Malaria Elimination in the Greater Mekong Subregion (GMS)

Malaria Policy Advisory Committee (MPAC)
2-4 October 2019
Malaria elimination in the GMS: Targets

By 2020 or earlier
- Transmission of *P. falciparum* malaria interrupted in all areas of multidrug resistance (and in Cambodia)
- All species of human malaria eliminated in Yunnan Province, China

By 2025
- *P. falciparum* malaria eliminated in all countries of the GMS
- All species of human malaria eliminated in Cambodia and Thailand

By 2030
- All species of human malaria eliminated in all countries of the GMS
• Updates on progress
• Priorities in the GMS
• WHO support to GMS
• Summary
Progress: Significant decrease in cases (2012-2019)

Source: WHO subregional database
Number of monthly cases in the GMS (2017-2019)

Case burden in Cambodia started to decrease in 2H 2018.

Source: WHO subregional database. Myanmar cases include only public sector data.
Progress toward *Pf* elimination

**Total confirmed cases (2016-2019)**

Source: WHO subregional database, excluding mixed cases.
Progress toward *Pf* elimination (2017 vs. 2018)

Changes in *Pf* + Mix Cases from 2017 to 2018

<table>
<thead>
<tr>
<th>Year</th>
<th>Country</th>
<th>Cases 2017</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>Myanmar</td>
<td>89110</td>
<td>-34%</td>
</tr>
<tr>
<td></td>
<td>Cambodia</td>
<td>-17912</td>
<td>-26%</td>
</tr>
<tr>
<td></td>
<td>Thailand</td>
<td>-7036</td>
<td>-39%</td>
</tr>
<tr>
<td></td>
<td>Lao PDR</td>
<td>97</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>Vietnam</td>
<td>118</td>
<td>4%</td>
</tr>
<tr>
<td>2018</td>
<td></td>
<td>63813</td>
<td>-28%</td>
</tr>
</tbody>
</table>

Source: WHO subregional database
Progress toward *Pv* elimination

**Total confirmed cases (2016-2019)**

- *P. falciparum* cases
- *P. vivax* cases

Source: WHO subregional database, excluding mixed cases.
Progress toward Pv elimination (2017 vs. 2018)

Changes in Pv + Mix Cases from 2017 to 2018

<table>
<thead>
<tr>
<th></th>
<th>2017</th>
<th>Thailand</th>
<th>Lao PDR</th>
<th>Vietnam</th>
<th>Myanmar</th>
<th>Cambodia</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>% change</td>
<td>-42%</td>
<td>-12%</td>
<td>2%</td>
<td>10%</td>
<td>125%</td>
<td>32%</td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>71768</td>
<td>-4010</td>
<td>-593</td>
<td>163</td>
<td>525</td>
<td>26779</td>
<td>94551</td>
</tr>
</tbody>
</table>

Source: WHO subregional database
In 1H 2019, approx. 79% of cases were \(Pv\) or \(Pv+Pf\).

Relative importance of \(Pv\) cases is likely to increase as countries approach elimination.

Insufficient or lack of implementation of radical cure with primaquine in Cambodia and Lao PDR.

Source: WHO subregional database. *Viet Nam data are provincial level.
### Percentage of \( P_v + \) Mix cases in GMS (2016-2019)

<table>
<thead>
<tr>
<th>Country</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>Jan-Jun 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cambodia</td>
<td>48%</td>
<td>46%</td>
<td>73%</td>
<td>87%</td>
</tr>
<tr>
<td>Lao PDR</td>
<td>63%</td>
<td>51%</td>
<td>47%</td>
<td>68%</td>
</tr>
<tr>
<td>Myanmar</td>
<td>43%</td>
<td>32%</td>
<td>51%</td>
<td>78%</td>
</tr>
<tr>
<td>Thailand</td>
<td>76%</td>
<td>84%</td>
<td>83%</td>
<td>80%</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>44%</td>
<td>37%</td>
<td>38%</td>
<td>34%</td>
</tr>
</tbody>
</table>

Source: WHO subregional database
Thailand is nearing Pf elimination

Pf + Mix cases in 2018
(n = 876 cases)

Source: WHO subregional database
Pf+Mix vs Pv in Cambodia (2014 - Aug 2019)

Source: WHO subregional database
Priorities in GMS (MPAC, April 2019)

• Targeting high-risk populations, including:
  → Forest goers in remote areas
  → Mobile and migrant populations

• Monitoring drug efficacy and updating/implementing national treatment guidelines, including:
  → Replacing ineffective first-line drugs and identifying second-line drugs
  → Implementing Pv radical cure

• Cross-border collaboration, including:
  → Regional data-sharing platform (RDSP)
  → Partner coordination

For each category, it is encouraged to explore innovative approaches
Priorities in GMS

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Cases are highly concentrated in a few health centres in Cambodia and Lao PDR.

In both Cambodia and Lao PDR, top 20 facilities account for approx. 40% of cases, while top 50 account for approx. 60% of cases (Jan-June, 2018).

Source: WHO subregional database. Cambodia/Lao PDR data are commune/HC level; Thailand data are district level; and Viet Nam data are provincial level.
Most cases are among forest goers (Results from UCSF and MSF)

Prevalence of all malaria parasites (RDT)
(% of all positive case, Champasak, Lao PDR)

- **Baseline** (n=4,942): 0.12
- **Forest goers (FTAT)** (n=2,906): 3.1
- **Villages (MTAT R1)** (n=17,821): 0.06
- **Village (MTAT R2)** (n=7,091): 0.1

Prevalence in malaria in ACD (PCR)
(% of positive Pf case, N=2772 (Preah Vihear, Cambodia))

- **No risk** (n=613): 0.0
- **Forest goers** (n=914): 2.5
- **Plantation** (n=850): 2.0
- **Rice Field** (n=165): 1.2

Source: UCSF (Lao PDR) and MSF (Cambodia).
Challenge: Forest sites are widely dispersed

Possible Forest Sites in Me Mang, Mondulkiri, Cambodia

Source: WHO subregional database
Mobility patterns, group size and access to communications differs significantly across forest goers. As a result, there is no one-size-fits-all solution to reaching forest goers.

To develop effective and tailored intervention strategies, it is helpful to work hand-in-hand with the community, government and partners.

This will also improve the ownership of the communities in resource-scarce settings.
Priorities in GMS

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Evolution and expansion of multidrug-resistant malaria in southeast Asia: a genomic epidemiology study


Summary

Background A multidrug-resistant co-lineage of *Plasmodium falciparum* malaria, named KEL1/PLA1, spread across Cambodia in 2008–13, causing high rates of treatment failure with the frontline combination therapy dihydroartemisinin-piperaquine. Here, we report on the evolution and spread of KEL1/PLA1 in subsequent years.

- 1. Emergence of KEL1 in different parts of SE Asia with notable localized geographic distribution.
- 2. Rapid expansion of a related group of parasites that shared a specific lineage of KEL1 and a specific lineage of plasmepsin amplification (PLA1) that caused DHA-PPQ treatment failure in western Cambodia.
- 3. KEL1/PLA1 co-lineage that has spread across the region and differentiated into sub-lineages that vary in geographical distribution and phenotype.
Determinants of dihydroartemisinin-piperaquine treatment failure in *Plasmodium falciparum* malaria in Cambodia, Thailand, and Vietnam: a prospective clinical, pharmacological, and genetic study


**Summary**

**Background**

The emergence and spread of resistance in *Plasmodium falciparum* malaria to artemisinin combination therapies in the Greater Mekong subregion poses a major threat to malaria control and elimination. The current study is part of a multi-country, open-label, randomised clinical trial (TRACCI, 2015–18) evaluating the efficacy, safety, and tolerability of triple artemisinin combination therapies. A very high rate of treatment failure after treatment with dihydroartemisinin-piperaquine was observed in Thailand, Cambodia, and Vietnam. The immediate public health importance of our findings prompted us to report the efficacy data on dihydroartemisinin-piperaquine and its determinants ahead of the results of the overall trial, which will be published later this year.
## Efficacy of ACTs in GMS (2010-2018)

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>N of studies</th>
<th>Tx failures min</th>
<th>Tx failures max</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Myanmar</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artemether-lumefantrine</td>
<td>2010-17</td>
<td>25</td>
<td>0.0</td>
<td>6.0</td>
</tr>
<tr>
<td>Artesunate-mefloquine</td>
<td>2011-13</td>
<td>5</td>
<td>0.0</td>
<td>2.2</td>
</tr>
<tr>
<td>Artesunate-pyronaridine</td>
<td>2017-18</td>
<td>4</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>DHA-piperaquine</td>
<td>2010-18</td>
<td>21</td>
<td>0.0</td>
<td>4.8</td>
</tr>
<tr>
<td><strong>Cambodia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artesunate-mefloquine</td>
<td>2011-18</td>
<td>18</td>
<td>0.0</td>
<td>1.8</td>
</tr>
<tr>
<td>Artesunate-pyronaridine</td>
<td>2017-18</td>
<td>4</td>
<td>0.0</td>
<td>3.3</td>
</tr>
<tr>
<td><strong>Lao PDR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artemether-lumefantrine</td>
<td>2010-17</td>
<td>9</td>
<td>0.0</td>
<td>17.2</td>
</tr>
<tr>
<td>DHA-piperaquine</td>
<td>2016-17</td>
<td>2</td>
<td>13.3</td>
<td>47.4</td>
</tr>
<tr>
<td>Artesunate-pyronaridine</td>
<td>2018-19</td>
<td>1</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Viet Nam</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DHA-piperaquine</td>
<td>2010-17</td>
<td>42</td>
<td>0.0</td>
<td>46.3</td>
</tr>
<tr>
<td>Artesunate-pyronaridine</td>
<td>2017-18</td>
<td>5</td>
<td>0.0</td>
<td>4.8</td>
</tr>
</tbody>
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Priorities in GMS

• Targeting high-risk populations, including:
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• Cross-border collaboration, including:
  → Regional data-sharing platform (RDSP)
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Cross-Country Collaboration: Regional Data Sharing Platform (RDSP)

- All GMS countries are sharing monthly surveillance data to the WHO RDSP
- RDSP enables monitoring toward malaria elimination, detailed data analysis, and sharing data across the Subregion (e.g. cross-border meetings).
WHO hosted an annual GMS surveillance meeting (Nov 2018), with the objectives to:

- Exchange information on surveillance progress and challenges in GMS countries
- Strengthen surveillance in elimination phase (e.g. case and foci-investigation)
- Discuss proposed mechanism to utilize the WHO RDSP for cross-border collaboration
- Brainstorm future priorities for surveillance

Next surveillance meeting scheduled for Nov 2019
Challenges for surveillance in GMS

### Key Areas of Work

**Data Collection and Reporting**
- Include surveillance data from partners and private sector
- Timely reporting of aggregated data to the national database
- Implement case-based surveillance and iDES

**Data Use**
- Analyse & share surveillance data especially sub-national levels
- Take timely programmatic actions

**Validation**
- Regular validation of surveillance data
- Surveillance assessment

### Challenges

- Analyse & share surveillance data especially sub-national levels
- Take timely programmatic actions
- Regular validation of surveillance data
- Surveillance assessment
- Include surveillance data from partners and private sector
- Timely reporting of aggregated data to the national database
- Implement case-based surveillance and iDES
Major Objectives

1. **Country Offices** continue support to national malaria elimination programmes

2. **HQ and Regional Offices** ensure timely technical support

3. **Mekong Malaria Elimination (MME) team** addresses partnership coordination and cross-country issues

MEAC: Malaria Elimination Advisory Committee; NMCP: National Malaria Control Programmes
WHO supports partner coordination and collaboration

• **Information:** Exchange information on activities. Regularly share key updates (e.g. new project, publication, meeting)

• **Coordination:** Ensure there are neither overlaps nor gaps in our activities. Maintain close contact among partners that operate in the same provinces/districts

• **Collaboration:** Establish joint projects with clear definitions of responsibilities for each partner and NMCP
WHO facilitates information exchange among partners through various mechanisms:

- Publications (e.g. annual publication, quarterly epidemiology summary)
- Partners’ mailing list (e.g. quarterly partner activity summary)
- MME website
- Subregional and national meetings
Partner Mapping with CHAI

Examples of results from partner mapping with CHAI

Partners working at national level (Lao PDR)

Source: WHO subregional database and CHAI survey
• GMS countries have substantially reduced the number of malaria cases from 2012-2018. In 2018 and the first half of 2019, countries have made significant progress towards *Pf* elimination, especially Cambodia, Myanmar and Thailand.

• From January to June 2019, approximately 79% of cases in the GMS were *Pv* or combined cases of *Pv* and *Pf*.

• The remaining cases are concentrated in small geographical areas among forest goers, requiring a focused and tailored strategy for these populations (inc. prophylaxis).

• WHO continues to support National Malaria Control Programmes to address challenges and priorities and the Mekong Malaria Elimination (MME) programme continues to support communication, partner coordination and cross-country activities.
Thank you
<table>
<thead>
<tr>
<th>Country</th>
<th>Overall</th>
<th>Pf+Mix</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td># of Cases 2017</td>
<td># of Cases 2018</td>
<td>% Change</td>
</tr>
<tr>
<td>Cambodia</td>
<td>46590</td>
<td>66386</td>
<td>42%</td>
</tr>
<tr>
<td>Lao PDR</td>
<td>9327</td>
<td>8909</td>
<td>-4%</td>
</tr>
<tr>
<td>Myanmar</td>
<td>85014</td>
<td>68752</td>
<td>-19%</td>
</tr>
<tr>
<td>Thailand</td>
<td>11396</td>
<td>6610</td>
<td>-42%</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>4542</td>
<td>4813</td>
<td>6%</td>
</tr>
</tbody>
</table>