Forest malaria in Myanmar: tracking landscapes at risk within a hidden diversity of environments.

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Malaria in the Greater Mekong subregion

→ *P. falciparum* & *P. vivax*
→ Progress over past 15 years
  - Decreasing incidence
  - Increasing % *P. vivax*
  - under threat from *P. falciparum* artemisinin & multidrug resistance
→ Increasing spatial heterogeneity
  - Hard to reach regions
  - Focus on « forest-goers »

*Figure 2.* Distribution of *P. falciparum* & *P. vivax* malaria cases in the GMS in 2021. Source: The Mekong Malaria Elimination Program, Bulletin March 2022.
- **Forest malaria in the GMS**
- **Malaria associated with forested regions at regional scale**
  - Ecological correlation
  - Ecological niche of major malaria vector *An. dirus* linked to forests (Obsomer)
  - Specific patterns in relation to deforestation described in Lao (Rerolle)

- **Malaria is associated with forest activities in individual case-control studies**
Forest malaria in the GMS

Different environments unlikely to support homogenous malaria vector population

Human activity patterns may allow transmission or not: seasonality, frequency+duration of exposure, population density and mixing in forest sites...

+ presence of a Human reservoir of parasites

Are all forested environments sharing the same risk of malaria?

Elimination phase:

→ Specific locations or types of locations (linked to specific activities) which could be targeted more accurately/specifically

→ Proxies of receptivity to define areas at higher risk of resurgence
Malaria Elimination Task Force (METF) in Karen State, Myanmar

Initiated in 2014 to drastically decrease malaria incidence and limit the spread of multidrug resistant *P. falciparum* beyond the GMS.

**Setting:** hard-to-reach mountainous and forested Eastern Karen State, Myanmar

**Intervention strategy:**

- Malaria posts (MP) in all villages (>1000 posts, 95% of villages)
- Identification of high prevalence hotspots and mass drug administration (70 hotspot communities).
- Routine surveillance through MP weekly reports
- Monitoring & evaluation to ensure continuous function of MP

**Objectives:** characterize environments associated with specific local malaria dynamics
**Outcome**

_P. falciparum & P. vivax_

INCIDENCE PROFILES

PAM-DTW clustering on functional data

(region scale)

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**Methods**

- **Covariates**
  - LULC classification
  - Elevation and slope data
  - Rainfall + temperature data

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**Analysis**

Association between malaria incidence profiles & forest environments

*Conditional inference trees + conditional random forest*

(region and township scales)

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**Outcome**

MAP OF ECO-EPIDEMIOLOGICAL ZONES

(region scale)
**INTRODUCTION**

**METHODS**

**RESULTS**

**DISCUSSION**

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**Outcome**

*P. falciparum & P. vivax*

**INCIDENCE PROFILES**

PAM-DTW clustering on functional data (region scale)

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**Raster data**

**LANDSCAPES** (region and township scales)

**CLIMATES** (region scale)

**MASS DRUG ADMINISTRATION**

**Covariates**

LULC classification

Elevation and slope data

Rainfall + temperature data

AHC on PCA

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Association between malaria incidence profiles & forest environments

*Conditional inference trees + conditional random forest*

(region and township scales)

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MAP OF ECO-EPIDEMIOLOGICAL ZONES

(region scale)
A. Outcome: defining groups villages sharing the same incidence dynamics over a 4-year period

- **Data**: clinical malaria incidence (*P. falciparum* & *P. vivax*) recorded by MP from 2016 to 2020 (n=662 villages)
- **Method**: clustering villages using PAM algorithm on DTW metric after functional transformation of incidence series.
- 2 sets of profiles: PF and PV separately

Raw data: weekly PF and PV incidence rate

![Raw data](image1.png)

Functional data

![Functional data](image2.png)

Dynamic time-warping distance matrix

![Distance calculation](image3.png)

Incidence profiles

![Incidence profiles](image4.png)
**Outcome**

*P. falciparum & P. vivax*

INCIDENCE PROFILES

PAM-DTW clustering on functional data
(region scale)

**Methods**

**Covariates**

- LULC classification
- Elevation and slope data
- Rainfall + temperature data

**Results**

Association between malaria incidence profiles & forest environments

*Conditional inference trees + conditional random forest*
(region and township scales)

**Discussion**

MAP OF ECO-EPIDEMIOLOGICAL ZONES
(region scale)
B. Environment data

Extraction using a 2-km hexagonal grid

**Landscape:**
- **altitude + slope**: GMTED 2010 digital elevation model
- **Landuse/landcover**: UMR ESPACE DEV team
  → Sentinel 2 de 2019 à 2020, 10m resolution
  → OBIA: object-based image analysis
  → ground-truthing with 300 random points (field team and Google Earth interpretation)

**Climate:**
- **Day and night temperature**: MODIS/006/MOD11A2 (1km resolution): monthly average over study period
- **Daily rainfall**: UCSB-CHG/CHIRPS/DAILY (5.5km resolution): average monthly cumulative over study period
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**Outcome**

*P. falciparum & P. vivax*

**INCIDENCE PROFILES**

- **PAM-DTW clustering on functional data** (region scale)

**Covariables**

- **Raster data**
  - LULC classification
  - Elevation and slope data
  - Rainfall + temperature data

**LANDSCAPES** (region and township scales)

**CLIMATES** (region scale)

**MASS DRUG ADMINISTRATION**

**Association between malaria incidence profiles & forest environments**

*Conditional inference trees + conditional random forest* (region and township scales)

**MAP OF ECO-EPIDEMIOLOGICAL ZONES** (region scale)
A. Incidence profiles

11 profiles for *P. falciparum* and *P. vivax* incidence.

Group villages sharing similar dynamics = amplitude, seasonality and trend.
B. Landscape and climate

• >70% of the region is covered with forest (sparse or dense)

• LULC included 10 classes

• LULC (% + fragmentation) + topography combined identified 17 Landscapes
  → 6 different major forest landscapes
  → 2 specific landscapes in the northern region

→ A wide diversity of landscapes identified within a forested region

• Gradients
  → pristine > anthropic
  → altitude/slope

• Types of agricultures (paddies vs slope)
C. Association between incidence profile and environment

Northern area

A

Node 1
Dense forest, sparse forest, cropland
N=370, p<0.001

≤ 2km

Node 2
Climate
N=140, p=0.044

> 2km

Node 5
Dense forest, sparse forest, cropland
N=230, p=0.012

≤ 19km

Node 6, N=207

> 19km

Node 7, N=23

B

P. falciparum incidence profiles
- Very low
- Low
- Cold 2016-2017
- Cold 2017-2018
- Cold 2018-2019
- Rainy 2017
- Rainy 2018
- Cold & Rainy decreasing
- Hotspot 1
- Hotspot 2
- V.350

Township boundary
P. falciparum CT (North-10km)
NODE 3
NODE 4
NODE 5
NODE 6
NODE 7
C. Association between incidence profile and environment

Mainly 1 climate and 2 landscapes associated with malaria-affected incidence profiles
### INTRODUCTION

#### METHODS

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**D. Eco-epidemiological zones**

**A. METF region vs. North area for P. falciparum**

<table>
<thead>
<tr>
<th>METF region</th>
<th>Midland (N3)</th>
<th>Not In Midland (N2)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2km DSC; Midland (N2)</td>
<td>129 (55.5)</td>
<td>0 (0)</td>
<td>129 (55.5)</td>
</tr>
<tr>
<td>≤2km DSC; foothills (N4)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>11 (4.7)</td>
</tr>
<tr>
<td>&gt;2km DSC (N8)</td>
<td>92 (39.9)</td>
<td>128 (52.8)</td>
<td>220 (84.7)</td>
</tr>
<tr>
<td>Not in North area</td>
<td>56 (5.3)</td>
<td>236 (35.6)</td>
<td>292 (44.1)</td>
</tr>
<tr>
<td>Total</td>
<td>277 (42)</td>
<td>385 (58)</td>
<td>662 (100)</td>
</tr>
</tbody>
</table>

⇒ 4 risk profiles

**B. METF region vs. North area for P. vivax**

<table>
<thead>
<tr>
<th>METF region, ≥8 km</th>
<th>Midland, South Midland (N2)</th>
<th>Not In Midland, ≤900m SG (N4)</th>
<th>Not In Midland, &gt;900m SG (N5)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not in North area</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>10 (1.5)</td>
<td>10 (1.5)</td>
</tr>
<tr>
<td>Midland, &gt;1.7km SG (N2)</td>
<td>0 (0)</td>
<td>5 (2.2)</td>
<td>134 (29.5)</td>
<td>139 (30)</td>
</tr>
<tr>
<td>Midland, &gt;2.5km SG (N4)</td>
<td>132 (9.9)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>132 (9.9)</td>
</tr>
<tr>
<td>Midland, &gt;7.5km SG (N5)</td>
<td>82 (12.4)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>82 (12.4)</td>
</tr>
<tr>
<td>Midland, &gt;7.5km SG (N9)</td>
<td>7 (1.1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>7 (1.1)</td>
</tr>
<tr>
<td>Not in North area</td>
<td>71 (10.7)</td>
<td>19 (2.9)</td>
<td>202 (30.5)</td>
<td>292 (44.1)</td>
</tr>
<tr>
<td>Total</td>
<td>292 (44.1)</td>
<td>24 (3.6)</td>
<td>346 (52.3)</td>
<td>662 (100)</td>
</tr>
</tbody>
</table>

⇒ 6 risk profiles

**C. P. falciparum vs. P. vivax**

<table>
<thead>
<tr>
<th>Pf</th>
<th>PV</th>
<th>Not In Midland; &gt;2km DSC</th>
<th>In Midland; +2km DSC</th>
<th>Foothills; &gt;2km DSC</th>
<th>In Midland; &gt;2km DSC</th>
</tr>
</thead>
<tbody>
<tr>
<td>In Midland, South Midland; &gt;900m SG; &gt;1.7km DSC</td>
<td>335 (50.4)</td>
<td>27 (0.4)</td>
<td>0 (0)</td>
<td>1 (0.15)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>In Midland, South Midland; &gt;900m SG; &gt;1.7km DSC</td>
<td>24 (3.6)</td>
<td>24 (0.4)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>In Midland, South Midland; &gt;2.5km DSC; &gt;7.5km DSC</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>10 (1.5)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>In Midland, South Midland; &gt;2.5km DSC</td>
<td>25 (3.7)</td>
<td>63 (9.5)</td>
<td>24 (4.9)</td>
<td>0 (0)</td>
<td>129 (19.6)</td>
</tr>
<tr>
<td>In Midland, South Midland; &gt;2.5km DSC; &gt;7.5km DSC</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>82 (12.4)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

⇒ 7 eco-epidemiological zones
D. Eco-epidemiological zones

7 eco-epidemiological zones with different environment, incidence trends and at-risk populations
D. Eco-epidemiological zones

7 eco-epidemiological zones with different environment, incidence trends and at-risk populations
Dense forest, sparse forest, Grass/shrubland

Traditional Karen “taung yar” slope agriculture
Mean elevation: 640m
Min elevation: 547m

% 0-5° = 10%
% 5-10° = 18%
% >10° = 71%

Dense forest, sparse forest, Cropland

Cropland located in broad valley bottoms indicative of wet rice paddies
Mean elevation: 223m
Max elevation: 342m

% 0-5° = 30%
% 5-10° = 27%
% >10° = 43%
3. **DISCUSSION**

- Large diversity of
  - malaria village-dynamics
  - forest landscapes
    - topography, ratio agriculture/forest, type of agriculture (no details on floristic composition)

- Malaria dynamics & environment association: broad > detailed profiles
  - 1 climate + 2 landscapes associated to malaria affected profiles

- 7 ecoepidemiological zones with different incidence patterns and at-risk population


3. **DISCUSSION**

- Forest is not a homogenous environment: it is shaped locally by humans and this results in different malaria risks
- Age distributions across zones suggest a gradient of **within versus outside village transmission**, linked to specific environments
- Post-MDA incidence analysis suggests **interventions impact differ between Z1 and Z3** (higher post-MDA incidence associated with DSC proximity)
- Suggests that the type of agriculture may be a proxy of **receptivity**
- Interest to target intervention and plan surveillance - especially in the light of current disruptions
METF communities in Karen State and partner organizations

SMRU: Francois Nosten, Gilles Delmas, Aung Myint Thu, Khin Maung Lwin, Jade D Rae & METF team

ESPACE-DEV + Institut Pasteur in Cambodia: Sokeang Hoeung, Vincent Herbreteau, Florian Girond & colleagues

SESSTIM: Jean Gaudart, Laurent Lehot, Sokhna Dieng


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INTRODUCTION

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SUP

CRF - Région – 10 km

A

\[ P. falciparum - METF - 10 km \]

Climate

Dense forest, sparse forest

Sparse forest, cropland

Majority sparse forest

Majority dense forest

Majority sparse forest, cropland

MDA before 2016

B

\[ P. vivax - METF - 10 km \]

Climate

Dense forest, sparse forest

Sparse forest, cropland

MDA after 2016

Majority sparse forest

Majority dense forest

CRF - Zone Nord – 10 km

A

\[ P. falciparum - North - 10 km \]

Dense forest, sparse forest, cropland

Dense forest, sparse forest, grassland

Majority sparse forest

Majority dense forest

Dense forest, sparse forest

Climate

MDA before 2016

B

\[ P. vivax - North - 10 km \]

Dense forest, sparse forest, cropland

Climate

Dense forest, sparse forest, grassland

MDA after 2016

Majority sparse forest

Majority dense forest

Majority sparse forest, cropland

Majority dense forest