

# OUTCOMES AND ACTION POINTS

FROM THE

## ANNUAL MEETING OF THE VIVAX WORKING GROUP – AUG 2021

### OUTCOMES – SUMMARY OF PRESENTATIONS AND DISCUSSIONS

The 2021 APMEN Vivax Working Group Annual Meeting was held online from 9-11<sup>th</sup> 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<sup>1</sup>. 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<sup>2</sup>. WHO guidance further provides a ‘good practice statement’ that the G6PD status of patients should be used to guide administration of primaquine for preventing

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

<sup>2</sup> World Health Organization. WHO Guidelines for malaria, 13 July 2021. Geneva: World Health Organization; 2021.

relapse<sup>2</sup>. 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 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<sup>3</sup>. Many published studies show considerable variation on patient adherence to PQ-14, ranging from 44% up to 98%<sup>4,5,6</sup>. *Individual patient counselling and medical supervision<sup>7</sup> 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<sup>8</sup> of tafenoquine in Myanmar, the Philippines and Vietnam is expected in 2022.

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<sup>3</sup> World Health Organization. Adherence to long-term therapies: evidence for action. World Health Organization; 2003.

<sup>4</sup> Cheoyman A, Ruenweerayut R, Muhamad P, Rungsahirunrat 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

<sup>5</sup> 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

<sup>6</sup> 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

<sup>7</sup> 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

<sup>8</sup> 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.

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-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](http://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:

<i>Knowledge collation &amp; dissemination</i>		
Action points	Status	Lead organization
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
<i>Implementation and Operational Research</i>		
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*

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

Menzies & APMEN VxWG

determine interest in being involved in OAT process

**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
- 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](mailto:GORCoP@path.org) for more details on materials and how to join and learn from the G6PD Operational Research Community of Practice

PAVE, FIND, Menzies and any partners involved in training on new tools

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

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Support dissemination of WHO-GMP timelines for policy guidance once available.

NMPs, APMEN VxWG and PAVE