Spatio-temporal modeling of weekly malaria incidence in children under 5 for early epidemic detection in Mozambique

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Outline

- Malaria
- Malaria burden in Mozambique
- Malaria Early Warning Systems
- The role of climate in malaria transmission
- Recent malaria trends in Mozambique
- Spatio-temporal model for predicting incidence
- Exceedance probabilities - modeling uncertainty
- Implementation
Malaria life cycle

Infection

Sporozoites

Liver

Merozoites

Transmission to mosquito

Asexual cycle

Gametocytes
WHO malaria facts

- 212 million cases worldwide in 2015
- Estimated 429,000 deaths, 92% of which were in Africa
- Deaths mostly occur in children under 5 years of age and in pregnant women
- There are 91 malaria endemic countries in the world
- 21% decrease in malaria incidence between 2010-2015
- 29% decrease in malaria mortality rates between 2010-2015
- In 2015, global funding for malaria was US$2.9 billion
- The US contributed 32% of the total funding
Malaria in Mozambique

- Population of nearly 28 million
- Estimated 8.3 million malaria cases and 15,000 deaths in 2015
Malaria transmission in Mozambique is highly seasonal and varies significantly geographically.

Highest transmission in the north and lowest in the south.

Unexpected increases in cases have occurred over the last several years that have resulted in significant morbidity and mortality.

Canal Endemico: designed to detect weekly case counts that are significantly higher than historical averages for that week.

Outbreaks are not detected in sufficient time to mount an effective response.
WHO Roll Back Malaria report in 2001 detailing the need for MEWS for Africa

2012 systematic review by Mabaso and Ndlovu summarized 35 articles on climate-driven malaria epidemic models - many more have been published since then

Most MEWS use time-series models with satellite weather data

Best models are those that make use of incidence data from continuously monitored populations at relatively small spatial scales (state, district, health facility)
Key components of MEWS

- Continuously monitored population at risk
- Historic case data on same population
- Independent variables associated with malaria transmission that can be forecasted into the future or that are associated at lagged time points that provide early enough warning so that individuals can plan a response
Temperature and rainfall are important to consider when trying to predict malaria.

The parasites survive best in ideal weather conditions.

Mosquitoes survive and are more active in ideal temperatures.

Rainfall creates new pools for mosquito breeding, but can also wash out existing pools.
Good climatic data for Africa can be derived from the Version A forcing data of the Famine Early Warning Systems Network Land Data Assimilation System (FLDAS)

Available from the National Aeronautics and Space Administration Goddard Earth Science Data and Information Services Center (https://earthdata.nasa.gov/about/daacs/daac-ges-disc)

The FLDAS data are available at daily temporal resolution and 0.1 degree spatial resolution
A MEWS for Mozambique

- Project funded by a Grand Challenges Explorations grant from the Bill & Melinda Gates Foundation
- Partners include: Lancaster University (UK), the Clinton Health Access Initiative, the National Institutes of Health and the National Malaria Control Program in Mozambique, National Center for Atmospheric Research
- Objective 1: to predict the probability that malaria incidence will exceed a policy relevant threshold 8 to 26 weeks in advance in each district in Mozambique
- Objective 2: Work with key stakeholders in Mozambique to develop a platform for implementing a MEWS
Weekly case reports of children under the age of five from 142 districts reporting in Mozambique between 2010-2017

Population data were obtained from WorldPop and the 2007 Mozambique census was used to determine the percentage of the population under 5 in each district
Under 5 malaria incidence per 1,000 population
Week 8, 2016
Malaria in Mozambique

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Malaria Early Warning System Mozambique

16/35
Malaria and climate in Mozambique

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Malaria Early Warning System Mozambique 17/35
Malaria and climate in Mozambique

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Malaria in Mozambique is temporally and spatially correlated

Cannot collect all relevant covariates to explain variation

Need to account for uncertainty in a prediction model for malaria

Model-based geostatistics (Diggle et. al, *Applied Statistics*, 1998) has been used to incorporate spatial correlation in environmental risk models for various diseases (Diggle et al., *Ann Trop Med Parasitology*, 2007; Giorgi et al., *Spatial and Spatio-temporal Epidemiology*, 2016) and to quantify the uncertainty in the predictions from these models (Diggle, et. al, *Stat Sci*, 2013; Giorgi, 2016)
Exceedance probability (EP): predictive probability that the relative risk exceeds a predefined threshold (or the multiplicative deviation from the expected level of incidence)

This MEWS aims to warn when incidence might exceed a level that is of public health concern

Taking action is then a context specific decision made by policy makers depending on the available resources
Spatio-temporal model

Let $Y_{it}$ denote the counts of reported children under 5 years with malaria for week $t$ in the $i$-th district, for $i = 1, \ldots, I = 142$ and $t = 1, \ldots, T = 313$ where $t = 1$ is the first epi-week of January 2010 and $t = 313$ is the last available epi-week of 2017. We assume that, conditionally on a spatio-temporally random effect, $S_{it}$, the $Y_{it}$ are mutually independent Poisson variables with mean

$$\lambda_{it} = m_{it} r_{it}$$

where $m_{it}$ is the population at risk,

$$\log\{r_{it}\} = d_{it}^T \beta + S_{it} \quad (1)$$

and $d_{it}$ is a vector of explanatory variables with associated coefficients $\beta$. 
Let $S_t^\top = (S_{it}, \ldots, S_{lt})^\top$; we then model $S_t$ using a stationary autoregressive process of the first order, i.e.

$$S_t = \gamma S_{t-1} + W_t, \gamma \in (0, 1)$$

where $W_t$ corresponds to temporal innovation following a multivariate Gaussian distribution with mean zero and covariance matrix $\Sigma$, such that

$$[\Sigma]_{ij} = \frac{\sigma^2}{|D_i||D_j|} \int_{D_i} \int_{D_j} \exp \left\{ \frac{||x_i - x_j||}{\phi} \right\} \, dx_i \, dx_j,$$

where: $|D|$ is the area encompassed by the boundaries of district $D$; $\sigma^2$ and $\phi$ are two scale parameters for the variance and spatial correlation of the process $W_t$; $||x_i - x_j||$ is the Euclidean distance between any two locations $x_i$ and $x_j$ in district $D_i$ and $D_j$, respectively.
Exceedance probability

EP is given by $e^{S_{it}}$, which measures the unexpected multiplicative deviation from the expected incidence level $e^{d^{T}_{it} \beta}$, expressed as

$$\text{Prob}(e^{S_{it}} > \ell | \text{data})$$

where $\ell$ is a predefined threshold.
Three models

- M1) use of climatic variables while ignoring any source of residual extra-Poisson variation
- M2) use of spatio-temporal random effects but no climatic variables
- M3) a spatio-temporal model which combines both climatic variables and spatio-temporal random effects
For each of the three models, two holdout sets were tested: 1) the last 8 weeks of data and 2) the last 26 weeks of data.

The remainder of the data were used to train the three models.

Model performance was compared using RMSE and 95% coverage probability (CP), defined as the proportion of observed malaria cases from the holdout data-set that fell within the 95% prediction intervals.
Model prediction performance

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Malaria Early Warning System Mozambique
District-level predictions

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Model predicting 26 weeks in advance

MACHAZE – 26 weeks

MASSANGENA – 26 weeks

CHIBABAVA – 26 weeks

SANGA – 26 weeks

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Model predicting 8 weeks in advance
http://www.lancaster.ac.uk/staff/haleac/healthatlas/
Health Atlas

Outcome: Mozambique Malaria Incidence 2017

Base map: Grey scale

Malaria Incidence 2017, week 8
District: MAVAGO
Population: 4965
240.4 cases/10^5 pop

Created in partnership with:
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Malaria Exceedance 2017, week 8
District: MAVAGO
Population: 4965
0.42 exceedance probability
Practical considerations

- Is 8 weeks advance notice enough time to organize a response?
- Model might require forecasted climate data, which will mean we need to work with a climatologist rather than simply downloading satellite data
- Need to connect to weekly case reports automatically
Thank you

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