Designing the GIS predicting regional malaria endemicity in Cambodia

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Malaria is a global public health issue.

A life-threatening disease caused by parasites that are transmitted to people through the bites of infected *Anopheles* mosquitoes.

Estimated malaria caused deaths in 2013 (Uncertainty range 367,000 – 755,000). (WHO, 2015)


584,000

WHO. Malaria Fact sheet No94, 2015
WHO-UNICEF. Child Health Epidemiology Reference Group, 2013
WHO. Trends in reported malaria incidence, 2000-2012
Artemisinin resistance is an emerging threat...

- Delayed parasite clearance in patients taking artemisinin combination therapy has been reported in Greater Mekong Subregions. (Ashley, 2014)

- If resistance to artemisinin develops and spreads to other large geographical areas, the public health consequences could be dire, as no alternative antimalarial medicine is now available. (WHO, 2015)

WHO. Malaria QA on artemisinin resistance, 2015
Ensuring appropriate course of treatment is an effective option for addressing artemisinin resistance.

**Issues of drug use in resistant malaria**

- Widespread availability of mono-therapy ([WHO, 2015](#))
- Counterfeit medicines ([Tabernero, 2014](#))
- Un-regulated use of antimalarials.

75% (95% CI, 49 - 90) with the standard 3-day dihydroartemisinin–piperaquine regimen, reported 1 year before.

WHO. Malaria QA on artemisinin resistance, 2015
High proportion of patient with parasitemia on day 3 and the gap from symptom (fever) resolution.

<table>
<thead>
<tr>
<th>Study site</th>
<th>No. of pts</th>
<th>Artesunate (mg/kg)</th>
<th>Artemisinin-Based Combination therapy</th>
<th>Median Duration of Fever (days)</th>
<th>Gametocytemia on Day 0 (%)</th>
<th>Positive for Parasitemia on Day3 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pailin</td>
<td>100</td>
<td>4</td>
<td>DP</td>
<td>2.5 (1.5-3.5)</td>
<td>19/100 (19)</td>
<td>65/98 (66)</td>
</tr>
<tr>
<td>Preah Vihear</td>
<td>120</td>
<td>2 or 4</td>
<td>DP</td>
<td>2.8 (2.0-3.0)</td>
<td>6/120 (5)</td>
<td>21/120 (18)</td>
</tr>
<tr>
<td>Ratanakiri</td>
<td>120</td>
<td>2 or 4</td>
<td>DP</td>
<td>2 (2-3)</td>
<td>7/120 (6)</td>
<td>8/119 (7)</td>
</tr>
<tr>
<td>Pursat</td>
<td>120</td>
<td>4</td>
<td>DP</td>
<td>3 (3-4)</td>
<td>22/120 (18)</td>
<td>71/118 (60)</td>
</tr>
</tbody>
</table>

*DP: dihydroartemisinin-piperaquine

Patent gametocytemia was more likely to develop in patients with slower parasite clearance (OR 2.40 95%CI, 1.53-3.76; p<0.001)

**Resistant malaria have a transmission advantage that may drive the spread of resistance after day 3.**

Community-based surveillance is feasible, but highly intensive... *(Cox, 2014)*

- Systems incorporating existing networks of village malaria workers (VMWs) to monitor day 3-positive *P. falciparum* cases were piloted*.  

  - **Day 0 : Preparing blood slides**
  - **Day 0-2 : Administering directly observed therapy (DOT)**
  - **Day 3 : Obtaining follow-up slides and transporting them to HC.**

*In Pailin, Pursat and Battambang province*
Pailin and Preah Vihear province where delayed artemisinin clearance was observed (Ashley, 2014), (Bosman, 2014)
Creating basal map

<table>
<thead>
<tr>
<th>Item</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Road, DEM, Pol. Boundary, Village dist.</td>
<td>Open development Cambodia</td>
</tr>
<tr>
<td>Hospital and health center location</td>
<td>Health coverage plan, ministry of health Cambodia, 2005</td>
</tr>
</tbody>
</table>

*Health center(♦) with 5km surrounding circle area covers most of populated village(●)
Think about what we can do through health GIS

Measuring the risk in “fine-scale”

For areas not well-covered
- Sufficient health resource delivery
- Reference for local healthcare staff recruitment

For cross-border transmission
- Arrange efficient cross-border screening in high risk area
How does GIS work under this situation?

- Predict areas at risk
- Estimate the effectiveness of intervention

- Spread of drug-resistance
- Poor quality medicines
- Inappropriate drug use
- Human mobility
- Issues in health resource distribution
Objective

• To identify the areas with high malaria endemicity where intensive monitoring and support is needed by creating fine scale risk map using spatial statistical risk modeling.
Method

Data collection;
Space satellite data
Surveillance data etc.

Modeling and statistics

Plotting the point estimated village level risks and interpolation
Change in the estimated prevalence and SMR of malaria in 2010-2013

Incidence (/1,000 pop.)
(Empirical bayes estimated)

SMR
(Empirical bayes estimated)
## Environmental and demographic variables collected

<table>
<thead>
<tr>
<th>Category</th>
<th>Items</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Climate</td>
<td>Precipitations(^{(1)})</td>
<td>WorldClim global climate data</td>
</tr>
<tr>
<td>Climate</td>
<td>Mean temperature(^{(1)})</td>
<td>WorldClim global climate data</td>
</tr>
<tr>
<td>Temperature</td>
<td>Land surface temperature (Day/Night)</td>
<td>MODIS data from LPDAAC MODIS Land Surface Temperature prod.</td>
</tr>
<tr>
<td>Topology</td>
<td>Topology Wetness Index(^{(2)})</td>
<td>Calculated from ASTER GDEM data</td>
</tr>
<tr>
<td>Plasmodium suitability</td>
<td><em>P.falciparum</em> and <em>P.vivax</em> temperature suitability index(^{(3)})</td>
<td>Malaria Atlas Project</td>
</tr>
<tr>
<td>Population density</td>
<td>Population density</td>
<td>WorldPop project Open development Cambodia</td>
</tr>
<tr>
<td>Land use/cover</td>
<td>Global Land cover data(^{(1)})</td>
<td>0.5 km MODIS-based Global Land Cover Climatology from USGS</td>
</tr>
</tbody>
</table>

\(^{(1)}\) Chikodzi D, J Geosciences and Geomatics, 2013 (1):1; 8-14  
\(^{(3)}\) Gething P.W. et.al, Parasite & Vectors, 2011 (4):92
Distance is related to the fitting of modeled risk.

**Correlation between log(EBSMR) and environmental variables**

**Coefficient of determination for selected models**

- **Model 1:** mean NDVI
- **Model 2:** # of months with mean NDVI >= 0.4
- **Model 3:** # of pixels with NDVI >= 0.4 in equal or more than 6 months
Linear regression model for predicting EBSMR

$log(EBSMR) = \beta_0 + \beta_1 NDVI_{mean,5000m} + \beta_2 NDWI_{1000m} + \beta_3 TWI_{1000m} + \beta_4 Temp + \beta_5 Pop + \beta_6 LLIN_{suf} + \varepsilon$

where

- $NDVI_{mean,5000m}$: mean normal difference vegetation index in 5000m circular buffer from village
- $NDWI_{1000m}$: mean difference water index in 1000m circular buffer
- $TWI_{1000m}$: Topological wetness index in 1000m circular buffer
- $Temp$: Plasmodium temperature suitability index
- $Pop$: Population density (/km²)
- $LLIN_{suf}$: Sufficient LLIN coverage

<table>
<thead>
<tr>
<th>Estimate</th>
<th>Std. Error</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta_0$</td>
<td>-15.690</td>
<td>4.81</td>
</tr>
<tr>
<td>$\beta_1$</td>
<td>8.814</td>
<td>2.074</td>
</tr>
<tr>
<td>$\beta_2$</td>
<td>-22.350</td>
<td>5.584</td>
</tr>
<tr>
<td>$\beta_3$</td>
<td>-1.152</td>
<td>0.655</td>
</tr>
<tr>
<td>$\beta_4$</td>
<td>0.00027</td>
<td>0.000047</td>
</tr>
<tr>
<td>$\beta_5$</td>
<td>-0.0057</td>
<td>0.002</td>
</tr>
<tr>
<td>$\beta_6$</td>
<td>-0.0426</td>
<td>0.0068</td>
</tr>
</tbody>
</table>

$***: P < 0.001$, $**: P < 0.01$, $.: P < 0.1$

adjusted $R^2 = 0.7326$, AIC = 161.6

A scatter plot showing the relationship between predicted and actual values.
Bayesian method for risk modeling

\[
\log(EBSMR) = \beta_0 + \beta_1 NDVI_{mean, 5000m} + \beta_2 NDWI_{1000m} + \beta_3 TWI_{1000m} + \beta_4 Temp + \beta_5 Pop + \beta_6 LLIN_{suf} + \varepsilon
\]

\[
\varepsilon \sim N(0, \sigma^2)
\]

<table>
<thead>
<tr>
<th>(\mu)</th>
<th>(Sd)</th>
<th>(Rhat^*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\beta_0)</td>
<td>-15.77790</td>
<td>4.91861</td>
</tr>
<tr>
<td>(\beta_1)</td>
<td>8.78043</td>
<td>2.07920</td>
</tr>
<tr>
<td>(\beta_2)</td>
<td>-22.41311</td>
<td>5.68282</td>
</tr>
<tr>
<td>(\beta_3)</td>
<td>-1.14354</td>
<td>0.65792</td>
</tr>
<tr>
<td>(\beta_4)</td>
<td>0.00027</td>
<td>0.00005</td>
</tr>
<tr>
<td>(\beta_5)</td>
<td>-0.00566</td>
<td>0.00201</td>
</tr>
<tr>
<td>(\beta_6)</td>
<td>-0.04262</td>
<td>0.00697</td>
</tr>
<tr>
<td>(\sigma)</td>
<td>0.50527</td>
<td>0.09195</td>
</tr>
</tbody>
</table>

*MCMC 10,000 times, burnin = 1,000, chain # = 3,000

*Gelman-Rubin statistics

DIC \sim 162.5
Observed vs. eSMR*

2010

Linear Regression Model
Bayese

2011

*estimated SMR

2012

2013
Mapping results (Pailin, 2010)
Mapping results (Preah Vihear, 2010)
Mapping results (IDW, Pailin, 2010)
Mapping results (Ordinal, kriging, Preah Vihear, 2010)
Is this map reliable?
Visual feature

From Malaria Atlas Project database (Moyes, 2013)

Fine-scale risk map (Preah Vihear province, 2010)
Verification of spatial risk model

- Compare with geocoded observed data
  - Pailin (Médecins Sans Frontières, 2005)
  - Preah Vihear (Incadona, 2007)

* t : Welch Two Sample t-test (Predicted vs Observed)
  
  - t = 0.59 (N.S.)
  - t = 0.40 (N.S.)

* r : Spearman's rank correlation
  
  - r = 0.66
  - r = 0.67

* t : Welch Two Sample t-test (Predicted vs Observed)
  r : Spearman's rank correlation
Discussion

• Compared with global-scale map
  - Different interpolation method
  - Variation and spatial density of source data
  - Needs for fine scale mapping for malaria elimination (Malaria Elimination Group, 2009) and drug resistance containment (Cox, 2014)

• Cross scale prediction
  - Accessibility for micro data
  - Managing spuriousness and unreliability for multi-scale prediction
  - Bayesian Approach (Keil, 2013) (Sturrok, 2014)
Next Step

- Improving accuracy of the model
  - Non-linear model such as general additive model
  - Bayesian approach for multivariate time series analysis

- Present the relationship between risks and containment status
Conclusion

• We created a fine scale risk map using surveillance data, remote sensing data and other demo/geographic data sources adjusted by distance from human communities.

• For more effective and practical applications, further studies are needed.
Reference

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Thank you!