Leptospirosis and Environment

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Summary

- What is Leptospirosis and which are the main questions
- Data sets: cases and climate
- Modelling:
  - basic model
  - climatic covariates: threshold and lags
- Problems and doubts...
Leptospirosis

- Bacterial zoonosis (*Leptospira sp*)
- Transmitted to humans through contact with urine from infected animals (rats in urban setting)
Leptospirosis

- Incubation period: 5 to 25 days
- Clinical manifestations:
  - self-limiting fever, with headache and muscle pain – easily taken for a bad cold or dengue fever
  - life-threatening disease – kidney failure, pulmonary haemorrhage, Weil's syndrome
- Early treatment! Dialysis mainly
Globally spread, affecting people on all continents.

Different epidemiological patterns:

- Sporadic disease, related with specific occupational exposures and recreational activities
- Slums and flooding in urban areas
In Brazil

- 10,000 reported cases per year in the major cities
- Under-registration
- 10-15% mortality when diagnosed; more due to late treatment
- Main suspected factors: poor sanitation, slum housing and flooding
Favela in Salvador
People living in slums – seroprevalence study estimates 23% at 50y, so what determines severe cases?

- different virulence according to the bacteria strain
- inoculant dose – related to behaviour (higher male prevalence – cleaning sewers) and environment
- previous immunity – how is it acquired? (a vaccine is on its way)
Does **rainfall** really cause epidemics of severe leptospirosis? Why?

- Reasoning: the rain clean up the rats holes, bringing to the soil surface leptospira
- Is it a linear relationship?

When to give an alarm to decrease fatalities – **threshold**
Questions

- Other environment factors: humidity & temperature
- Time delay
  - duration of incubation period – related to inoculant dosis
  - duration of the *Leptospira* on the soil – related with temperature and moisture on the soil
Data

- Salvador surveillance system
- Cases: weekly aggregated
- Climate covariates:
  - Mean weekly temperature (°C)
  - Mean weekly relative humidity (%)
  - Weekly accumulated rainfall (mm)
The basic model

\[ Y(t) \sim \text{Poisson}(\mu_t) \]
\[ \ln(\mu_t) = \beta_t + \phi_t \]

where:

\[ \beta_t = 2 \beta_{t-1} - \beta_{t-2} + \epsilon_t \quad (2^{\text{nd}} \text{ order random walk prior}) \]
\[ \phi_t \sim \mathcal{N}(0, \sigma^2) \quad (\text{temporal random effect, accounting for overdispersion}) \]

Fitted in BayesX

(www.stat.uni-muenchen.de/~bayesx/bayesx.html)
- Seasonality
- Downward general trend?
Including climate covs

Which are the important temporal lags?
Is the corresponding effect linear?

\[
\ln(\mu_t) = \beta_t + \phi_t + \sum_{k=0}^{5} \psi_k(x_{t-k})
\]

\(\psi_k()\) is a nonparametric spline
\(x_{t-5}, \ldots, x_t\) measures humidity OR temperature OR rainfall
\(k\) lags, from the same week \(k = 0\) up to the 5\(^{th}\) previous one
Lags and Linearity

Relative humidity (%)

Temperature (°C)

Rainfall (mm)
Rain > 5mm

Comparison of DIC of models with different thresholds
Rain > 5mm

- Chosen based on.... civil defence information as well
\[ \ln(\mu_t) = \mu_0 + \beta_t + \phi_t + 
+ \beta_{H1}(Humid_1) + \beta_{H2}(Humid_2) + 
+ \beta_{T1}(Temp_1) + \beta_{T2}(Temp_2) + 
+ \beta_{R1}(Rain_1) + \beta_{R2}(Rain_2) + \beta_{R3}(Rain_3) + \beta_{R4}(Rain_4) \]
<table>
<thead>
<tr>
<th>Variables</th>
<th>Relative risk exp(β)</th>
<th>2.5% quantile</th>
<th>97.5% quantile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean relative humidity, week(t-1)</td>
<td>1.045834</td>
<td>1.024385</td>
<td>1.067776</td>
</tr>
<tr>
<td>Mean relative humidity, week(t-2)</td>
<td>1.055043</td>
<td>1.032454</td>
<td>1.078136</td>
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<tr>
<td>Mean temperature, week(t-1)</td>
<td>0.945387</td>
<td>0.873472</td>
<td>1.020173</td>
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<tr>
<td>Mean temperature, week(t-2)</td>
<td>1.055784</td>
<td>0.976662</td>
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<tr>
<td>Num. days rain &gt; 5mm, week(t-1)</td>
<td>1.150296</td>
<td>1.093561</td>
<td>1.210880</td>
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<tr>
<td>Num. days rain &gt; 5mm, week(t-2)</td>
<td>1.117894</td>
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<td>Num. days rain &gt; 5mm, week(t-3)</td>
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<td>1.109781</td>
</tr>
<tr>
<td>Num. days rain &gt; 5mm, week(t-4)</td>
<td>1.063815</td>
<td>1.023835</td>
<td>1.106515</td>
</tr>
</tbody>
</table>
Conclusions

- Leptospirosis depends upon:
  - rainfall (up to 4 weeks previously),
  - humidity (up to 2 weeks previously),
  - not temperature.

- Alert to public health and guidelines to emergency doctors
climate related – *el niño* phenomena?

structural changes in favelas – no!

sanitation – Blue Bahia (World Bank project) was entirely devoted to touristic areas
Statistical problems

- Better models to discover the rainfall threshold?
- How to analyse the lagged effect?
  - Colinearity!
  - Polynomial distributed lag models (package pdl in R)
Future research

- Space-time analysis – data is now localised in small area, in a GIS, with level curves (1m) and socio-economic covariates

- The *Natural history of severe leptospirosis* project (NIH grant) – a longitudinal study going on in Pauda-Lima favela, already in its 3rd visit

- Vaccine – phase 1
Acknowledgements

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