a key challenge for programs in the use of vivax radical cure. Thus, once those populations are accessed, ensuring their return to facilities. Relatedly, for highly mobile populations, completing supervised treatment, or verifying supervised treatment is something that continues to scupper national programs.
- With referral being a key strategy for programs, often from community level upwards, there was a sense that once patients feel better, they would not follow the referral recommendation from community volunteers.
- Availability of diagnostics and radical cure where patients are presenting - private sector utilisation is high in some countries for example, in Pakistan it is estimated that 50% of vivax patients present to private facilities. However, primaquine is available only in the private sector in Pakistan and their use of national treatment guidance is in doubt.
- While community level testing and treatment was described by some as the ideal approach, others highlighted that incorporating volunteers with no clinical training was a challenge in their health systems. For example, community malaria volunteers do not have access to primaquine and are required to refer patients to health facilities. Similarly, G6PD testing is not available at community level in Afghanistan and thus referral is the only option for community volunteers to use.
- Conflict and insecurity are factors that prevents access to facilities for patients (e.g. along the Thai-Myanmar border, Assam and West Bengal boarder areas).

7.6. NMP and partners needs

Treatment adherence: NMPs almost universally expressed the need for strategies to increase patient adherence generally, and specifically among remote and mobile populations. Emphasis from those discussions was on the need to have carefully constructed strategies that would sufficiently address gaps. Suggestions included the need for pre-packaging of blood and liver-stage treatment to improve patient adherence.

Access to remote populations: Echoing the session on discussion of access strategies, several NMPs and partners requested more information on strategies to increase access among remote populations. One suggestion was for a 'one-stop service' approach to vivax for migrants, where migrants could be screened, tested and treated in one facility rather than referred to any other levels. Additionally, participants

expressed the need to have more effective ways to track mobile migrants to ensure their access to treatment services.

Improvement of referral pathways: Given the number of countries using this as a strategy – participants felt that more information, evidence collation, or research is required to understand how to improve referral pathways.

Better diagnostic tools either to better identify species, or test for G6PD at health facility levels.

Chemoprophylaxis as a potential tool for internal migrants moving between high and low transmission areas.

Pharmacovigilance to monitor patient side effects

Better data was requested on the rate of loss of patients to follow-up and the potential impact of that on vivax transmission. It was felt that this type of information would support advocacy within the ministry of health to highlight the challenges in deploying current vivax radical cure tools. Similarly, several participants felt that data on patient follow up was important to monitor outputs related to adherence.

National or regional level **facilitation of cross-border discussions** and research collaboration was requested. In addition, participants suggested the formation of **national taskforces** spanning multiple governmental departments to support a multisectoral approach that could increase access.

Finally, **Implementation and Operational Research** requested by participants **included research on how to train Community Workers to use G6PD tests and administer radical cure** and how to involve communities more proactively in malaria elimination.

Pharmacovigilance is essential to monitor for side effects for remote populations.

Planned research known to NMPs and partners

- Several countries are planning to undertake feasibility studies to determine the use of shorter course treatments with Qn-G6PD tests at different levels of the health system including Thailand and Papua New Guinea.
- In PNG, there are plans to pilot Qn-G6PD use by outreach teams with linkages to Village Malaria Workers.
- In Nepal, work is needed to genotype malaria cases presenting at cross-border areas to identify the origin areas of the infection
- In Thailand, the DVBD is planning to investigate the potential role of focal Mass Drug Administration in active malaria foci or proactive MDA among forest goers.
- More information on planned and ongoing operational research is available at vivaxmalaria.org

7.7. Questions, answers, and comments with and from participants

Q1. Is Chemoprophylaxis (for Pf) used in Swaziland as well as they were being used for internal migration and is close to elimination phase?

Dr Kevin Baird responded by stating that Southern Africa has a serious challenging time for elimination and seems to be turning to chemoprophylaxis. In the Indonesian context, travel often reintroduces outbreaks and keeps recurring partly due to the lack of strong advocacy for domestic travel to these areas.

Q2. How are the higher-level health facilities measured? How many patients went to higher levels as requested?

Dr Soy Ty emphasized the close network of VMWs and the touch points in Cambodia. When the patient is identified, they connect to the health centers for provision of services. Based on this experience, a very high number of *P. vivax* patients reached out to health facilities. Cambodia recently started *P. vivax* radical cure, and witnessed that a number of patients who get multiple relapses reach out to the volunteers for provision of services at the health facility. This is a testament to the effectiveness of this referral mechanism but needs to be monitored closely.

Q3. Is there any advantage for MDA for those countries that are nearing malaria elimination?

The role of MDA in near elimination countries such as Malaysia is dependent on the locality to conduct MDA for malaria outbreak. The locality needs to be stable with regards to population movement. Therefore, the selection of the locality has to be flexible for comprehensive coverage. The other challenge is the use of PQ or TQ since a very accurate quantitative G6PD essay is needed. These conditions are necessary to avoid bringing the whole population to conduct G6PD testing. Given these considerations, it is not feasible to do MDA now. For Malaysia, people were brought from the locality to the facility where G6PD would be carried out. Fortunately, Malaysia was able to test for this G6PD using qualitative methods. Although a small number of people were missed out for testing (e.g. those born outside of the locality).

Q4. What is the issue in Vietnam whereby testing is not allowed by CSOs currently - is it a legal/legislation issue? Does any country have experience in changing this approach? and how?

- Jenny Kerrison (RAM): responded by saying that "task shifting" is also not allowed in Indonesia and village cadres/volunteers are not allowed to do test and treat but they have a MoH decree in place and this allows MoH to control the use of lay volunteers e.g. RAM has a small grant to train village volunteers to test, treat and educate in one border district in West Timor. Implementation is done by MoH and Provincial Health malaria managers.
- Josselyn Neukom: the range of policies (and practices) related to community level case management in the region has been discussed at several regional forums. Within the GMS, policies in countries such as Cambodia and Myanmar endorse community level case management. Learning from these examples may help other countries assess benefits and risks associated with task sharing. The CSO Platform recently recommended an independent regional review of the varying policies and practices in this area.

- Maxine Whittaker: Aceh Province in Indonesia had a multisectoral committee and embedded in the provincial development plan at the high level was eliminating malaria as a priority. When APMEN did a study tour there, it was felt that this was part of the success.

Mascot Competition

A mascot competition was held for the three-day meeting with the aim to make everyone smile. The winning pictures were selected and the award went to the flowers from Professor Maxine Whittaker and Dr Htin Kyaw Thu.

Flowers by Professor Maxine Whittaker

Flowers by Dr Htin Kyaw Thu

Closing Remarks

The three-day meeting was adjourned with closing remarks by **Dr Karma Lhazeen**, Chair of the APMEN Vivax Working Group and **Ms Amita Chebbi**, Senior Director for APMEN.

APLMA had established a Senior Official's meeting as a platform to provide this kind of engagement beyond health, beyond malaria, and to secure senior political buy-in. Dr Maxime Whittaker highlighted the fact that multisectoral collaboration needs to occur at the senior level but equally at the sub-national level to have multisectoral committees at the district level, provincial level and it is by working jointly that we can achieve the elimination goal.

There are implications for donor transitions (e.g. procurement policies), especially relevant for the GMS related to Global Fund transition out of the region by 2023 and maintaining a more modest presence and a modest level of support.

This requires follow-up and conversations that needs to take place. The 2019 meeting's outcome was the options assessment tool that the Working Group is now developing and this year's meeting will also lead to some specific outputs and outcomes in the coming days and months.

Annex One: Comments and Additional Questions from the chat box

Note: These comments and questions were made by participants through the Chatbox function. Due to the limited time available, those listed below were not answered during the annual meeting.

Day 1

Session 1

- Caroline Lynch for Dr Gonzalo: you mentioned that there are other platforms that will increase stability - could you elaborate on those? Where are they in the pipeline?
- Prudence Hamade: Have WHO developed any clear recommendations on the management of G6DP deficient people pregnant women and infants?
- Rishikesh Kumar: In your view, what are the most challenging impediments to malaria eradication in India?
- Rishikesh Kumar: What is the maximum tolerable dose of primaquine which can be given to a vivax patient with normal G6PD activity?
- Nelson Chin for Dr Neena: What is the current management approach in dealing with sub-microscopic malaria?
- Josselyn Neukom for Dr Neena: is it possible to share the average time required for each of the 3 stages of WHO's pathway?
- Kemi Tesfazghi for Dr Neena: How are we ensuring that countries are receiving the guidance as not prescriptive and that one size does not fit all?
- Abhijit Sharma for Dr Neena: I would like to know any specific guideline focusing the overlap of COVID-malaria link and any presumptive malaria treatment scenario in this context as per you?
- Josselyn Neukom for Dr Penny: Can you share more information about the expected timeline for the conclusion of the ASEAN 3-country review of TQ?
- Yucheng Tsai: Could you mention again what is the updated timeline for WHO prequalification on G6PD tests? What would be the recommendations for countries to start to use the G6PD tests at point-of-cares before it's WHO PQ? (e.g. any and what kind of QA/QC needed?)

Poster Session

- Estrella Lasry-GF: What malaria RDT is used?
- Abhijit Sharma: Any spontaneous adverse event reporting been carried out as part of the process?
- EIJKMAN _Ari Satyagraha: How do you ensure the volunteers are actually following up the patients?
- Benedikt Ley: What ratio of volunteer to population have you found to be feasible and effective?
- Win Han Oo, Burnet Institute: Do all malaria suspected clients go to government facilities when you refer? What if they are undocumented migrants? Lastly, how do you manage migrant workers to complete the 1-3-7 works? In another word, what is the success rate of 1-3-7 strategy in this area?

- Richard Kowel: Is there any specific strategy in logistic delivery for the community volunteers and malaria post?
- Tayzar Tun: How do you test G6PD deficiency in remote villages? Refer to government facilities?
- Prudence Hamade: what do you do with G6DP deficient patients?

NMP Group Work Discussion

- Prudence Hamade: Have you in Thailand found that Tafenoquine is needed or would primaquine with different dosage regimes be sufficient to achieve elimination in the next 9 years?
- Josselyn Neukom for Dr Karma and Carrie: will there be time during this meeting, or perhaps in a follow-on session to learn more about the countries that have 6-7 vivax studies planned/underway/completed? It would be interesting to see the breadth of vivax research underway in these 4 or so countries to help other countries think further about what is needed to inform optimal implementation of safe, scaled radical cure.
- Benedikt Ley: what G6PD test did you use?
- Estrella Lasry-GF: Are only symptomatic patients included or is there any active case detection?
- How is the testing done in terms of compliance to the treatment algorithm and also treatment adherence?
- Any challenge in transit into G6PD qualitative to quantitative tests or if you are mixing different kinds of tests in different areas?
- From Gonzalo Domingo to Everyone: were there any challenges transitioning from the qualitative G6PD test to the quantitative test?
- Liony Fransisca to everyone: 1. do you use mixed biosensor and RDT for diagnosis for different areas? 2. what are the Primaquine regimen used? 3. how is the treatment adherence for primaquine when you use CHW? 4. how long this has been done (for vivax) and how successful is it so far?
- Kamala Ley-Thriemer to everyone: do you have an idea on the quality of training and what level of training is needed to perform biosensor reliable? and what is need for refresher training?
- Gonzalo Domingo to Everyone: how is the research team monitoring how well the testing is being done and the level of compliance to the treatment algorithm?
- Benedikt Ley to everyone: How do you ensure testing quality among MPW?
- Estrella Lasry-GF to everyone: Are females systematically being referred?

Day 2

- Is 1-3-7 a part of surveillance system in Malaysia?

Day 3

Session 6

- Question for Dr Leo: How did you manage to get the different sectors together and how long did it take? Was there a lot of advocacy needed?

- Does OptiDx require that both accessibility studies and geospatial localization of testing sites (community to hospital) be done to be implemented?
- Question for Dr Lieven: Do migration patterns shift regularly, how do you plan for this?
- Question for Dr Rosalind: What data would you need from country programs to go into the model? Is there data that you must have and other data that is not necessary but would strengthen the model?
- Question for Dr Quaye: Can you tell us through what mechanisms you contact other sectors e.g. education, military, agricultural – is this through other government ministries or otherwise?

Annex Two: Country action points for APMEN VxWG

Afghanistan

- Determine budgetary needs for roll out Qn-G6PD
- Action point to determine whether enough data for evidence brief on G6PD in Afghanistan -or surrounding/neighbouring countries with similar ethnicity

Bhutan

- Identify any further support needed for implementation of Qn-G6PD
- Provide updated training materials, supervision checklists and competency assessments to NMP

Lao PDR

- Liaise with CMPE to underscore current TQ label with CQ only

Myanmar

- Share G6PD evidence brief with new NMP members

Philippines

- Action point to determine whether there have been any studies on patient compliance in Philippines

Solomon Islands

- Request more detail on PSMC in Sols from NMP or partners
- Determine whether there is any evidence on reasons for Health worker hesitancy in administering primaquine
- Determine whether any research is planned for Qn-G6PD feasibility in Solomon Islands and if not, whether this may be feasible to pilot.

Annex Three: APMEN Vivax Working Group Annual Meeting 2021 Agenda

AGENDA

2021 ANNUAL MEETING: APMEN Vivax Working Group

APMEN ASIA PACIFIC MALARIA ELIMINATION NETWORK

DAY 1: "PIPELINE TO POLICY" (9-Aug-2021, Monday)

13:00-13:20 **Opening, agenda & workplan**	Opening (Dr Sarthak Das) Introductions & agenda (Dr Karma Lhazeen)	
13:20-14:20 **Out of the pipeline**	Higher sensitivity vivax diagnostics & G6PD tests (Dr Gonzalo Domingo) WHO current guidance for treatment of malaria & process for policy change (Dr Neena Valecha) Updates on latest tools for vivax radical cure treatment (Penny Grewal)	**Chair: Dr Kamala Thriemer** Menzies School of Health Research
14:25-15:30 **Policy change process**	Introduction, overview and Operational Research database (Dr Bipin Adhikari) APMEN VxWG 2019 roadmaps & groupwork session (Dr Phyoe Yarzar)	**Chair: Dr Prudence Hamade** Malaria Consortium

DAY 2: "TO POLICY AND TOWARDS OPTIMIZED IMPLEMENTATION" (10-Aug-2021, Tuesday)

13:00-14:10 **Priorities, options assessment and policy mapping**	Introduction to a prioritisation framework for the Asia Pacific region (Dr Caroline Lynch) Policy processes & implications for future policy changes (Varunika Ruwanpura) An Options Assessment Toolkit to assist decision-making (Dr Manash Shrestha)	**Chair: Dr Prayuth Sudathip** DVBD, Thailand **Dr Neena Valecha**, WHO
14:15-15:10 **Improving current practices Early experiences with G6PD testing & patient compliance/adherence**	Experiences with adherence from countries that have reached elimination (Dr Kamini Mendis) Implementing G6PD point of care tests – early experiences (Dr Chansuda Wongsrichanalai)	**Chair: Dr Lek Dysoley** CNM, Cambodia

DAY 3: "TOWARDS OPTIMIZED IMPLEMENTATION" (11-Aug-2021, Wednesday)

13:00-13:50 **'Show me the vivax!'**	Targeting new tools to achieve impact (FIND) Lightning talks on Access & multisectoral approaches (Malaria Consortium, RBM et al)	**Chair: Dr Leo Makita** MoH, Papua New Guinea
13:55-14:40 **How are you accessing vivax patients?**	Groupwork – strategies for increasing radical cure among remote populations (Yucheng Tsai)	**Chair: Dr Hamida Hamid** NMLCP, Afghanistan
14:40-15:00 **Perspectives from APMEN**	Perspectives from APMEN (VxWG Advisory Council)	**Chair: Dr Leonard Boaz** NVBDC, Solomon Islands

The timings are Singapore Time & may vary slightly