A System Dynamics Approach to Malaria and Climate Change:
A Case Study along the Thai-Myanmar Border

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Outline of Presentation

1. Motivations
2. Background of Malaria (issues, progress, and challenges)
   - Regional (the GMS), Thailand
   - Thai-Myanmar border areas (inc. immigration and other specific challenges)
3. System Dynamics (SD) Approach
   - Why SD?
   - Other approaches (Statistics, Mathematical models)
4. Model Development for Malaria
   - Reference mode
   - Underlying feedback loops/Stock-flow diagramming (and non-linearity)
   - Exogenous seasonality (climate and distant effects), …
5. Model-based Experimentation for control/policy analysis
6. Summary and Ways forward
7. References
1. Motivations

1. Trans-boundary issues, along with others:
   - Biodiversity loss, forest fires/haze, droughts/flooding
2. Location of our university (MFU):
   - Thailand’s North most (border), strategic (in the GMS)
3. Opportunities of SD recognized for public health control
   (Homer 2006, Amer. J of PH; Sterman 2000, Business Dynamics/Modeling Epidemics, … )
4. Limited research on malaria: In Thailand and the GMS
   - More on descriptive and forecasting, less on control strategy
5. Author’s background: SD (and GIS, Optimization)
   - With several applications to natural resources/env. issues
   - Used to work (as GIS expert) on Dioxin (from Vietnam war)
   - Co-authoring with a PhD student in public health
6. Initial study with SD for more collaborative and in-depth research:
   - On Malaria and other public health issues (Thailand/GMS)
   - More understanding and data required!
2. Background: Malaria Issues in the GMS

There are about 300 million cases, and 1 million deaths from malaria globally each year.

Human malaria parasites are in the genus *Plasmodium*, and include *P. falciparum*, *P. malariae*, *P. ovale*, *P. vivax* and *P. knowlesi*.

*Plasmodium falciparum* is most common, and accounts for 80% of malaria cases, and 90% of malaria deaths globally.

3 anopheline mosquito species, *Anopheles dirus*, *Anopheles minimus*, and *Anopheles Maculatus* are responsible for malaria in the GMS.
2. Background: Malaria Issues in the GMS

Malaria control over the last 20 years:
Significant progress: Vietnam, Thailand, and Yunnan Province of China

Moderate progress: Cambodia and Laos (but malaria remains a serious threat there)

Limited progress: in Myanmar (with rising malaria rates and accounting for more than 50% of malaria cases, and 75% of malaria deaths in the GMS)

The distribution of each country’s highest malaria incidence rates indicate that malaria is concentrated in border areas across the GMS (trans-boundary issues)

These borders are characterized by forest and forest fringe areas with high malaria transmission, poor geographical accessibility, high Malaria epidemiology is closely linked with the physical environment, including climate

The most prevalent malaria vectors are *Anopheles dirus*, which breeds predominantly in forested areas, and *Anopheles minimus*, which is widespread in the forest fringe areas. Most of the population in this Subregion lives in rice-growing areas and the plains, which are generally free of malaria transmission. The at-risk population are those who live in remote villages in or close to forested areas, which are not only where malaria vectors thrive but also where accessibility to health services is poorest.

Another factor affecting the malaria situation is the distribution of parasite species within the Region. The type of malaria parasite has implications on the severity of illness, risk of death, and the
2. Background: Malaria Issues in Thailand

The *Plasmodium falciparum* and *Plasmodium vivax* human malaria parasites are predominant in Thailand.

3 anopheline species complexes, *Anopheles dirus*, *Anopheles minimus*, and *Anopheles maculatus*, are primary malaria vectors in the country.
Background: Malaria Issues in Thailand

Thai provinces with the highest malaria cases, 2003

Thai provinces with the highest malaria mortality rate (per 100,000 pop.), 2002

Province – wise distribution of Annual Parasite Incident (API) in Thailand, 2009

Legend

API, Thailand 2009

- 0
- 0.01 - 0.5
- 0.51 - 1.0
- 1.01 - 5.0
- 5.01 - 10.0
- more than 10.0

1. Tak (10,278)
2. Yala (3,051)
3. Kanchanaburi (2,659)
4. Chanthaburi (2,628)
5. Mae Hong Son (1,929)
6. Chiang Mai (1,732)
7. Prachuap Khiri Khan (1,437)
8. Ubon Ratchathani (1,186)
9. Nakhon Sri Thammarat (1,166)
10. Chumphon (1,080)

1. Mae Hong Son (5.87)
2. Tak (4.97)
3. Kanchanaburi (4.14)
4. Chanthaburi (2.98)
5. Prachuap Khiri Khan (2.88)
6. Chumphon (2.76)
7. Chiang Mai (2.76)
8. Mukdahan (1.48)
9. Phetchaburi (1.3)
10. Phrae (1.24)
2. Background: Malaria Issues in Thailand

Malaria incidence in North-western border provinces of Thailand: 1999-2004
2. Background: Malaria Control Progress Thailand

Organization chart of agencies working on malaria prevention in Tak Province, Thailand.
2. Background: Malaria Challenges for Thailand (from Myanmar)

Reported Malaria Morbidity Rate (/1000) in Myanmar, 2000-2008

Reported Malaria Mortality Rate / 100000 in Myanmar, 2000-2008
2. Background: Malaria Challenges in Thailand

An example of the dynamics underlying the evolution of drug resistance:
- Starting freq. of resistance: 10±8
- Increasing by 5% per parasite generation.

The principle factors determining the rate of evolving resistance, possible remedial action to slow it, and some of the drawbacks associated with implementing these actions

<table>
<thead>
<tr>
<th>Factor</th>
<th>Remedial action</th>
<th>Drawbacks</th>
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<tbody>
<tr>
<td>Resistance appears very rapidly</td>
<td>Effective sentinel studies</td>
<td>Cost</td>
</tr>
<tr>
<td>Starting frequency of resistance</td>
<td>Use drugs in combination</td>
<td>Initial cost may be twice as much</td>
</tr>
<tr>
<td>Amount and pattern of drug usage</td>
<td>Minimize drug use</td>
<td>Lose prophylactic benefits of drug</td>
</tr>
<tr>
<td>Drug half-life</td>
<td>Modify drug structure to minimize half-life</td>
<td>Delay in treatment may be fatal or debilitating</td>
</tr>
<tr>
<td>Number of genes required to encode resistance</td>
<td>Use drugs with widespread metabolic actions</td>
<td>Lose prophylactic benefits of drug</td>
</tr>
<tr>
<td>Level of sexual recombination in the parasite</td>
<td>Use drugs in combination</td>
<td>Compliance problems if multiple doses required</td>
</tr>
<tr>
<td>Genetic basis of resistance</td>
<td>Management: e.g. reduce clonal multiplicity in malaria</td>
<td>Regulatory permission</td>
</tr>
<tr>
<td>Intrahost dynamics and ‘crowding’ effects</td>
<td>May be able to increase drug dosages</td>
<td>None, if available</td>
</tr>
<tr>
<td>Number of individual parasites in an infection</td>
<td>Management: reduce parasite load per host</td>
<td>Initial cost may be twice as much</td>
</tr>
<tr>
<td></td>
<td>Management: reduce parasite load per host</td>
<td>Cost, may not be feasible</td>
</tr>
<tr>
<td></td>
<td>Use drugs in combination</td>
<td>Cost, compliance and regulatory approval</td>
</tr>
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<td></td>
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<td>Cost of, e.g. earlier diagnosis, better nutrition</td>
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The expansion and intensity of multi-drug resistant *Plasmodium falciparum* is the most serious development to occur the last several decades.
2. Background: Malaria Challenges in Thailand
3. System Dynamics (SD)

1. History of SD
   - Developed from mid-1950s, initiated by Jay Forester (MIT)
   - Based on feedback loop/control theory + computer simulation + differential equations
   - Applied mainly to Industrial, Urban, World Dynamics, and to business/resource/ecosystem and public health

2. Philosophy/Advantages of SD
   - System behavior: mainly from system structure
   - For feedback systems: with feedback loops (positive and negative)
   - Useful for improving understanding (esp. cause-effects), and policy analysis
   - Flexible (esp. quantification), less math required, can be used by policy makers

3. Related approaches
   **Statistic:** To learn about the behavior of a system a rest (while SD about how a system changes over time, then for possible control).
   -> Another issue: correlation may not imply causality!

   **Predictive models:** To predict the value of an important variable at some point in the future (to provide best possible forecast of the future state of the system (how to improve general understanding to guide research?)),
   -> So easy to understanding (prediction can be judged as right or wrong)

   **GIS:** More about how things changes over geographical areas

   **Mathematical models:** More complicated, difficult to obtain analytical solutions (need to make simplifying assumptions), not easy to understand by non-mathematicians
   -> Limited real-world applications (esp. for policy analyis)
3. System Dynamics: Literature Review on Malaria and related research

1. System Dynamics (SD)
   - Extensive and successful applications to AIDS/HIV
   - Moderate applications to basic SIR models and health control
   - Some applications to Malaria (but mainly for one event)

2. Math Modeling
   - Many applications to Malaria (but more on proving stability, less on control strategies)

3. Statistics:
   - Many on Malaria (but mainly to detect patterns of occurrence, including seasonality)

4. GIS
   - Some on Malaria (with Spatial analysis: Cluster detection, Spatial auto-correlation)

5. Optimization
   - Limited applications seen on Malaria

6. Management models of malaria policy analysis
   - Very limited applications seen on Malaria

-> Need to have relevant models for malaria understanding and policy analysis, especially to deal with seasonal patterns, trans-boundary effects, drug-resistance, and persisting situations
4. Model development

4.1. Problem identification

Areas:
Northern Thailand
Thai-Myanmar border

Malaria Problems:
- Persisting (over time)
- Cyclic patterns
- Seasonal characteristics
  - 01 high peak (May-Jun-Jul)
  - 01 low peak (Oct-Nov)

Source: Childs et al. (2005), Spatiotemporal patterns of malaria incidence in northern Thailand. Transactions of the Royal Society of Tropical Medicine and Hygiene (2006) 100, 623–631
4. Model development

4.1. Problem identification: Similar seasonality in other countries: India (left), Yunnan (right)

Source: Gupta et al. (2009), *Patterns of Plasmodium vivax and Plasmodium falciparum malaria underscore importance of data collection from private health care facilities in India*. Malaria Journal 8.
4. Model development

4.2. Feedback loops/stock-flow diagramming

2 main sub-systems:
- Human (Host)
- Mosquitoes (Vector)

Contagion/spreading loop:
- To link the 2 sub-systems
- Positive feedback loop (reinforcing)

Depletion loops:
- Similar for each (H/V)
- Move from S to I

Recovery and immune loops:
- Only for Human

Birth and death loops:
- Similar for both (but M is faster)

Exogenous inputs/effects (seasonal):
Mosquitoes:
- More breeding in rainy season

Human:
- Farming exposure (farming calendar)
- Labor immigration (from Myanmar)
- Infective arrival (from Myanmar)
4. Model development
4.3. Reproduction of Reference Mode

Major Assumptions:

- Human biting by mosquitoes: randomly (for 3 H groups), so non-linear here
- Mosquitoes: Basic cycle only
- Immunity: can be acquired and lost for Humans only
- Exogenous Inputs:
  Migration (labor + infective)
  Rainfall pattern (for M)
- Initial values:
  1000 for both H and M (only for Susceptible)
  Some for Infective humans

Simulation result (with VENSIM):
- Persisting, 2 peaks per year
- Phase delay: from H to M
- Almost stable cyclic pattern (between 50% to 10%)
4. Model development
4.3. Reproduction of Reference Mode
(3 years for better visualization)

Simulation results:
- Phase characteristics
  From S to I (and Immune)
  For both H and M
- Magnitude characteristics
- Frequency characteristics
- Total humans and mosquitoes
5. Model Experimentation

5.1. Preliminary Results:
- Which comes first (infective human or infective mosquitoes):
  Not important (same patterns)
- Without immigration (trans-boundary effects):
  Infectious human can be substantially reduced
  (depending on susceptible human)
- Without seasonal human exposure (on farms, in the forest, …):
  Unlikely to generate seasonal patterns in infection (both H and M)
- Traditional control measures (mosquito bed netting, spraying, partial treatment, ):
  Not so effective (especially in wide forest areas)

5.2. Future Experimentation:
- Control at various levels (primary, secondary, tertiary)
- How to control immigrations (especially from infective humans):
  Need some joint actions along the borders?
- Control at source: vaccination possible and affordable?
- Identify possible effects from and control under climate change
- Cost effectiveness:
  - For various control measures and possible combinations
  - Priority actions (from most sensitive areas) for more control efforts pooled

Also need to better understand the malaria dynamics in the study areas, then improve the model to be more closely with the real-world situations!
6. Summary and Ways Forward

1. Summary:
   - **Initial Progress**
     - Development of a SD for malaria to:
       - Identifying underlying feedback loops (responsible …)
       - Developing stock-flow diagramming
       - Reproducing malaria behavior (reasonable assumptions)
       - Some preliminary experimentation for policy analysis
   - **Limitations** (mainly due to time and resource constraints)
     - Uncertainty of estimation of various factors:
       - Human migration patterns
       - Mosquitoes population dynamics (size, type, growth, ..)
     - No much experimentation conducted with the model
     - No analysis of cost-effectiveness of various control measures

2. Ways forward (next steps)
   - **Overcoming the above limitations**
     - Working more closely with key stakeholders (esc. Experts in Malaria)
     - Improving ground understanding (through field surveys)
     - Improving the model to be more representative and reliable
   - Developing and (model-based) testing effective control strategies
Thank you very much for your attention and

Look for more research collaboration

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