Malaria, river-blindness and plague: three case studies in spatial modelling of tropical diseases

Emanuele Giorgi and Peter J. Diggle

Lancaster Medical School, Lancaster University, Lancaster, UK



LSHTM, 24 April 2015

Emanuele Giorgi and Peter J. Diggle

1 Combining data from multiple surveys of different quality:

e.g. randomised and non-randomised surveys.

1 Combining data from multiple surveys of different quality:

e.g. randomised and non-randomised surveys.

Spatially structured zero-inflation: chance finding or disease-free community?

1 Combining data from multiple surveys of different quality:

e.g. randomised and non-randomised surveys.

- 2 Spatially structured zero-inflation: chance finding or disease-free community?
- 3 Analysis of spatio-temporal data at multiple spatial-scales: how to integrate district-level disease case reports with high resolution environmental data?

 Malaria: combining data from a community and a (biased) school-based surveys in Nyanza Province, Kenya.

- Malaria: combining data from a community and a (biased) school-based surveys in Nyanza Province, Kenya.
- **River-blindness:** geostatistical modelling of spatially-structured zero inflation in prevalence data from Mozambique, Malawi and Tanzania.

- Malaria: combining data from a community and a (biased) school-based surveys in Nyanza Province, Kenya.
- **River-blindness:** geostatistical modelling of spatially-structured zero inflation in prevalence data from Mozambique, Malawi and Tanzania.
- Plague: spatio-temporal analysis of monthly plague incidence from 2000 to 2007 in Madagascar.

Malaria mapping in Nyanza Province



Malaria mapping in Nyanza Province



Statistical issues

- Different unmeasured risk factors for malaria.
- Joint model or gold-standard data only?

- $r_d(x)$ = ``odds for the disease''
- $r_s(x)$ = ``odds within the survey''
- $r_c(x)$ = ``relative odds between participants and non-participants to the survey''

- $r_d(x)$ = ``odds for the disease''
- $r_s(x)$ = ``odds within the survey''
- $r_c(x)$ = ``relative odds between participants and non-participants to the survey''

 $r_s(x) = r_d(x) \times r_c(x)$

- $r_d(x)$ = ``odds for the disease''
- $r_s(x)$ = ``odds within the survey''
- $r_c(x)$ = ``relative odds between participants and non-participants to the survey''

$$r_s(x) = r_d(x) \times r_c(x) \iff \log\{r_s(x)\} = \frac{S(x)}{S(x)} + B(x)$$
(1)

- $r_d(x)$ = ``odds for the disease''
- $r_s(x)$ = ``odds within the survey''
- $r_c(x)$ = ``relative odds between participants and non-participants to the survey''

$$r_s(x) = r_d(x) \times r_c(x) \iff \log\{r_s(x)\} = S(x) + B(x)$$
 (1)

• $Y_{ijk}|S(x_{ij}), B(x_{ij}) \sim \text{Bernoulli}(p_{ijk})$ (i=``survey", j=``household", k=```individual'').

- $r_d(x)$ = ``odds for the disease''
- $r_s(x)$ = ``odds within the survey''
- $r_c(x)$ = ``relative odds between participants and non-participants to the survey''

$$r_s(x) = r_d(x) \times r_c(x) \iff \log\{r_s(x)\} = S(x) + B(x)$$
 (1)

- $Y_{ijk}|S(x_{ij}), B(x_{ij}) \sim \text{Bernoulli}(p_{ijk})$ (i=``survey", j=``household", k=```individual'').
- $\log\{p_{ijk}/(1+p_{ijk})\} = d_{ijk}^{\top}\beta + S(x_{ij}) + B(x_{ij});$ $B(x) = 0, \forall x \in \mathbb{R}^2$ if i is "community".

Term	Estimate	$95\%~{ m Cl}$
Intercept	-1.412	(-2.303, -0.521)
Age	-0.141	(-0.174, -0.109)
Rachuonyo District	2.006	(1.228, 2.785)
Socio-Economic-Status	-0.121	(-0.169, -0.072)
School survey	-0.761	(-1.354, -0.167)
Age (bias)	0.094	(0.046, 0.142)

Results (2)

Mapping of (a) $r_c(x)$ and (b) $1 - P(0.9 < r_c(x) < 1.1|y)$.





Emanuele Giorgi and Peter J. Diggle

Gain/loss in the accuracy for the estimates of S(x).



River blindness



Rapid epidemiological mapping of onchocerciasis





Prevalence estimates in the 20 APOC countries



Prevalence estimates in the 20 APOC countries



Statistical issue

 $\mathbf{1}$ 3,320 villages with no case and 11,154 villages with at least one case.

2 Accounting for zero-inflation: how to identify disease-free areas?

• Standard model: $Y|S(x) \sim \text{Bin}(\cdot; n, p(x))$ where

$$\log\{p(x)/(1-p(x))\} = \mu + S(x).$$

• Standard model: $Y|S(x) \sim \text{Bin}(\cdot; n, p(x))$ where

$$\log\{p(x)/(1-p(x))\} = \mu + S(x).$$

Allowing for zero-inflation:

$$P(Y = y | S_1(x), S_2(x), D(x)) = \begin{cases} \pi(x) + (1 - \pi(x)) \text{Bin}(0; n, p(x)) & \text{if } y = 0\\ (1 - \pi(x)) \text{Bin}(y; n, p(x)) & \text{if } y > 0 \end{cases}$$

• Standard model: $Y|S(x) \sim Bin(\cdot; n, p(x))$ where

$$\log\{p(x)/(1-p(x))\} = \mu + S(x).$$

Allowing for zero-inflation:

$$P(Y = y | S_1(x), S_2(x), D(x)) = \begin{cases} \pi(x) + (1 - \pi(x)) \text{Bin}(0; n, p(x)) & \text{if } y = 0\\ (1 - \pi(x)) \text{Bin}(y; n, p(x)) & \text{if } y > 0 \end{cases}$$

where

• Standard model: $Y|S(x) \sim Bin(\cdot; n, p(x))$ where

$$\log\{p(x)/(1-p(x))\} = \mu + S(x).$$

Allowing for zero-inflation:

$$P(Y = y | S_1(x), S_2(x), D(x)) = \begin{cases} \pi(x) + (1 - \pi(x)) \operatorname{Bin}(0; n, p(x)) & \text{if } y = 0\\ (1 - \pi(x)) \operatorname{Bin}(y; n, p(x)) & \text{if } y > 0 \end{cases}$$

where

In the next example $D(x) = 0, \forall x$.

Mapping in Mozambique - Malawi - Tanzania (1)



Mapping in Mozambique - Malawi - Tanzania (2)





Emanuele Giorgi and Peter J. Diggle

Spatial modelling of tropical diseases 13 / 21



Plague in Madagascar





Plague in Madagascar





Statistical issue

- Ecological bias.
- How to integrate spatially continuous data with district-level case reports?

Emanuele Giorgi and Peter J. Diggle

• $N_{i,t}$ = ``number of cases in the i-th district at time t''

- $N_{i,t}$ = ``number of cases in the i-th district at time $t^{\prime\prime}$
- $\lambda(x,t)$ = ''intensity of an inhomogeneous Poisson process at location x and time $t^{\prime\prime}$

- $N_{i,t}$ = ``number of cases in the i-th district at time $t^{\prime\prime}$
- $\lambda(x,t)$ = ''intensity of an inhomogeneous Poisson process at location x and time $t^{\prime\prime}$
- $N_{i,t} \sim \operatorname{Poisson}\left(\int_t^{t+1} \int_{A_i} \lambda(u,v) \, du \, dv\right).$

- $N_{i,t}$ = ``number of cases in the i-th district at time $t^{\prime\prime}$
- $\lambda(x,t)$ = ''intensity of an inhomogeneous Poisson process at location x and time $t^{\prime\prime}$
- $N_{i,t} \sim \operatorname{Poisson}\left(\int_t^{t+1} \int_{A_i} \lambda(u,v) \, du \, dv\right).$

•
$$\int_t^{t+1} \int_{A_i} \lambda(u, v) \, du \, dv \approx \Delta \sum_{j=1}^{n_{i,t}} \lambda(x_j, t).$$

- $N_{i,t}$ = ``number of cases in the *i*-th district at time $t^{\prime\prime}$
- $\lambda(x,t)$ = ``intensity of an inhomogeneous Poisson process at location x and time $t^{\prime\prime}$
- $N_{i,t} \sim \operatorname{Poisson}\left(\int_t^{t+1} \int_{A_i} \lambda(u,v) \, du \, dv\right).$
- $\int_t^{t+1} \int_{A_i} \lambda(u, v) \, du \, dv \approx \Delta \sum_{j=1}^{n_{i,t}} \lambda(x_j, t).$
- $\mathcal{X}_{i,t} = \{X_{j,t} \in A_i\} | N_{i,t} = n_{i,t}$ has multinomial distribution with probabilities

$$p_k = rac{\lambda(x_k,t)}{\sum_{j=1}^{n_{i,t}}\lambda(x_j,t)}$$
, for $k = 1, \dots, n_{i,t}$.

• m(x,t) = ``number of susceptibles at location x and time $t^{\prime\prime}$

- m(x,t) = ``number of susceptibles at location x and time $t^{\prime\prime}$
- $\lambda(x,t) = m(x,t) \exp\{d(x,t)^\top \beta + S(x) + V(t)\},\$

- m(x,t) = ``number of susceptibles at location x and time $t^{\prime\prime}$
- $\lambda(x,t) = m(x,t) \exp\{d(x,t)^\top \beta + S(x) + V(t)\},\$

 $d(x,t)^{\top}\beta = \beta_1 + \beta_2 \operatorname{temp}(x,t) + \beta_3 \operatorname{rain}(x,t) + \beta_3 \operatorname{rain$

- m(x,t) = ``number of susceptibles at location x and time $t^{\prime\prime}$
- $\lambda(x,t) = m(x,t) \exp\{d(x,t)^\top \beta + S(x) + V(t)\},\$

$$d(x,t)^{\top}\beta = \beta_1 + \beta_2 \operatorname{temp}(x,t) + \beta_3 \operatorname{rain}(x,t) + \\ \beta_4 I(\operatorname{elev}(x) > 800m) + \beta_5 \operatorname{elev}(x) + \\ \beta_6 \operatorname{elev}(x) \times I(\operatorname{elev}(x) > 800m) +$$

- m(x,t) = ``number of susceptibles at location x and time $t^{\prime\prime}$
- $\lambda(x,t) = m(x,t) \exp\{d(x,t)^\top \beta + S(x) + V(t)\},\$

$$d(x,t)^{\top}\beta = \beta_1 + \beta_2 \operatorname{temp}(x,t) + \beta_3 \operatorname{rain}(x,t) + \\ \beta_4 I(\operatorname{elev}(x) > 800m) + \beta_5 \operatorname{elev}(x) + \\ \beta_6 \operatorname{elev}(x) \times I(\operatorname{elev}(x) > 800m) + \\ \beta_7 \log\{\operatorname{pop}(x)\} +$$

- m(x,t) = ``number of susceptibles at location x and time $t^{\prime\prime}$
- $\lambda(x,t) = m(x,t) \exp\{d(x,t)^\top \beta + S(x) + V(t)\},\$

$$\begin{aligned} d(x,t)^{\top}\beta &= \beta_1 + \beta_2 \mathsf{temp}(x,t) + \beta_3 \mathsf{rain}(x,t) + \\ & \beta_4 I(\mathsf{elev}(x) > 800m) + \beta_5 \mathsf{elev}(x) + \\ & \beta_6 \mathsf{elev}(x) \times I(\mathsf{elev}(x) > 800m) + \\ & \beta_7 \log\{\mathsf{pop}(x)\} + \\ & [\beta_8 + \beta_9 \mathsf{temp}(x,t) + \beta_{10} \mathsf{rain}(x,t)] \sin(2\pi t/12) + \\ & [\beta_{11} + \beta_{12} \mathsf{temp}(x,t) + \beta_{13} \mathsf{rain}(x,t)] \cos(2\pi t/12) \end{aligned}$$

- m(x,t) = ``number of susceptibles at location x and time $t^{\prime\prime}$
- $\lambda(x,t) = m(x,t) \exp\{d(x,t)^\top \beta + S(x) + V(t)\},\$

$$\begin{split} d(x,t)^{\top}\beta &= \beta_1 + \beta_2 \mathrm{temp}(x,t) + \beta_3 \mathrm{rain}(x,t) + \\ & \beta_4 I(\mathrm{elev}(x) > 800m) + \beta_5 \mathrm{elev}(x) + \\ & \beta_6 \mathrm{elev}(x) \times I(\mathrm{elev}(x) > 800m) + \\ & \beta_7 \log\{\mathrm{pop}(x)\} + \\ & [\beta_8 + \beta_9 \mathrm{temp}(x,t) + \beta_{10} \mathrm{rain}(x,t)] \sin(2\pi t/12) + \\ & [\beta_{11} + \beta_{12} \mathrm{temp}(x,t) + \beta_{13} \mathrm{rain}(x,t)] \cos(2\pi t/12) \\ S(x) &= S_i, \text{ if } x \in \mathrm{district}_i \end{split}$$

- m(x,t) = ``number of susceptibles at location x and time $t^{\prime\prime}$
- $\lambda(x,t) = m(x,t) \exp\{d(x,t)^\top \beta + S(x) + V(t)\},\$

$$\begin{array}{lcl} d(x,t)^{\top}\beta &=& \beta_{1} + \beta_{2} \mathrm{temp}(x,t) + \beta_{3} \mathrm{rain}(x,t) + \\ && \beta_{4}I(\mathrm{elev}(x) > 800m) + \beta_{5} \mathrm{elev}(x) + \\ && \beta_{6} \mathrm{elev}(x) \times I(\mathrm{elev}(x) > 800m) + \\ && \beta_{7} \log\{\mathrm{pop}(x)\} + \\ && \left[\beta_{8} + \beta_{9} \mathrm{temp}(x,t) + \beta_{10} \mathrm{rain}(x,t)\right] \sin(2\pi t/12) + \\ && \left[\beta_{11} + \beta_{12} \mathrm{temp}(x,t) + \beta_{13} \mathrm{rain}(x,t)\right] \cos(2\pi t/12) \\ && S(x) &=& S_{i}, \text{ if } x \in \mathrm{district}_{i} \\ && V(t) & | & V(t-1), \dots, V(0) = V(t) \mid V(t-1) \end{array}$$

Results (1)

Term	Estimate	95% Cl	
β_1	-41.301	(-54.246, -30.104)	
β_2	0.055	(-0.008, 0.125)	
β_3	0.028	(-0.009, 0.061)	
β_4	22.241	(10.566, 35.322)	
β_5	0.027	(0.011, 0.043)	
β_6	-0.024	(-0.041, -0.008)	
β_7	0.069	(0.014, 0.140)	
β_8	0.735	(-0.103, 1.444)	
β_9	-0.293	(-0.314, -0.269)	
β_{10}	0.025	(-0.003, 0.053)	
β_{11}	5.017	(4.513, 5.498)	
β_{12}	0.040	(0.007, 0.078)	
β_{13}	-0.026	(-0.063, 0.013)	



Spatial residuals





How to account for spatio-temporally structured bias?

- How to account for spatio-temporally structured bias?
- Alternative modelling approaches to zero-inflation.
 - 1 Admitting discontinuities in prevalence.
 - 2 Constraining prevalence to smoothly approach zero.

- How to account for spatio-temporally structured bias?
- Alternative modelling approaches to zero-inflation.
 - 1 Admitting discontinuities in prevalence.
 - 2 Constraining prevalence to smoothly approach zero.
- Comparison of the mechanistic approach with empirical models.

- How to account for spatio-temporally structured bias?
- Alternative modelling approaches to zero-inflation.
 - 1 Admitting discontinuities in prevalence.
 - 2 Constraining prevalence to smoothly approach zero.
- Comparison of the mechanistic approach with empirical models.
- Acknowledgements: Gillian Stresman (LSHTM), Jennifer Stevenson (LSHTM), Hans Remme (Ornex), Cyril Caminade (Liverpool), Matthew Baylis (Liverpool).

- How to account for spatio-temporally structured bias?
- Alternative modelling approaches to zero-inflation.
 - 1 Admitting discontinuities in prevalence.
 - 2 Constraining prevalence to smoothly approach zero.
- Comparison of the mechanistic approach with empirical models.
- Acknowledgements: Gillian Stresman (LSHTM), Jennifer Stevenson (LSHTM), Hans Remme (Ornex), Cyril Caminade (Liverpool), Matthew Baylis (Liverpool).

Thanks for your attention.