Supplementary materials to "Optimizing test and treat options for Vivax malaria: an option assessment toolkit (OAT) for Asia Pacific National Malaria Control Programs"

Table S1: Demographic characteristics of responding experts for BAT modified e-Delphi

Characteristics		Round one		Round two	
		Number (n=21)	**Percentage (%)**	**Number (n=20)**	**Percentage (%)**
Region	South East Asia	11	55	12	60
	Western Pacific	4	20	3	15
	Global	3	15	3	15
	Eastern Mediterranean	2	10	2	10
Gender	Female	13	62	12	60
	Male	8	38	8	40
Affiliation	Academic/Research institution	19	90	18	90
	Government Agency	1	5	1	5
	NGO	1	5	1	5
	Other	1	5	1	5
Expertise	Treatment of vivax malaria	16	76	15	75
	Malaria Epidemiology	16	76	15	75
	Diagnostics and Surveillance	14	67	13	65
	Pathology and Pathogenesis of vivax malaria	9	43	9	45
	Health Policy	4	19	4	20
	Entomology and Vector control	4	19	3	15
	Other	3	14	3	15
	Behavioral Science	1	5	1	5

Table S2: Comparison of originally intended composition of toolkit and final composition

S. No	Tools	Status	Rationale
1	**Baseline assessment template (BAT)** *previously named as Readiness assessment template.*	**Included**	Assess readiness of malaria program for vivax elimination.
2	**Scenarios** representative of Asia Pacific region	**Included**	Scenario representative of the region for epidemiological, health system and political economic context.
3	**Scenario based test and treat options**	**Included**	Optimal test and radical cure treatment options of vivax, based on the scenarios
4	**Step-by-step guidance** on how to use the OAT toolkit (based on documentation of the process and engagement with NMPs)	**Included**	Assists NMPs to use the toolkits
5	**Evidence briefs** on efficacy and effectiveness of current radical cure drugs and latest information on high sensitivity rapid diagnostic tests (HS-RDTs), G6PD screening tests, and radical cure options near end of pipeline	Abandoned	Evidence is continuously evolving and new evidence needs to be added continuously to revise OAT.
6	NMP **weighting tool** for different variables	Abandoned	Too complex, limited data available
7	**Approaches** for optimized radical cure tools	**Included**	Outlines the policy change process and considerations for policy change and implementation.
8	Policy options evaluation matrix	Abandoned	Too complex and not user friendly
9	Policy uncertainties and potential mitigation actions template	Abandoned	Too complex, data may not be available
10	**Decision tree**	Abandoned	NMPs felt it would not be useful

Table S3: The 25 factors initially included in the BAT and the reasons for their inclusion or exclusion

S. No	Factors	Status	Rationale
	Epidemiological domain		
1.	Vivax malaria caseload	Added after NMP feedback	Representation of phases of malaria program
2.	Geographic variations in vivax cases within the country	Excluded after NMP feedback	Influences implementation decision and approaches but less relevant for policy decisions.
3.	Efficacy and Effectiveness of current radical cure treatment regimen	Retained after NMP feedback	Given context may influence policy and implementation decisions
4.	Vulnerable populations at risk	Excluded after NMP feedback	Policy is prepared to address wider population
5.	Vivax relapse periodicity (predicted) (*additional factor**)	Excluded after NMP feedback	Limited information with NMPs
6.	Chloroquine resistance (*additional factor**)	Excluded after NMP feedback	Limited information with NMPs
7.	G6PD deficiency prevalence	Retained after NMP feedback	Given context may influence policy on radical cure.
	Implementation domain		
8.	Access to radical cure treatment regimen	Retained after NMP feedback	Assess the strength of health system
9.	Coverage of current radical cure regimen	Excluded after NMP feedback	Does not influence vivax radical cure policy
10.	Healthcare worker adherence to guidelines	Retained after NMP feedback	Assess the strength of health system
11.	Patient adherence	Retained after NMP feedback	
12.	Pharmacovigilance	Retained after NMP feedback	
13.	Logistics and supply chain	Excluded after NMP feedback	Does not influence vivax radical cure policy
14.	Human resources	Retained after NMP feedback	
15.	Quality of training and supervision to healthcare workers	Excluded after NMP feedback	Does not influence vivax radical cure policy
	Enabling factor Political and economic domain		
16.	Antimalarial policy change processes	Excluded after NMP feedback	Important to map out but not through the baseline assessment
17.	Political will for vivax elimination	**Retained after NMP feedback**	Commitment of NMPs for elimination target
18.	Acceptance/ interest/appetite for alternative solutions with different risk/benefits to current regimes	**Retained after NMP feedback**	Influences vivax radical cure policy and included as factor "risk aversion"

S. No	Factors	Status	Rationale
19.	Ease of policy implementation	Excluded after NMP feedback	Important to map out but not through the baseline assessment
20.	Administrative feasibility	Excluded after NMP feedback	Does not explicitly influence vivax radical cure policy
21.	Economic burden of vivax	Excluded after NMP feedback	Important to map out but not through the baseline assessment
22.	Cost-effectiveness analysis of radical cure tools	Excluded after NMP feedback	Relevant for later tools developed
23.	Public spending for malaria	Retained after NMP feedback	Combined as a single factor of 'Budget"
24.	External donor funding	Retained after NMP feedback	
25.	Income inequality	Excluded after NMP feedback	Does not explicitly influence vivax radical cure policy

*additional factors were suggested in the development phase by the initial core team, based on literature reviews and discussions.

Table S4: Ranking of factors included in the BAT by the NMP participants

Country		**Solomon Islands**	**Afghanistan**	**Vietnam**
	Specific factors			
1. How do you rate the importance of this factor/question for assessment of your readiness for vivax elimination?	phase of malaria program	High	High	High
2. How do you rate the importance of this factor/question for your assessment of readiness for vivax elimination?	vivax case load	High	High	High
3. How do you rate the importance of this factor/question for assessment of your readiness for vivax elimination?	G6PD prevalence	High	Low	High
4. How do you rate the importance of this factor/question for assessment of your readiness for vivax elimination?	G6PD def. heterogeneity	High	High	High
5. How do you rate the importance of this factor/question for assessment of your readiness for vivax elimination?	Blood stage treatment	High	Moderate	High
6. How do you rate the importance of this factor/question for assessment of your readiness for vivax elimination?	liver stage treatment	High	High	High
7. How do you rate the importance of this factor/question for assessment of your readiness for vivax elimination?	Antirelapse efficacy	High	High	High
8.1 How do you rate the importance of this factor/question for assessment of your readiness for vivax elimination?	functioning of referral system - referral initiation	Moderate	Moderate	High
8.2 How do you rate the importance of this factor/question for assessment of your readiness for vivax elimination?	functioning of referral system - referral completion	Moderate	moderate	High
9.1 How do you rate the importance of this factor/question for assessment of your readiness for vivax elimination?	Patient adherence - proportion	High	High	High
9.2 How do you rate the importance of this factor/question for assessment of your readiness for vivax elimination?	patient adherence - supervised	Moderate	High	High

Country		**Solomon Islands**	**Afghanistan**	**Vietnam**
10. How do you rate the importance of this factor/question for assessment of your readiness for vivax elimination?	human resource-health workers available	High	High	High
11. How do you rate the importance of this factor/question for assessment of your readiness for vivax elimination?	Pharmacovigilance	High	High	Moderate
12. How do you rate the importance of this factor/question for assessment of your readiness for vivax elimination?	budget	Moderate	High	Moderate
13. How do you rate the importance of this factor/question for assessment of your readiness for vivax elimination?	political will	Moderate	Moderate	High
14. How do you rate the importance of this factor/question for assessment of your readiness for vivax elimination?	Risk aversion	High	High	High

Table S5: Results from round one of first modified e-Delphi to validate the factors included in the BAT

Factor	Number of respondents who think the factor is important for readiness assessment and/or decision making on test and treat combinations	% Agreement	Threshold agreement achieved
1) Epidemiological Domain			
i) Phase of malaria program	19	90	Yes
ii) Vivax caseload	20	95	Yes
iii) G6PD deficiency prevalence	21	100	Yes
iv) G6PD deficiency heterogeneity	21	100	Yes
v) Blood stage treatment	18	86	Yes
vi) Liver stage treatment	19	90	Yes
vii) Antirelapse efficacy	20	95	Yes
2) Implementation Domain			
i) a. Referral system (referral initiation rate)	21	100	Yes
b. Referral system (referral completion rate)	20	95	Yes
ii) a. Human resource (available in community)	21	100	Yes
b. Human resource (HW compliance rate)	21	100	Yes
iii) a. Patient adherence (adherence rate)	21	100	Yes
b. Patient adherence (supervised treatment)	21	100	Yes
iv) Pharmacovigilance	20	95	Yes
3) Enabling Domain			
i) Budget	18	86	Yes
i) Political will	13	**62**	**No**
ii) Risk aversion	19	90	Yes

Table S6: Response on the factors in round two of the first modified e-Delphi

Factor		Number of respondents who think the factor is important for readiness assessment and/or decision making on test and treat combinations	Total respondents who answered yes/no	% Agreement	Threshold agreement achieved
I)	**Epidemiological Factors**				
i)	Severity of G6PD deficiency*	15	19	79	Yes
ii)	Safety of radical cure regimen*	16	19	84	Yes
II)	**Implementation Factors**				
i)	Feasibility of evidence use*	20**	20	100	Yes
III)	**Enabling Factors**				
i)	Political will	14	18	78	Yes

**Additional factor suggested in round one included in round two to reach agreement*

*** if response= Yes: it ranges from somewhat to a lot (somewhat: 6/20,30%; moderate: 7/20, 35%; a lot: 7/20, 35%)*

Table S7: Additional factors suggested by experts

Additional factors suggested by experts in round 1	Status	Rationale	Status in round 2 Delphi
Vivax case heterogeneity	Not taken forward to round two after internal discussion	Influence on implementation decision and approaches but less on policy related to vivax radical cure	
Severity of G6PD deficiency	Retained for round 2	Important for radical cure treatment policy, challenges lie with data availability	Experts agreed on its importance
Safety of radical cure	Retained for round 2	Affects NMPs decision making process on vivax radical cure	Experts agreed on its importance
Feasibility of evidence use	Retained for round 2	Important on considering policy changes and its implementation	Experts agreed on its importance
Variant type of enzyme CYP2D6 gene	Not taken forward to round two after internal discussion	Limited data with NMPs	
Insecticide resistance	Not taken forward to round two after internal discussion	Important for overall malaria control but less relevant for treatment policy change	
Quality of malaria commodities	Not taken forward to round two after internal discussion	Important for overall malaria control but less relevant for treatment policy change	
Existence of community outreach.	Not taken forward to round two after internal discussion	Important for overall malaria control, addressed by the factors in the implementation factors	

Table S8: Responses on the questions in each factor/ additional factor BAT (Round two of the first modified e-Delphi)

Factor	Question	Total respondents who answered yes/no	Number of respondents who agree that the question/categorization adequately captures the factor	% Agreement	Threshold agreement achieved
Severity of G6PD deficiency	What level of severity of G6PD deficiency is the most common in your country?	13	8	**61%**	**No**
Political will	13.a Do you think the question "Who was the chief guest in the last World Malaria Day event in your country?" is adequate for capturing this factor?	14	5	**36%**	**No**
			Central tendency	Range	
Antirelapse efficacy	adequate antirelapse efficacy (defined as risk of recurrence and not risk/ probability of recurrence free) at six months for decision-making for any given radical cure regimen	20	Mean: 85.5%	50-100%	Yes
Safety of radical cure regimen (Upper limit of SAE) *	Upper limit of severe hemolytic events requiring transfusion related to 8-aminoquinolines, adequate to consider it safe enough?	13	<1/100,000 = 6/13 (46%) <1/10,000 = 5/13 (38%) <1/1,000 = 2/13 (15%)	<1/100,000 – <1/1,000	NA

*this factor was initially considered important for BAT related to radical cure treatment but later it was removed citing the unavailability of data.

Table S9: Detailed responses on the questions and categorizations in each factor BAT (Round one of the first modified e-Delphi)

Factor	Question	Categorization	Total respondents who answered yes/no	Number of respondents who agree that the question/categorization adequately captures the factor	% Agreement	Threshold agreement achieved
Phase of malaria program	1.a What is the phase of malaria program in your country?" is adequate for capturing this factor?		16	14	87%	Yes
		1.b We have classified Phase of malaria program into four categories, based on WHO, 2008, as: a) Control (slide or RDT positivity rate ≥5), b) Pre-elimination (slide or RDT positivity rate <5%), c) Elimination (<1 case/1000 population at risk per year), d) Prevention of reintroduction (3 years of 0 locally acquired cases)	13	10	77%	Yes
Vivax caseload	2.a Do you think the question "What is the number of annual reported cases of vivax in your country?" is adequate for capturing this factor?		18	14	78%	Yes.
		2.b We have classified Vivax caseload into seven categories, adapted from Battle & Baird, 2021, as: a) >100000, b) 10001-100000, c) 1001-10000, d) 101-1000, e) 1-100, f) 0 g) Unknown	13	10	77%	Yes

Factor	Question	Categorization	Total respondents who answered yes/no	Number of respondents who agree that the question/categorization adequately captures the factor	% Agreement	Threshold agreement achieved
G6PD deficiency prevalence	3.a Do you think the question "What is the level of G6PD deficiency (defined as less than 30% G6PD activity) in your country?" is adequate for capturing this factor?		17	14	82%	Yes
		3.a Do you think the question "What is the level of G6PD deficiency (defined as less than 30% G6PD activity) in your country?" is adequate for capturing this factor?	14	13	93%	Yes
G6PD deficiency heterogeneity	4.a Do you think the question "How would you describe the spatial heterogeneity of G6PD deficiency in your country?" is adequate for capturing this factor?		18	14	78%	Yes
		4.b We have classified G6PD deficiency heterogeneity into three categories as: a) Heterogeneous, b) Non-heterogeneous, c) Don't know	12	10	83%	Yes
Blood stage treatment	5.a Do you think the question "What is the blood stage treatment used for uncomplicated vivax in your country?" is adequate for capturing this factor?		18	17	94%	Yes
		5.b We have classified Blood stage treatment into two categories as: a) Chloroquine, and b) Artemisinin Combination Therapy	15	15	100%	Yes

Factor	Question	Categorization	Total respondents who answered yes/no	Number of respondents who agree that the question/categorization adequately captures the factor	% Agreement	Threshold agreement achieved
Liver stage treatment	6.a Do you think the question "What are the current radical cure regimen/s (one or more options) for uncomplicated vivax malaria recommended by the national treatment guidelines in your country?" is adequate for capturing this factor?		19	18	95%	Yes
		6.b We have classified the current recommended Liver stage treatment into six categories as: a) PQ14days (0.25mg/kg/day for a total 3.5mg/kg), b) PQ14days (0.5mg/kg/day for a total 7mg/kg), c) PQ8weekly (0.75mg/kg/week for a total 6mg/kg), d) PQ7days (0.5mg/kg/day for a total 3.5mg/kg) e) None, f) Others (specify)	16	14	87%	Yes
Antirelapse efficacy	7.a Do you think the question "Antirelapse efficacy data is available for which radical cure drug regimen/s in your country or similar settings?" is adequate for capturing this factor?		18	15	83%	Yes
		7.d What should be an appropriate threshold (%) for adequate antirelapse efficacy (defined as risk of recurrence and not as risk/probability of recurrence free) at six months for decision-making for any given radical cure regimen?	17	Mean: 52.8 Range: 5-95		No*

Factor	Question	Categorization	Total respondents who answered yes/no	Number of respondents who agree that the question/categorization adequately captures the factor	% Agreement	Threshold agreement achieved
Referral system						
Functioning of referral system (a. What is the estimated proportion of vivax patients referred from initial point of malaria diagnosis to higher centers?)	8.1a Do you think the question "What is the estimated proportion of vivax patients referred from initial point of malaria diagnosis to higher centers?" is adequate for capturing this factor?		19	18	95%	Yes
		8.1b We have classified Referral initiation rate into five categories, adapted from Measure Evaluation, 2013, as: a) <10%, b) >10-50%, c) >50-80%, d) >80-100%, and e) Don't know	15	15	100 %	Yes
Functioning of referral system (b. What is the estimated proportion of referred vivax patients that complete referral at receiving health facility?)	8.2a Do you think the question "What is the estimated proportion of referred vivax patients that complete referral at receiving health facility?" is adequate for capturing this factor?		17	15	88%	Yes
		8.2b We have classified Referral completion rate into five categories, adapted from Measure Evaluation, 2013, as: a) <10%, b) >10-50%, c) >50-80%, d) >80-100%, and e) Don't know	13	13	100%	Yes

Factor	Question	Categorization	Total respondents who answered yes/no	Number of respondents who agree that the question/categorization adequately captures the factor	% Agreement	Threshold agreement achieved
Human resource						
Human resource (What kind of health workers are available at the community level for malaria case management?)	9.1a Do you think the question "What kind of health workers are available at the community level for malaria case management?" is adequate for capturing this factor?		20	16	80%	Yes
		9.1b We have classified Human resource into five categories as a) HW not available at community level; b) HW available but cannot test, treat, or track; c) HW available and can test and track but cannot treat; d) HW available and can test, treat, and track for patient adherence e) Don't know	15	12	80%	Yes
Human Resource (What do you think is the estimated proportion of health workers at different levels of the health system who adhere to current or new treatment protocols?)	9.2a Do you think the question "What do you think is the estimated proportion of health workers at different levels of the health system who adhere to current or new treatment protocols?" is adequate for capturing this factor?		18	14	78%	Yes
		9.2b We have classified the estimated Health Worker compliance rate into four categories as: a) <50%, b) 50-80%, c) >80%, and d) Don't know	14	14	100%	Yes

Factor	Question	Categorization	Total respondents who answered yes/no	Number of respondents who agree that the question/categorization adequately captures the factor	% Agreement	Threshold agreement achieved
Patient adherence						
Patient adherence (What do you think is the estimated proportion of patients who adhere to the full treatment regimen of the current recommended radical cure drugs?)	10.1a Do you think the question "What do you think is the estimated proportion of patients who adhere to the full treatment regimen of the current recommended radical cure drugs?" is adequate for capturing this factor?		21	20	95%	Yes
		10.1b We have classified the estimated patient adherence rate into four categories, adapted from Kim et al, 2018 and Burnier, 2019, as: a) <50%, b) 50-80%, c) >80%, and d) Don't know	17	17	100%	Yes
Patient adherence (Is supervised treatment or any other interventions being implemented at a large scale to improve patient adherence to radical cure of vivax in your country?)	10.2a Do you think the question "Is supervised treatment or any other interventions being implemented at a large scale to improve patient adherence to radical cure of vivax in your country?" is adequate for capturing this factor?		19	18	94%	Yes
		10.2b We have classified implementation of supervised treatment or any other interventions into three categories as: a) Yes, b) No, c) Don't know	15	14	95%	Yes

Factor	Question	Categorization	Total respondents who answered yes/no	Number of respondents who agree that the question/categorization adequately captures the factor	% Agreement	Threshold agreement achieved
Pharmacovigilance	11.a Do you think the question "What is the status of adverse event reporting for any disease in the last 12 months in your country?" is adequate for capturing this factor?		15	12	80%	Yes
		11.b We have classified Pharmacovigilance into four categories as: a) Adverse Event usually recorded and reported, b) Adverse Event sometimes recorded and reported, c) Adverse Event not recorded or reported, and d) Don't know	12	11	91%	Yes
Budget	12.a Do you think the question "What percentage of the annual budget for malaria is funded by the national government?" is adequate for capturing this factor?		17	13	76%	Yes
		12.b We have classified Budget as the percentage of the annual budget for malaria is funded by the national government.	11**	8	73%	No
Political will	13.a Do you think the question "Who was the chief guest in the last World Malaria Day event in your country?" is adequate for capturing this factor?		9**	6	67%	No
		13.b We have classified Political will with the proxy of the highest-level chief guest in the last World Malaria Day event in your country as a) Prime Minister, b) Health Minister, c) Health/Permanent Secretary, d) Director General, e) Director of Department, or f) Others (specify)	6**	6	100%	No

Factor	Question	Categorization	Total respondents who answered yes/no	Number of respondents who agree that the question/categorization adequately captures the factor	% Agreement	Threshold agreement achieved
Risk aversion	14.a Do you think the question "What percentage of time was spent discussing patient safety compared to efficacy and implementation issues of 8-aminoquinolines in the last Technical Working Group (TWG) meeting which discussed on treatment policy change for vivax malaria in your country?" is adequate for capturing this factor?		15	14	93%	Yes
		14.b We have classified Risk aversion with the proxy of the percentage of time spent discussing "patient safety" compared to "efficacy" and "implementation issues of 8-aminoquinolines" in the country's last Technical Working Group (TWG) meeting which discussed on treatment policy change for vivax malaria.	14	14	100%	Yes

**Consensus not reached due to a wide variation*

***Minimum 12 respondents not reached*

Table S10: Responses on the categorizations in each factor/ additional factor BAT (Round two Delphi)

Factor	Categorization	Total respondents who answered yes/no	Number of respondents who agree that the question/categorization adequately captures the factor	% Agreement	Threshold agreement achieved
Severity of G6PD deficiency	We have classified the Severity of G6PD deficiency into 4 categories, adapted from Malaria Policy Advisory Group, WHO 2022 as: 1. Class A: <20% median activity with chronic non-spherocytic hemolytic anemia (CNSHA) 2. Class B: <45% median activity with triggered acute hemolytic anemia (AHA) 3. Class C: 60-150% median activity without hemolytic risk 4. Class U: Any variant with unknown clinical significance and median activity	8*	7	87%	No
Budget	12.b We have classified Budget as the percentage of the annual budget for malaria is funded by the national government.	14	5	36%	No

**Minimum 12 respondents not reached*

Table S11: Overview of scenario using simplified version of BAT

Scenario 1 (*Best case scenario*)	**Scenario 2 (*At the finish line*)**	**Scenario 3 (*Running*)**	**Scenario 4 (*Walking*)**	**Scenario 5 (*Worst case scenario/sleeping*)**
• No indigenous vivax cases	• Low vivax caseload • Efficacy for low-dose PQ evident	• Low vivax caseload • Efficacy for low-dose PQ evident	• High vivax caseload • Efficacy for high dose PQ	• High vivax caseload • No data on Efficacy for PQ
• Strong health system readiness	• Strong health system readiness	• Weak health system readiness	• Weak health system readiness	• No data/ Weak health system readiness
• Strong high-level political will	• Low risk aversion • Strong high-level political will	• Low risk aversion • Strong high level political will	• High risk aversion • Strong high level political will	• Low/ High risk aversion • Weak high level political will

Table S12. Overview of 11 scenarios

	THEUNA	FLOESAL	CREOSO	OTROS	ACRINES	JOBLIL	PLOJI	GLAERA	ECHA	USPOS	BLAOR
Enabling domain											
Budget (domestic funding)	Moderate to High	Moderate to High	Low to Moderate	Moderate	Moderate	High	Low	Low to Moderate	Low to Moderate	Low	Low
Political will	High	High	Moderate to High	Moderate to High	Moderate to High	Moderate	Low to moderate	Moderate	Low	Low	Low
Risk aversion of decision makers for future malaria policy options	Moderate	Moderate	Moderate	low	Low	Moderate	High	**High**	Moderate - High	Low-Moderate	Low
Implementation domain											
Referral initiation rate	High	High	Very low	Moderate	Low to Moderate	Moderate	Low	Very low or don't know	Very low or don't know	Very low or don't know	Don't know
Referral completion rate	High	High	High	High	High	Moderate	Low	Very low or don't know	Very low or don't know	Very low or don't know	Don't know
HW availability: community-level case management	HW can test and track but cannot treat	HW can test and track but cannot treat	HW can test and track but cannot treat	HW can test and track but cannot treat	HW can test track but cannot treat	HW can test, treat, and track patient adherence	HW can test and track but cannot treat	HW can test and track but cannot treat	HW can test and track but cannot treat	HW can test and track but cannot treat	HW can test and track but cannot treat
HW compliance with protocols	High	High	Moderate to High	Moderate to High	Moderate to High	Moderate to High	Low or don't know	Low or don't know	Low or don't know	low	Don't know
Supervised treatment for patient adherence	Yes	Yes	Yes	Yes	Yes/No	Yes/No	Yes/No	No	No	No	No

	THEUNA	FLOESAL	CREOSO	OTROS	ACRINES	JOBLIL	PLOJI	GLAERA	ECHA	USPOS	BLAOR
Patient adherence rate	High	High	Moderate to High	Low to Moderate	Moderate	Moderate	Low or don't know	Low or don't know	Low or don't know	No	No
Pharmacovigilance	High	High	Moderate	Moderate to High	Moderate to High	Low to Moderate	Low	Low	Low	Low or don't know	Don't know
Epidemiological domain											
Malaria program phase	Prevention of re-introduction & Elimination	Prevention of re-introduction with outbreaks	Elimination	Elimination	Elimination	Elimination	Pre-elimination	Control	Control	Control	control
Vivax caseload	0	1-10,000	1-10,000	1-10,000	1-10,000	1-10,000	>10,000	>10,000	>10,000	>10,000	>10,000
G6PD Def. Prevalence	Common	common	Common	Common	**High**	Rare	Common – High	Common–High	Common - High	Common - High	Don't know
Most common G6PD variants	Kaiping / Canton/ don't know	Kaiping/ Canton/ don't know	Mediterranean/ Orissa/ don't know	Union/ Viangchan	Mahidol/ Viangchan	Don't know	Mahidol/ Viangchan	Viangchan/ Union/Vanua Lava	Mediterranean, Orissa, Kerala-Kalyan	Don't know	Don't know
Current liver-stage treatment	PQ14 (3.5mg/kg) / PQ8Wk	PQ14 (3.5mg/kg)/ PQ8Wk	PQ14 (3.5mg/kg) / PQ8Wk	PQ14 (3.5mg/kg)/ PQ8Wk	PQ14 (3.5mg/kg) / PQ8Wk	PQ14 (3.5mg/kg) / PQ8Wk	PQ14 (3.5mg/kg)/ PQ8Wk	PQ14 (3.5mg/kg) / PQ8Wk	PQ14 (3.5mg/kg) /PQ8Wk	PQ14 (3.5mg/kg) /PQ8Wk	PQ14 (3.5mg/kg) / PQ8Wk
Anti-relapse efficacy data	No data available	No data available	Adequate (Risk of recurrence at 6 months at 1%, but >10% at 1 year)	Adequate (The risk of recurrence at 6 months around 10%)	**Inadequate** (The risk of recurrence at 6 months around 20%)	Inadequate (The risk of recurrence at 6 months around 20%)	Adequate (The risk of recurrence at 6 months around 10%)	**Inadequate** (The risk of recurrence at 6 months around 40%)	Adequate (The risk of recurrence at 6 months around 10%, but >10% at 1 year)	Inadequate (The risk of recurrence at 6 months around 40%)	No data available

	THEUNA	FLOESAL	CREOSO	OTROS	ACRINES	JOBLIL	PLOJI	GLAERA	ECHA	USPOS	BLAOR
Delphi first round top options matching (out of 12 questions)	100% match with Floesal	100% match with Theuna	100% match with Otros	100% match with Creoso	83% (i.e.10/12) match with Otros, Creoso, and Joblil	83% (i.e.10/12) match with Otros, Creoso, and Acrines	75% (i.e. 9/12) match with Glaera 66% (8/12) match with Joblil	75% (i.e. 9/12) match with Ploji 66% (8/12) match with Echa	91% (11/12) match with Uspos. 100% match with Blaor	91% (11/12) match with Echa and Blaor	91% (11/12) match with Uspos. 100% match with Echa

Table S13: Scenario-based test and treat options (expert agreement on responses from Delphi- Qualitative and quantitative G6PD testing)

Scenario	Optimal G6PD test	Liver-stage treatment option/s			
		With **CQ** as the blood-stage treatment		With **ACT** as the blood-stage treatment	
		For G6PD Normal (% of experts)	**For G6PD intermediate (% of experts)**	**For G6PD Normal (% of experts)**	**For G6PD intermediate (% of experts)**
1. Theuna-Floesal	Point of care Quantitative test for G6PD	TQ (74%)	PQ14 (low dose) (74%)	PQ7 (high dose) (84%)	PQ14 (low dose) (68%)
		PQ7 (high dose) (26%)	PQ7 (low dose) (26%)	PQ14 (high dose) (16%)	PQ7 (low dose) (32%)
2. Creoso-Ortos	Point of care Quantitative test for G6PD	TQ (89%)	PQ14 (low dose) (68%)	PQ7 (high dose) (84%)	PQ14 (low dose) (68%)
		PQ7 (high dose) (11%)	PQ14 (high dose) (32%)	PQ14 (high dose) (16%)	PQ7 (low dose) (32%)
3. Acrines	Point of care Quantitative test for G6PD	TQ (84%)	PQ14 (low dose) (68%)	PQ7 (high dose) (74%)	PQ14 (low dose) (58%)
		PQ14 (high dose) (16%)	PQ14 (high dose) (32%)	PQ14 (high dose) (26%)	PQ14 (high dose) (42%)
4. Joblil	Point of care Quantitative test for G6PD	TQ (95%)	PQ14 (low dose)(53%)	PQ7 (high dose) *(84%)	PQ14 (low dose) (63%)
		PQ7 (high dose) (5%)	PQ7 (low dose) (42%)	PQ14 (high dose) (16%)	PQ7 (low dose) (37%)
5. Ploji	Point of care Qualitative test for G6PD	TQ (68%)	PQ14 (low dose) (21%)	PQ7 (high dose) *(79%)	PQ14 (low dose) (68%)
		PQ14 (low dose) (21%)	PQ7 (low dose) (31%)	PQ14 (low dose) (21%)	PQ7 (low dose) (32%)
6. Glaera	Point of care Quantitative test for G6PD	TQ (89%)	PQ7 (low dose) (89 %)	PQ7 (high dose) *(84%)	PQ14 (low dose) (53%)
		PQ7 (high dose) (11%)	PQ7(high dose) (11%)	PQ14 (low dose) (16%)	PQ7 (low dose) (47%)
7. Echa-Blaor	Point of care Qualitative test for G6PD	PQ7 (high dose) *(84%)	PQ14 (low dose) (68%)	PQ7 (high dose) *(74%)	PQ14 (low dose) (74%)
		PQ14 (low dose) (16%)	PQ7 (high dose) (32%)	PQ14 (low dose) (26%)	PQ7 (low dose) (26%)
8. Uspos	Point of care Qualitative test for G6PD	TQ (68%)	PQ7 (low dose) (53%)	PQ7 (high dose) * (84%)	PQ14 (low dose) (79%)
		PQ7 (high dose) (32%)	PQ14 (low dose) (37%)	PQ14 (high dose) (16%)	PQ14 (high dose) (21%)

**Replaced by PQ14 (high dose) in G6PD normal patients when presented to NMCP at the annual meeting in Dec 2022, given the issued WHO recommendation against high dose PQ7 in Nov 2022.*

Fig. S1: Scenario CREOSO-OTROS

Enabling factors:

Budget: The proportion of NMP activities that are funded domestically ranges from low (≤30%) to moderate (31-89%) with external technical assistance available from the donor agencies.

Political will: The country has a moderate to high political will to achieve elimination. A Health/Permanent Secretary or a head of state like the Prime Minister attends the 'World Malaria Day' event in advocacy and commitment to sustain the achievements made.

Risk aversion of decision makers for future malaria policy options: The Ministry of Health and National Malaria Program have low to moderate risk aversion. During NMPs Technical Working Group (TWG) meetings, less or equal time is spent discussing 'patient safety' compared to 'efficacy' and 'implementation issues of 8-aminoquinolines'.

Implementation factors:

Referral initiation rate: The proportion of vivax patients who get referred to a higher-level health facility after getting diagnosed at the community level can vary from very low (<10%) to moderate (>50-80%).

Referral completion rate: A high proportion of referred vivax patients (i.e., >80%) avail treatment at a higher-level facility.

Community level case management: There are health workers in the community who can test to confirm malaria and track but cannot treat.

Health worker compliance rate: A moderate (50-80%) to high (>80%) proportion of health workers are estimated to comply with treatment protocols.

Patient adherence rate: The proportion of vivax patients who adhere to recommended radical cure can vary from low (<50%) to high (>80%).

Interventions to improve patient adherence: The MOH in Creoso-Otros admits vivax malaria patients to hospital to provide DOT or provide supervised treatment like scheduled follow-up by community to ensure adherence to the treatment.

Epidemiological factors:

Malaria program phase: The Creoso-Otros countries are in the Elimination phase with <1 case/1000 population at risk/year.

Vivax caseload: The countries report vivax cases ranging from 1-10,000 per annum.

G6PD deficiency prevalence: The G6PD deficiency prevalence is estimated as common (1-10%).

Liver stage treatment: The recommended current radical cure regime is PQ at a low dose (3.5mg/kg total dose) given over 14 days or a weekly dose (0.75mg/kg) for 8 weeks.

Antirelapse efficacy: The efficacy of PQ14 low dose is estimated as adequate. The risk of recurrence of the current PQ 14 day treatment is estimated to be around 1-10% at 6 months.

Fig. S2: Scenario ACRINES

Enabling factors:

Budget: The proportion of NMP activities that are funded domestically is moderate (31-89%) with external technical assistance available from the donor agencies.

Political will: There is moderate to high political will to sustain the elimination. A Health/Permanent Secretary or a head of state like the Prime Minister attends the 'World Malaria Day' event in advocacy and commitment to sustain the achievements made.

Risk aversion of decision makers for future malaria policy options: Risk aversion is low. During NMPs Technical Working Group (TWG) meetings, less time is spent thinking through 'patient safety' compared to 'efficacy' and 'implementation issues of 8-aminoquinolines'.

Implementation factors:

Referral initiation rate: Low (10-50%) to moderate (>50-80%) proportion of vivax patients get referred to a higher-level health facility after getting diagnosed at the community level.

Referral completion rate: A high proportion of referred vivax patients (i.e., >80%) avail treatment at a higher-level facility.

Community level case management: There are health workers in the community who can test to confirm malaria and track but cannot treat.

Health worker compliance rate: A moderate (50-80%) to high (>80%) proportion of health workers are estimated to comply with treatment protocols.

Patient adherence rate: Adherence to radical cure is moderate (50-80%).

Interventions to improve patient adherence: Acrines may provide supervised treatment like the scheduled follow-up to ensure adherence to the treatment or supervised treatment does not exist.

Epidemiological factors:

Malaria program phase: The Acrines countries are in the elimination phase with <1 case/1000 population at risk/year.

Vivax caseload: The countries report vivax cases ranging from 1-10,000 per annum.

G6PD deficiency prevalence: The G6PD deficiency prevalence is estimated as high (>10%).

Liver stage treatment: The recommended current radical cure regime is PQ at a low dose (3.5mg/kg total dose) given over 14 days or weekly dose (0.75mg/kg) for 8 weeks.

Antirelapse efficacy: The efficacy of PQ14 low dose is estimated as inadequate. The risk of recurrence of the current PQ 14 day treatment at 6 months is estimated around 20%.

Fig. S3: Scenario JOBLIL

Enabling factors:

Budget: The proportion of NMP activities that are funded domestically is high (≥ 90%). However, remaining gaps in funds along with external technical assistance are available from the donor agencies.

Political will: The country has a moderate political will to progress to elimination. The Health/Permanent Secretary attends the 'World Malaria Day' event in advocacy and commitment to sustain the achievements made.

Risk aversion of decision makers for future malaria policy options: Risk aversion is moderate. During NMPs Technical Working Group (TWG) meetings equal time is spent discussing 'patient safety' as it is for 'efficacy' and 'implementation issues of 8-aminoquinolines'.

Implementation factors:

Referral initiation rate: A moderate proportion of vivax patients (i.e., 50-80%) get referred to a higher-level health facility after getting diagnosed at the community level.

Referral completion rate: Moderate proportion of referred vivax patients (i.e., 50-80%) avail treatment at a higher-level facility.

Community level case management: There are health workers at the community level that can test to confirm malaria treat and track patients for adherence.

Health worker compliance rate: A moderate (50-80%) to high (>80%) proportion of health workers are estimated to comply with treatment protocols.

Patient adherence rate: Adherence to radical cure is moderate (50-80%).

Interventions to improve patient adherence: Joblil may provide supervised treatment like a scheduled follow-up to ensure adherence to the treatment of supervised treatment does not exist.

Epidemiological factors:

Malaria program phase: The countries in Joblil are in the elimination phase, defined as <1 case/1,000 populations at risk per year.

Vivax caseload: The countries are characterized by an annual caseload of vivax ranging from 1-10,000.

G6PD deficiency prevalence: The G6PD deficiency prevalence is estimated as rare (<1%).

Liver stage treatment: The recommended current radical cure regime is PQ at a low dose (3.5mg/kg total dose) given over 14 days or weekly dose (0.75mg/kg) for 8 weeks.

Antirelapse efficacy: The efficacy of the current PQ14 treatment is unknown. However, regionally, it is estimated that risk of recurrence at 6 months is 20%.

Fig. S4: Scenario PLOJI

Enabling factors:

Budget: The proportion of NMP activities that are funded domestically is low (≤30%). However, remaining gaps in funds along with external technical assistance are available from the donor agencies.

Political will: The country has a low to moderate political will to progress to elimination. Either no high ranking official or the Health/Permanent Secretary attends the 'World Malaria Day' event in advocacy and commitment to sustain the achievements made.

Risk aversion of decision makers for future malaria policy options: Risk aversion is High. During NMPs Technical Working Group (TWG) meetings, more time is spent discussing 'patient safety' than 'efficacy' and 'implementation issues of 8-aminoquinolines'.

Implementation factors:

Referral initiation rate: A low proportion of vivax patients (i.e.,10-50%) get referred to a higher-level health facility after getting diagnosed at the community level.

Referral completion rate: A low proportion of referred vivax patients (i.e.,10-50%) avail treatment at a higher-level facility.

Community level case management Health workers at the community level can test to confirm malaria and track but cannot treat cases.

Health worker compliance rate: A low proportion (<50%) of health workers is estimated to comply with treatment protocols or data on their compliance rate is not available.

Patient adherence rate: Data on adherence to radial cure is either not available or low (<50%) if available.

Interventions to improve patient adherence: Ploji may provide supervised treatment like the scheduled follow-up to ensure adherence to the treatment or supervised treatment does not exist.

Epidemiological factors:

Malaria program phase: The Ploji countries are in the pre-elimination phase, defined as <5% slide or RDT positivity rate.

Vivax caseload: The countries are characterized by an annual vivax caseload of >10,000.

G6PD deficiency prevalence: The G6PD deficiency prevalence is estimated as common (1-10%) to high (>10%).

Liver stage treatment: The recommended current radical cure regime is PQ at a low dose (3.5mg/kg total dose) given over 14 days or weekly dose (0.75mg/kg) for 8 weeks.

Antirelapse efficacy: The estimated efficacy of current PQ14 treatment is adequate. The risk of recurrence at 6 months in this scenario is 10%.

Fig. S5: Scenario GLAERA

Enabling factors:

Budget: The proportion of NMP activities that are funded domestically is low (≤30%) to moderate (31-89%). The remaining gaps in funds along with external technical assistance are available from the donor agencies.

Political will: The country has a moderate political will to progress to elimination. The Health/Permanent Secretary attends the 'World malaria Day' event in advocacy and commitment to sustain the achievements made.

Risk aversion of decision makers for future malaria policy options: Risk aversion is High. During NMPs Technical Working Group (TWG) meetings, more time is spent discussing 'patient safety' than 'efficacy' and 'implementation issues of 8-aminoquinolines'.

Implementation factors:

Referral initiation rate: Very low proportion of vivax patients (i.e., <10%) get referred to a higher-level health facility after getting diagnosed at the community level or data is not available for initiation of referral.

Referral completion rate: Very low proportion of referred vivax patients (i.e., <10%) avail treatment at a higher-level facility, or data is not available for completion of referral.

Community level case management: Health workers at the community level can test to confirm malaria and track but cannot treat cases.

Health worker compliance rate: A low proportion of health workers (i.e., <50%) are estimated to comply with national malaria treatment protocols or data on their compliance rate is not available.

Patient adherence rate: Adherence to radial cure is low (<50%).

Interventions to improve patient adherence: No supervision of treatment or other interventions to improve patient adherence are implemented.

Epidemiological factors:

Malaria program phase: The countries in Glaera are in control phase, defined by slide or RDT positivity rate ≥ 5%.

Vivax caseload: The countries are characterized by an annual vivax caseload of >10,000.

G6PD deficiency prevalence: The G6PD deficiency prevalence is estimated as common (1-10%) to high (>10%).

Liver stage treatment: The recommended current radical cure regime is PQ at a low dose (3.5mg/kg total dose) given over 14 days or weekly dose (0.75mg/kg) for 8 weeks.

Antirelapse efficacy: The estimated efficacy of the current PQ14 treatment is inadequate. The risk of recurrence at 6 months is 40%.

Fig. S6: Scenario ECHA-BLAOR

Enabling factors:

Budget: The proportion of NMP activities that are funded domestically is low (≤30%) to moderate (31-89%). Remaining gaps in funds along with external technical assistance are available from the donor agencies

Political will: The country has a low political will to sustain progress to elimination. No High-ranking official attends the 'World Malaria Day' event in advocacy and commitment to sustain the achievements made.

Risk aversion of decision makers for future malaria policy options: Risk aversion among the Ministry of Health and National Malaria Program can vary from moderate to high, or it cannot be ascertained. During NMPs Technical Working Group (TWG) meetings, equal or more time is spent discussing 'patient safety' compared to 'efficacy' and 'implementation issues of 8-aminoquinolines' or TWG meetings are held sporadically.

Implementation factors:

Referral initiation rate: Very low proportion of vivax patients (i.e., <10%) get referred to a higher-level health facility after getting diagnosed at the community level or data is not available for initiation of referral.

Referral completion rate: Very low proportion of referred vivax patients (i.e., <10%) avail treatment at a higher-level facility, or data is not available for completion of referral.

Community level case management: Health workers at the community level that can test to confirm malaria and track but cannot treat cases.

Health worker compliance rate: A low proportion of health workers (i.e., <50%) are estimated to comply with national malaria treatment protocols or data on their compliance rate is not available.

Patient adherence: Adherence to radial cure is low (<50%) or data may not be available.

Interventions to improve patient adherence: No supervision of treatment or other interventions to improve patient adherence are implemented.

Epidemiological factors:

Malaria program phase: Echa-Blaor countries are in the control phase, defined by slide or RDT positivity rate ≥ 5%.

Vivax caseload: The countries are characterized by an annual vivax caseload of >10,000.

G6PD deficiency prevalence: The G6PD deficiency prevalence is estimated as common (1-10%) to high (>10%) or the data may not be available.

Liver stage treatment: The recommended current radical cure regime is PQ at a low dose (3.5mg/kg total dose) given over 14 days or weekly dose (0.75mg/kg) for 8 weeks.

Antirelapse efficacy: The estimated efficacy of the current PQ14 treatment is adequate. The risk of recurrence at 6 months is 1%, but >10% at 1 year. However, the data may not be available in some cases.

Fig. S7: Scenario USPOS

Enabling factors:

Budget: The proportion of NMP activities that are funded domestically is low (≤30%). External donor funds supporting the NMP are limited.

Political will: The political situation is unstable and political will is low.

Risk aversion of decision makers for future malaria policy options: Due to the unstable political situation, the risk aversion cannot be ascertained, and the Technical Working Group (TWG) meetings are only held sporadically.

Implementation factors:

In this scenario, the public health system is not fully functional due to political instability. Therefore, all implementation factors are categorized in their lowest range.

Referral initiation rate: Very low proportion of vivax patients (i.e., <10%) get referred to a higher-level health facility after getting diagnosed at the community level, or data is not available for initiation of referral.

Referral completion rate: Very low proportion of referred vivax patients (i.e., <10%) avail treatment at a higher-level facility, or data is not available for completion of referral.

Community level case management: Health workers at the community level that can test to confirm malaria and track, but cannot treat cases.

Health worker compliance rate: A low proportion of health workers (i.e., <50%) are estimated to comply with national malaria treatment protocols, or data on their compliance rate to protocols is not available.

Patient adherence: Adherence to radial cure is low (<50%), or data may not be available.

Epidemiological factors:

Malaria program phase: Uspos countries are in the control phase, defined by slide or RDT positivity rate of ≥ 5%.

Vivax caseload: The countries are characterized by an annual vivax caseload of >10,000.

G6PD deficiency prevalence: The G6PD deficiency prevalence is estimated as common (1-10%) to high (>10%).

Liver stage treatment: The recommended current radical cure regime is PQ at a low dose (3.5mg/kg total dose) given over 14 days or weekly dose (0.75mg/kg) for 8 weeks.

Antirelapse efficacy: The estimated efficacy of the current PQ14 treatment is inadequate. The risk of recurrence at 6 months is around 40%.

Text S1: Approach tools:

Objective:

- Outline policy change process considerations and highlight different implementation strategies/approaches for each combination of radical cure options.
- Plan the next steps to use OAT beyond 2022

Description

This groupwork should enable the NMPs to visualize the policy change process and provide their own recommendations for effective implementation of the chosen test and treat combination. Specific approaches will include strategies on targeted allocation of resources, tests and treatments, improving access, adherence, advocacy, and awareness for the radical cure combinations.

WHEN should this consideration be used?

The consideration for policy change and approaches to implement more effective test and treat combinations for vivax malaria must be made if country has been missing out the target for malaria elimination due to vivax malaria.

WHO should be responsible for this process?

The NMP should take the lead role and after deciding the optimal radical cure option, the TWG and NMP can draw valuable insights from this tool to proceed and plan for reaching the 2030 malaria elimination target.

WHY was there a need for this consideration for policy change?

While some countries may have an existing systemic approach to tackle policy changes routinely, some countries may lack such routine approaches and therefore, they may to understand the processes and approaches involved.

Policy change may take very long in some countries but with availability of the evidences for policy decision such processes can be fast tracked. Towards the 2030 malaria elimination target there is need to fast track the process of management of vivax malaria.

HOW should it be done?

The NMPs should identify the need for change the vivax clinical management based on the scenario. NMP and TWG should access the Expert technical guidance on test and treat policy and adapt/develop a clinical management guideline. Then the clinical guideline should put up to relevant authority for consideration for policy change and then finally approval.

Considerations for policy change and implementation of vivax radical cure

Policy changes processes:

- **Who do you need to convene to change policy to the selected test and treat options**?
    - ~ What committees are normally convened to consider a policy change? In some countries, this might include a Technical Working Group and National Drug Committee?
    - ~ How often do that group/committee meet to review new test and treat options? When is the next meeting?
    - ~ What other processes need to be considered (e.g. application for Essential Medicines List)? Are there pilot study requirements, are those required before or after test and drug registration?
    - ~ Identify where you think you may need to undertake advocacy for policy change and resources to support implementation (e.g. immigration dept, HMIS, pharmacovigilance units)
    - ~ Consider making adapted versions of the evidence summaries and registration updates that were provided during earlier parts of the meeting. Consider using making country experiences available to key decision makers (e.g., through technical working group)

Implementation factors

Targeting & access

- ~ Has your program undertaken sub-national tailoring or stratification?
- ~ If yes:
    - o When was it undertaken most recently?

- Is it feasible to allocate test and treatment options chosen *initially* in the high burden strata identified through SNT or stratification?
- From the access session in which we discussed ways to achieve access – please consider which options discussed may have been most feasible for your context, whether a mix of strategies is required or how you think it is best to achieve access where vivax caseloads are highest?
- Think about access to remote, mobile or border populations – is a system such as 'buddy health' feasible for your setting?

~ If no consider the following.

- Criteria from CHAI on where to place G6PD analyzers.

Text S2: Step by step guideline:

Introduction

The vision of WHO and the global malaria community is a world free of malaria. As part of this vision, the Global Malaria Technical Strategy 2018-2030 set ambitious global targets for 2030. Countries that have controlled malaria *Plasmodium falciparum* malaria cases are reducing but as this happens, the proportion of cases due to *Plasmodium vivax* has increased. *P. vivax* tolerates a wider range of environmental conditions than *P. falciparum* and therefore has a wider geographical range. In countries where both *Plasmodium falciparum* and *P. vivax* are present, the burden of disease due to *P. vivax* is more difficult to reduce because the parasite forms a dormant stage in the liver (hypnozoites). Dormant hypnozoites are more difficult to detect because the parasite density is typically low and dormant hypnozoites residing in the liver cannot be detected with existing diagnostic tests. Hypnozoites can give rise to multiple relapses and contribute to significant morbidity and onward transmission. *P. vivax* can be transmitted from humans to mosquitoes before infected people develop symptoms. The hypnozoites can only be eliminated through treatment with drugs belonging to the 8-aminoquinoline class, which can produce serious side effects (haemolytic anaemia) in patients who have G6PD deficiency, and such treatment is contraindicated in vulnerable population groups such as infants and pregnant or breastfeeding women.

WHO recognizes that safe and effective radical treatment of vivax malaria currently requires two diagnoses (confirmation of *P. vivax* parasites and glucose-6-phosphate dehydrogenase (G6PD) status). As point-of-care G6PD tests become available, these services will need to be implemented alongside malaria diagnostic testing to ensure optimal treatment to prevent *P. vivax* relapse. For elimination to succeed, greater attention must be given to *P. vivax,* a parasite less well understood than P. *falciparum*. Vivax malaria presents multiple challenges and needs specific strategies.

The control and elimination of malaria depends on resolute political commitment to universal health care, inclusive of malaria prevention, diagnosis and treatment as part of both primary health care systems and broader development initiatives.

Human and financial resources will be required to appropriately support safe and effective implementation of G6PD testing services and improved radical treatment of vivax malaria. The services, both public and private, and medical

products need to be safe and effective and delivered in a timely, equitable, efficient and integrated manner. High-quality and integrated delivery are important for reducing both the burden of malaria and the potential for onward transmission of parasites.

To keep ahead of the disease will require a culture of learning and adapting with the capacity to effectively generate and use knowledge to identify gaps, health disparities and existing inequalities, monitor progress, and seek and adopt transformative approaches and new interventions that have the potential to accelerate the progress towards elimination goal of 2030.

Background and rationale

As countries in the Asia Pacific strive towards elimination of malaria by 2030 and many countries may have eliminated *P. falciparum*, finishing the elimination job by treating and reducing the transmission of *Plasmodium vivax* is of paramount importance. For elimination to succeed, attention must be also given to *P. vivax P. vivax* and treatment requires a radical cure that cures both the blood-stage and liver stage infections.

Currently, primaquine is the only widely available and WHO-recommended drug against hypnozoites. However, the prolonged administration of PQ for 14 days to 8 weeks brings about issues of adherence with many patients failing to complete the recommended treatment regimen and there is a risk associated with most treatments, including 8-Aaminoquinolines especially for G6PD deficient patients. Recent advances in near-patient or point-of-care G6PD deficiency screening and shorter course 8-aminoquinoline treatment are rapidly changing the landscape of radical cure of vivax malaria available for National Malaria Programs (NMPs).

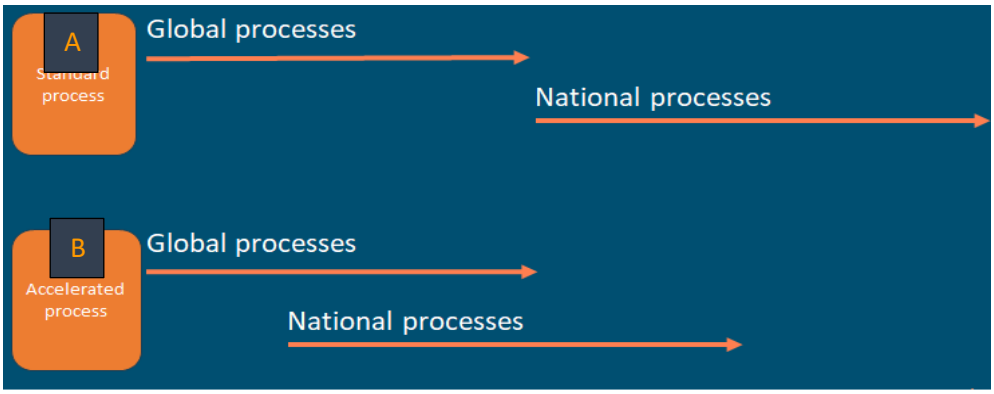
While NMPs await the WHO's global policy guidance on these advances, they need to consider different contextual factors related to their countries vivax burden, health system capacity, and availability of resources to support changes to their policies and practices.

This Options Assessment Toolkit (OAT) was developed to enable NMPs systematically determine optimal radical cure options for their given environments. Where multiple options are available to policy makers, evidence shows that delays in decision-making occurs. Additionally, malaria program policy changes are often triggered in reaction to WHO recommendations from the Global Malaria Program (see figure 1a). This more proactive approach using the

OAT for decision-making and identification of activities to strengthen support mechanisms to facilitate effective use of new tools, can shorten delays once WHO recommendations are available from the global level and potentially reduce the size of stairs along the loss of effectiveness stairway.

The OAT has been co-developed through participatory research methods approach which included validation of the various elements with NMPs and experts engaged in designing the research process and the toolkit.

Figure 1: Conceptual timelines for reactive (A) and proactive (B) approaches to decision-making



What is OAT and why do it?

The OAT kit consists of:

1) Baseline Assessment Template (BAT)
2) Status of new tools for vivax case management
3) Scenarios representing the Asia Pacific region.
4) Scenario based test and treat options.
5) Considerations for policy change and, approaches to implement Test and Treat combinations.

These tools are expected to be used by the NMPs and their stakeholders working in antimalarial response in the country/region and facilitate accelerated decision making for optimal radical cure for vivax malaria and accelerate towards achieving malaria elimination.

Table 1: OAT elements, description, objective and intended use/user.

Tool	Description	Objective	Intended use/user
1. Baseline assessment template (BAT)	This template includes specific variables under three broad factors of epidemiological, implementation (health system), and enabling (political and economic) factors	Facilitate the NMPs in assessing their current situation of readiness for vivax elimination.	For use by the TWG at the start of the process for considering changing antimalarial policy or improving current vivax treatment guidelines.
2. Status of new tools for vivax case management	This tool will provide the latest and comprehensive evidence on high-sensitivity RDTs, G6PD testing, different regimens of primaquine, and tafenoquine, along with their pediatric formulations for informing NMPs.	Inform the NMPs with the latest evidence on different diagnostics, G6PD screening, and radical cure regimens.	The NMPs can use these evidence decks (i.e., slides) as a reference and as an information sharing tool.
3. Scenarios representing Asia Pacific region	This tool describes eight possible contextual scenarios depicting the status of malaria elimination/control in the Asia Pacific region, taking into consideration the readiness of health system and politico-economic factors, along with vivax malaria-specific epidemiological factors.	Aid the NMPs in viewing different contextual and health system features of scenarios of malaria elimination in the region.	The NMP and TWG can map the range of scenarios possible in the region and identify which scenario their country likely falls into.
4. Scenario based test and treat options.	This document will list the expert-recommended optimal combinations of G6PD testing and radical cure treatment regimens for each scenario.	Enable the NMPs to assess the combinations of radical cure options for their current scenario. Allow the NMPs to view what the experts think and visualize potential future scenarios and radical cure tool combinations as burden reduces in higher-burden countries.	The TWG to discuss in detail the options recommended by the experts, their feasibility for local country context, and then identify what is optimal for their conditions

Tool	Description	Objective	Intended use/user
5. Considerations for policy change and approaches to implement Test and Treat combinations	This tool will enable the NMPs to visualize the policy change process and provide recommendations for effective implementation of the chosen test and treat combination. Specific approaches will include strategies on improving access, adherence, allocation of resources, advocacy, and awareness for the radical cure combinations.	Outline policy change process considerations and highlight different implementation strategies/approaches for each combination of radical cure options.	After deciding the optimal radical cure option, the TWG and NMP can draw valuable insights from this tool to proceed and plan for reaching the 2030 malaria elimination target.

OAT elements

1. Baseline Assessment Template (BAT)

Objective

To enable NMPs to assess the current readiness for vivax elimination in their country context.

Description

BAT provides a comprehensive framework of specific variables for assessment of the enabling factors, implementing factors and epidemiological factors and identify gaps that need strengthening in order to improve / update test and treat for vivax malaria.

WHEN should this Baseline assessment template be used?

The baseline assessment template should be used when the NMP requires to update/revise vivax malaria test and treat policy and needs to know the current status so that they can choose from the various test and treat options recommended that best suits the local context.

WHO should do the baseline assessment?

The NMPs should lead the baseline assessments in each country and identify their stakeholders in the Ministry of Health (HMIS, Research Unit, AFD, PPD, District Health Services, Pharmacy Department Clinical Laboratory and Public Health Labs, etc.) and Allied Health Agencies (Medical Council, Drug Regulatory Authority, etc.) who can provide the information on various aspects of health financing and health system.

WHY was there a need for a baseline assessment template?

Countries in the Asia Pacific region are in different phases of malaria programming and have diverse challenges. A standard, tested, baseline assessment template (BAT) can enable NMPs to focus on critical information that needs to be considered while revising or updating the treatment policy for vivax malaria.

HOW should it be done?

NMPs should take the lead role in completing the baseline assessment template. Firstly, the NMPs should fill up all the information the program confidently can fill up. NMPs should identify relevant stakeholders and consult them for relevant information. If there is already an existing committee that program works with routinely such committees should support the program. If there is no such committee a committee with relevant stakeholders may be formed to complete the assessment. All information filled up should be backed up with evidence and references listed for authenticity. Where there is lack of information if need be, a study or research may be needed in future so such gaps should also be identified and listed.

How long should this element take?

As per the experience shared by a few NMPs, the filling up of the BAT has just taken just about 30-60 minutes to fill but it may vary from country to country based on various factors.

2. Status of new tools for vivax case management

Objective: Inform the NMPs with the latest evidence on different diagnostics, G6PD screening, and radical cure regimens.

Description:

- WHEN should this Baseline assessment template be used?
- WHO should do the baseline assessment?
- WHY was there a need for a baseline assessment template?
- HOW should it be done?
- How long should this element take?

3. **Scenarios representing the Asia Pacific region.**

Objective: Aid the NMPs in viewing different contextual and health system features of scenarios of malaria elimination in the region.

Description:

- WHEN should this Baseline assessment template be used?
- WHO should do the baseline assessment?
- WHY was there a need for a baseline assessment template?
- HOW should it be done?
- How long should this element take?

4. scenario based test and treat options.

Objective: Enable the NMPs to assess the combinations of G6PD testing and radical cure options for their current scenario. Also, allow the NMPs to view what the experts think and visualize potential future scenarios and radical cure tool combinations as burden reduces in higher-burden countries.

Description:

- WHEN should this Baseline assessment template be used?
- WHO should do the baseline assessment?
- WHY was there a need for a baseline assessment template?
- HOW should it be done?
- How long should this element take?

5. Considerations for policy change and approaches to implement Test and Treat combinations.

Objective: Outline policy change process considerations and highlight different implementation strategies/approaches for each combination of radical cure options.

Description:

- WHEN should this Baseline assessment template be used?
- WHO should do the baseline assessment?
- WHY was there a need for a baseline assessment template?
- HOW should it be done?
- How long should this element take?

Table: Baseline assessment template domains, questions, variables, stakeholders list and source of information (*each country may have different names for their committees)*

Domain	Questions in BAT	Variables	Stakeholders	Source of information
Epidemiology	What is the phase of malaria program in your country?	Prevention of re-introduction Elimination Pre-elimination Control	Technical Working Group (or country equivalent)	National strategic plan, annual malaria report; world malaria report
	What is the number of annual reported cases of vivax in your country?	0 1-10,000 >10,000	HMIS and WHO	Annual malaria program report; annual health bulletin; world malaria report
	What is the level of G6PD deficiency (defined as less than 30% G6PD activity) in your country?	Rare (<1%) Common (1%-10%) High (>10%) Don't know	Clinical laboratory/study report	Laboratory report; study report (national or local); collation of small-scale national studies, if no data available (Howes et al 2012)
	Antirelapse efficacy data (≥85% efficacy at six months) is available for which radical cure drug regimen/s in your country or similar settings?	Adequate (>85% recurrence-free at six months) Inadequate (<85% recurrence-free at six months)	Research unit/ethical committee	National or regional randomized controlled trial data; National Drug regulatory Authority such as FDA; and Ethical Committee where study protocols are submitted.

Domain	Questions in BAT	Variables	Stakeholders	Source of information
Implementation	What is the estimated proportion of vivax patients referred from initial point of malaria diagnosis to higher health centers?	High (>80%)	Health facility in-charge, data managers, researchers	Health facility referral registers report/study report
		Moderate (>50%-80%)		
		Low (>10%-50%)		
		Very low (<10%)		
		Do not know		
	What is the estimated proportion of referred vivax patients that complete referral at receiving health facility	High (>80%)	Health facility incharge, data managers, researchers	Health facility report/study report (national or local)
		Moderate (>50%-80%)		
		Low (>10%-50%)		
		Very low (<10%)		
		Do not know		
	What activities are allowed by the Ministry of Health for health workers at the community level for malaria case management?	HW can test, treat, and track patient adherence	Medical council & drug regulatory authority	Malaria treatment guideline; medical council & drug regulatory authority regulations; labour force and employment surveys; health facility assessment and routine administrative information
		HW can test and track but cannot treat		
		HW available but cannot test, treat and track		
		Do not know.		
		High (>80%)		

Domain	Questions in BAT	Variables	Stakeholders	Source of information
	What do you think is the estimated proportion of health workers at different levels of the health system who adhere to current or new treatment protocol?	Moderate (>50%-80%) Low (<50%) Don't know	Pharmacy unit in health facilities	Pharmacy register, study report (national or local), routine case records
	What do you think is the estimated proportion of patients who adhere to the full treatment regimen of current recommended radical cure of drugs?	High (>80%) Moderate (>50%-80%) Low (<50%) Don't know	Research partners	National or local survey
	Is supervised treatment or any other intervention being implemented at a large scale to improve patient adherence to current recommended radical cure of vivax in your country? (Policy on supervised treatment)	Yes No Don’t know	Pharmacy unit in health facilities	National strategic plan, national treatment guidelines, pharmacy register, study report
	What is the status of adverse event reporting for any diseases in the last 12 months in your country? (Pharmacovigilance)	High (AE usually recorded and reported from health facility to national level) Moderate (AE sometimes recorded and reported health facility to national level)	Pharmacy in health facility & drug regulatory authority	Report from drug regulatory authority pharmacovigilance unit (or national pharmacovigilance unit not linked with FDA)

Domain	Questions in BAT	Variables	Stakeholders		Source of information
		Low (AE not recorded or reported health facility to national level)			
		Do not know			
Enabling	What Percentage of time was spent discussing "patient safety" compared to "efficacy" and implementation issues pf "8-aminoduinolines (PQ, TQ) in the last Technical Working Group (TWG) meeting which discussed on treatment policy change for vivax malaria in your country?	High (More time spent on discussing safety compared to efficacy)	TWG members		TWG meeting report
		Moderate (equal time spent on discussing safety compared to efficacy)			
		Low (Less time spent on discussing safety compared to efficacy)			
	What percentage of the annual budget for malaria is funded by the national government?	High (≥90%)	PPD/AFD/MOH		Annual budget report
		Moderate (19-89%)			
		Low (≤20%)			
	Who was the chief guest in the last World Malaria Day event in your country?	High (Head of state attends World Malaria Day events)	NMP	NMP	WMD report
		Moderate (Permanent Secretary			

Domain	Questions in BAT	Variables	Stakeholders		Source of information
		attends World Malaria Day events)			
		Low (No high-ranking official attends World Malaria Day events)			

Table 2: Step by step guidance for BAT

S No.	**ACTIVITIES**	
	PHASE 1: ASSESSMENT INITIATION	
1.1	Establish Committee (Steering Committee /TWG)	
1.2	Formulate the roles and responsibilities of Committee	
1.3	Sensitize the Committee on the Baseline Assessment Template	
1.4	Develop Concept note /protocol development	
1.5	Customize the data collection tools	
1.6	Ethical approvals id studies needed	
1.7	Planning activities (meetings/field visits/studies etc.) with timelines and budget	
	PHASE 2: DATA COLLECTION & REVIEW	
2.1	Conduct Desk review and identify information gaps that needs to be collected	
2.2	Field visits to collect/verify data	
2.3	identify survey/study needed	
2.4	Data quality assessment	
	PHASE 3: DATA ANALYSIS OUTPUTS	
3.1	Collate outputs of desk reviews	
3.2	Collate outputs of field visits	
3.3	Aggregate data from desk reviews, field visits studies and other sources	
3.4	Manage and clean data	
3.5	Data analysis	
	PHASE 4: REPORT FINALIZATION AND DISSEMEINATION	
4.1	Final Report	
4.2	Identify gaps that need to be addressed and recommendations	
4.3	Prepare presentations for dissemination	
4.4	Technical briefs and reports	