One Health: Spatial Statistics at the border of human and veterinary health

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Background

- Some common threads weave through human and veterinary epidemiology in geo-referenced applications.
- There are also unique aspects that arise particularly in veterinary applications.
- Major area of veterinary uniqueness is the focus on infectious disease spread and the degree to which detailed information is available in veterinary applications.
Some common threads

- Data format and quality
  - Case diagnosis gives rise to spatially and temporally referenced event data
  - This is essentially a point process in space and time
  - Hence many common point process-based methods could be applied.

- Case ascertainment can be difficult and depends on reporting biases or surveillance coverage.
- Aggregation of case events to small areas or over time periods yields count data within those areas
Unique Aspects: human

- Confidentiality limits the spatial scale of analysis
- Confidentiality can limit the publication of georeferenced disease events
- Diagnoses are better differentiated and case ascertainment can be better managed than in some veterinary applications
- Interventions in infections may be more difficult
- Behavioral interventions easier
Unique aspects: veterinary

- Aggregated units often inherit diagnoses:
  - A case diagnosis can lead to an infected premise designation and so a farm level effect results
- Proximity of animals can increase the likelihood of transmission
- Infectious disease spread can be more closely observed and to a degree controlled
- Wild populations can lack good measures of population density and/or structure.
- Disease in wild populations can be difficult to detect: hunter surveys, dung surveys, remote sensing?
CWD in cervids

- Chronic Wasting disease (CWD) is a prion disease which is endemic in deer herds in northern US states
- Hunting is also endemic in many of these states
- In Wisconsin hunter stations are the destination for legitimate deer kill and once delivered they are autopsied
- Hunter surveys yield data with some unique issues:
  - Selection bias ...preferences of hunters
  - Population estimates based on such data are also biased
- Prion disease can be found during autopsy
- Could also be indicated from dung surveys

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Hunter survey Wisconsin 2002-2006

- Harvested deer:
  - Black (DEZ)
  - Grey (HRZ)
Infected deer (n=618)
CWD data

- Data includes
  - GPS location
  - Time of hunting
  - Age at harvest
  - Sex
  - Disease status
- Data does not include a population estimate
- This is not a simple point process also however
  - when harvested, the deer is censored in different ways
    - Infected deer are left censored, non-infected are right censored
  - A semi-parametric survival model has been utilized (Lawson and Song, 2010)
Estimated non-infection survival probability 2002-2006

Figure 5: Image maps of the estimated survival probability \( \exp(-(H_0 + \hat{H}_1) \exp(Z_0 \hat{\beta})) \) over time; (a) 2002, (b) 2003, (c) 2004, (d) 2005 and (e) 2006. The X-axis of the image maps is longitude and Y-axis of the image maps is latitude.
CWD: infection or not?

- It is not clear whether CWD has an infectious etiology
- Or whether deer can be affected from some environmental source
- Hence direct modeling of infection is difficult to validate
- Mobility of herds also make this type of modeling problematic (especially with annual data)
- This is overlain by the inevitable hunter biases
- Effect of population density is also difficult to assess.
References


FMD in Cumbria, NW England

- Another form of data that can be encountered is aggregated count data.
- During the large scale foot and mouth epidemic in Cumbria NW England in 2001 veterinary surveillance was intensive.
- As FMD can be spread quickly it was important to be able to detect infection striking any farm unit in the area concerned. In this case infected premise (IP) is the data unit. The number of these in an area is clearly important.
FMD first 6 time periods case/pop ratios (row-wise)
The unique effect of culling

- In the case of this FMD outbreak a special form of intervention was used: ring culling
- Ring culling: culling all herds within a distance $X$ of a discovered case infection
- Important for stopping the spread of the disease
- However, makes it harder to predict the behavior as culls will lead to censoring of data: i.e. animals will be culled whether they have disease or not.
To model infection mechanism OR to describe the spread

- With any infectious disease it is possible to consider different approach to modeling.
- For non-infectious diseases it is adequate to simply describe the distribution of risk via such tools as random effect models (CAR models; geostatistical models).
- It's known that for most spatial risk distributions random effect models including spatial correlation effects do very well in recovering true risk.
However

- For infectious disease spatial and temporal spread it could be important to model *mechanism* of transmission.
- This must involve interaction between units at least at the individual level (even if not observed)
- Hence......
SIR formulation

- A common model assumed is a compartment model such as the SIR model (susceptible-infected-removed).
Basic SIR model

- Susceptible population (S)
- Infective (I)
- Removed (R)

- Also SEIR includes Exposed group also
How can counts be modelled?

- Observe new incident infections (Infectives)
- We know previous infective numbers
- We know the population (susceptibles)
- Removal?
  - Can assume a given rate

- Difference representation of the SIR
FMD models: Model I

\[ I_{ij} \sim bin(\rho, y_{ij}) \]

or

\[ y_{ij} = \rho I_{ij} \]

- Model assumes that the observed count \( I_{ij} \) is a proportion of the true infectives
- The observed infectives depend on the previous true infective count
FMD models: Model II

- Accounting model

\[ I_{ij} \sim \text{Pois}(S_{ij} \cdot f(I_{ij-1})) \]
\[ S_{ij+1} \sim N(\mu_{ij+1}, \sigma_s^2) \]
\[ \mu_{ij+1} = S_{ij} - I_{ij} - R_{ij} \]
\[ R_{ij} \sim N(\beta I_{ij}, \sigma_R^2) \]
Model 2

- How to parameterize the dependence on the previous infectives?

\[
\log \pi_{ij} = \log S_{ij} + \log f(I_{ij-1})
\]
Simple Dependencies

1) \( \log f(I_{ij-1}) = \log I_{ij-1} + b_0 + b_i \)

OR

2) \( \log f(I_{ij-1}) = b_0 + \log[I_{ij-1} + \sum_{l \in \delta_i} I_{lj-1}] \)

where \( b_i \) is a random effect.
FMD Models

**Notation**

- $l_{ij}$: infective premise count
- $y_{ij}$: true IP count
- $n_{ij}$: total number of premises

**Underascertainment**

$$y_{ij} = \beta l_{ij}$$

**Initial Model**

$$l_{ij} \sim \text{bin}(p_{ij}, n_{ij})$$

However the rate is low and so a Poisson approximation may be useful: $l_{ij} \sim \text{Pois}(\mu_{ij})$ where $\mu_{ij} = S_{ij} \cdot f(l_{i,j-1})$ and where $S_{ij} = n_{ij}$
FMD specific issues

- We know the removal due to culling
- We have the (almost) fully ascertained infectives (IPs)
- Finite population of premises which varies in time.
- Also want to estimate termination
FMD Model Dependencies

- We will model the rate of infection:
  - Model I: dependence on previous IPs
  - Model II: dependence on IPs and counts
  - Model III/IV: dependence on lagged neighbors

- Note: the SIR accounting equation is fixed in this case:

\[ n_{ij} = n_{i,j-1} - R_{i,j-1} - I_{i,j-1} \]
Poisson SIR

Model I: \( \log f(l_{i,j-1}) = \alpha_0 + \alpha_c l_{i,j-1} + v_i + u_i \)

Model II: \( \log f(l_{i,j-1}) = \alpha_0 + \alpha_c l_{i,j-1} + \alpha_p n_{i,j-1} + v_i + u_i \)

Model III: \( \log f(l_{i,j-1}) = \alpha_0 + \alpha_{c1} l_{i,j-1} + \alpha_{c2} \sum_{k \in \delta_i} l_{k,j-1} + v_i + u_i \)

Model IV: \( \log f(l_{i,j-1}) = \alpha_0 + \alpha_{c1} l_{i,j-1} + \alpha_{c2} \sum_{k \in \delta_i} l_{k,j-1} + \alpha_p n_{i,j-1} + v_i + u_i \)
FMD data and Model I fitting

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# Results for all FMD Models

<table>
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<tr>
<th>Model</th>
<th>random effects</th>
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<th>Deviance</th>
<th>pD</th>
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Model 2: posterior Mean estimates

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Detecting termination

- Can assess termination using monotone means ie continually descending mean estimates flag termination

\[ \mu_{ij} < \mu_{i,j-1} < \mu_{i,j-2} < \mu_{i,j-3} \ldots \]
Some References on FMD and BDM


What is common?

- Modeling spatial disease risk variation based on aggregate count data in small areas:
  - via generalised linear mixed models which include spatial correlation
  - Many examples of this in the veterinary literature
- Cluster detection:
  - Detection of clustering or ‘unusual’ aggregation of disease is both a theme in human and veterinary epidemiology
  - Leads to isolation of high risk but also targeting of interventions
What is less common (or at least less studied)?

- Zoonosis and its complications
- Many diseases affect both humans and animals
- Animals can be seen as sentinels (chickens for West Nile in California)
- Hosts or vectors?
- Whether there is transmission between animal and human there could be a useful focus on joint analysis of the data from the two sources.
West Nile in California (counties)
Tularemia in Finland

- Final example is one where zoonosis can be addressed at least in the sense of being able to examine/model both human cases and animal cases together.
- Tularemia type B strain is a mosquito borne disease commonly found in Scandinavia and it affects the rodent and human populations. Causes skin lesions, fever and can be life-threatening.
- Transmission to humans is usually by mosquito
- Humans can be infected from drinking water infected by rodents (mainly voles in Finland), or by skin contact with infected animals or aerosols
Available data

- We have access to regional data on human cases and rodent cases for a period of 1995-2012
- Human data is of the form of counts of confirmed cases
- The rodent data is categorical and can only be either binary or three level.
  - The binary version is peak/non-peak
  - The categorical version is background/increasing/decreasing
- Collected bi-annually at 30 locations and imputed to hospital regions (20) (Rosssow et al., 2015, *Euro Surveillance*)
- Rodent known cycles of 3-4 years
Number of laboratory confirmed cases and timing of vole population peaks (1995-2013)
Human SIRs (1995-1998)
Joint modeling

- Possible approaches:
  - Consider rodent count/state as syndromic variable
  - Consider joint modeling of rodent and human data
    - Can be useful when prediction of both human and rodent variation is important
    - If cross infection is important then joint modeling may be essential
    - If missingness is important (in human and rodent data) then joint modeling may be essential
Joint modeling of Tularemia

- Definitions:
  - Human case count $h_{it}$
  - Rodent state (binary) $r_{it}$
    (obtained at a networks if sites and interpolated to district level)
  - for $i$ th spatial unit and $t$ th temporal unit
    - 20 health districts
    - 18 years
human \_it = h \_it \sim Poisson(e_i, \theta \_it) \\
\log(\theta \_it) = \alpha ^h + u ^h_i + v ^h_i + \delta ^h \_it \\
\delta ^h \_it = \beta ^h_i \delta ^r \_it-1 \\
\beta ^h_i = \beta ^p_i r ^n _it-1 + \beta ^n_i (1-r _it-1) \\
rodent \_it = r _it \sim Bernoulli(p _it) \\
\logit(p _it) = \alpha ^r + u ^r _i + v ^r _i + \nu ^{sr} _k + \nu ^{sr} _k + \delta ^r \_it
Prior distributions

\[ \alpha^h \sim N(0, \tau_{\alpha^h}^{-1}); \alpha^r \sim N(0, \tau_{\alpha^r}^{-1}) \]
\[ \delta_{it}^h \sim N(0, \tau_{\delta^h}^{-1}); \delta_{it}^r \sim N(0, \tau_{\delta^r}^{-1}) \]
\[ u_i^h \sim ICAR(\tau_{u^h}^{-1}); v_i^h \sim N(0, \tau_{v^h}^{-1}) \]
\[ u_i^r \sim ICAR(\tau_{u^r}^{-1}); v_i^r \sim N(0, \tau_{v^r}^{-1}) \]
\[ u_{kr}^{sr} \sim ICAR(\tau_{u^{sr}}^{-1}); v_{kr}^{sr} \sim N(0, \tau_{v^{sr}}^{-1}) \]
\[ \beta_i^p \sim N(0, \tau_{\beta^p}^{-1}); \beta_i^n \sim N(0, \tau_{\beta^n}^{-1}) \]
\[ \tau_* \sim Uniform(0,10). \]
Linking Rodents and Humans

\[ \delta_{it}^h = \beta_i \delta_{it-1}^r \]

\[ \beta_i = \beta_i^p r_{it-1} + \beta_i^n (1 - r_{it-1}) \]
Positive and negative dependence on rodent state (DP and DN)

\[ \beta_i^p, \beta_i^n \]

\[ DP_i = \frac{\exp(\beta_i^p)}{\exp(\beta_i^p) + 1} \]

\[ DN_i = \frac{\exp(\beta_i^n)}{\exp(\beta_i^n) + 1} \]
Maps of 95% lower limit (left), mean (middle) and 95% upper limit of DP for each health district in Finland.
Maps of 95% lower limit (left), mean (middle) and 95% upper limit of DN for each health district in Finland.
Conclusion

- I have highlighted the unique and also common threads that run through geo-veterinary and geo-human applications
- One Health really focusses on the interaction between human and veterinary disease incidence
- Hence approaches that integrate and find common ground in the modeling disease risk are going to be of increasing importance in the future
- In addition sensitivity to unique aspects of the spatial distribution of human and animal risk will always be important
Spatial epidemiology references

Thank you!