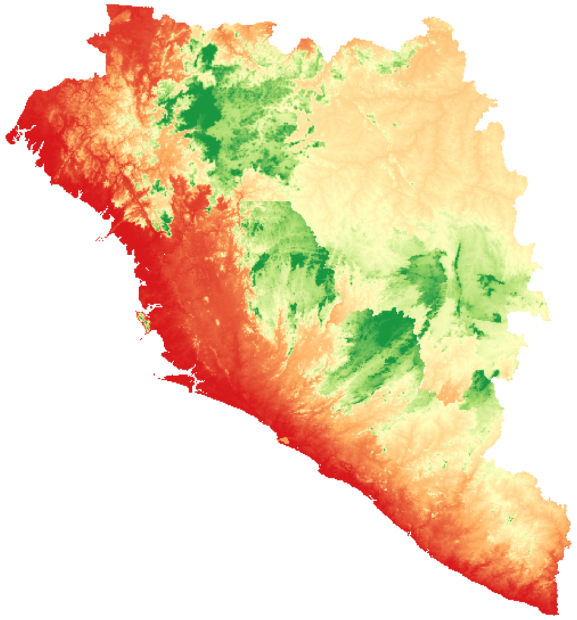

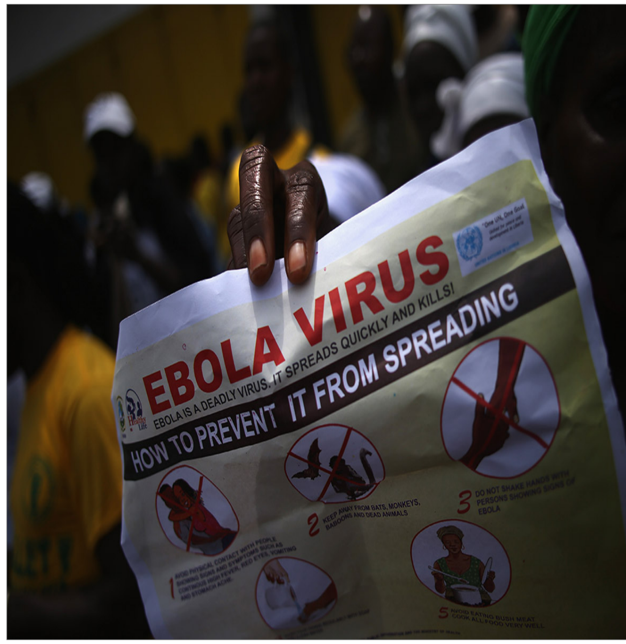

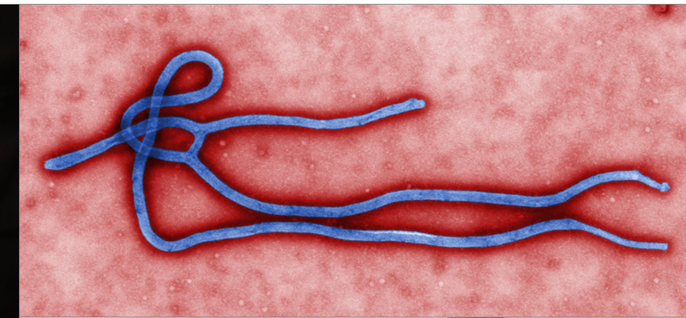

Spatial determinants of Ebola virus disease risk for the West African epidemic

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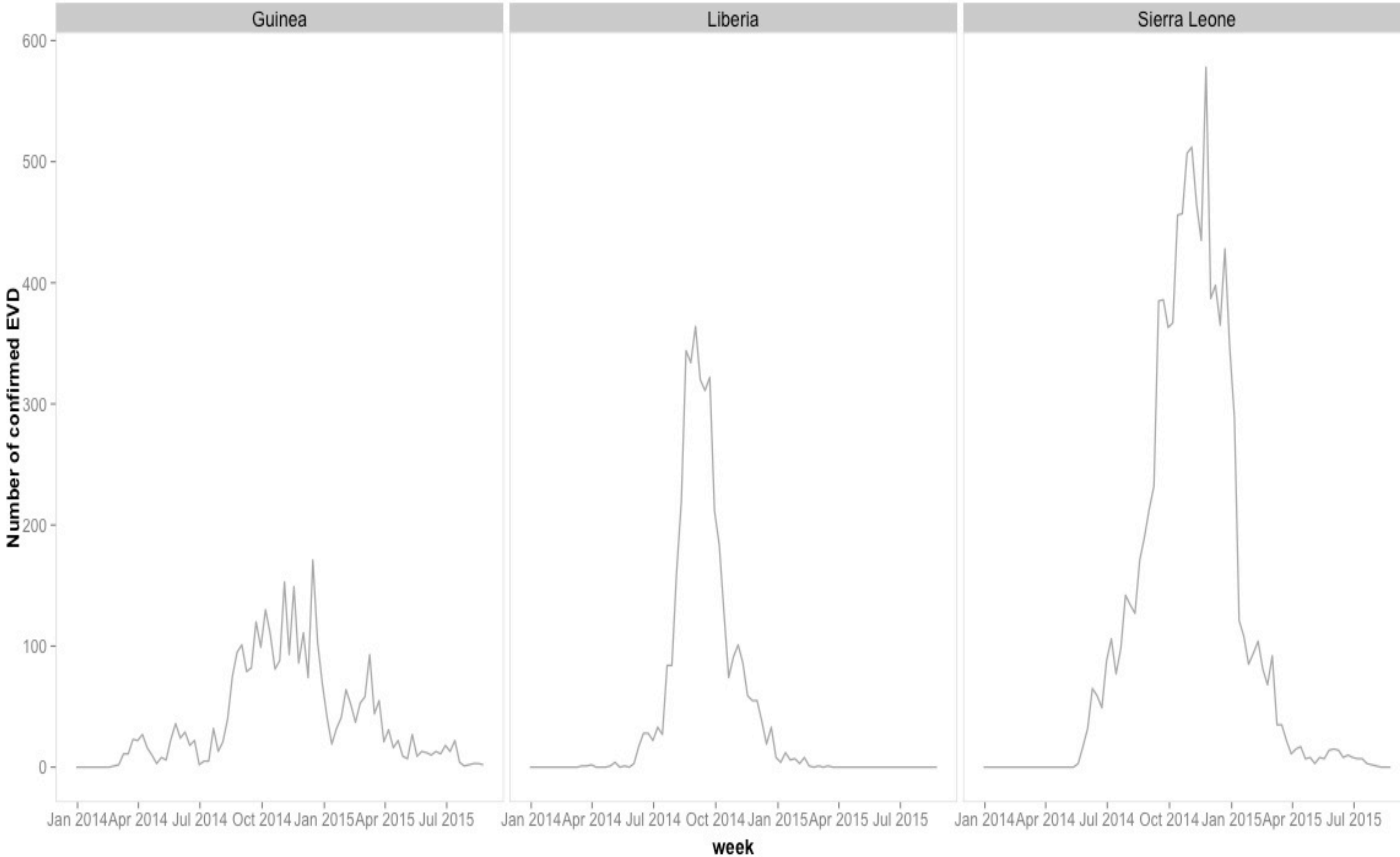
12 June 2018
Workshop on causal adjustment in the presence of spatial dependence
Centre de Recherches Mathématiques

EVD West Africa

- 15,261 confirmed cases with a 74% mortality rate
- Index case: a child who had contact with a fruit bat
- Numerous factors contributed to the human-to-human spread of Ebola virus disease (EVD)
  - Caring for infected individuals, funeral preparations, inadequate healthcare infrastructure
  - Frequency and breadth influenced by population density and mobile populations

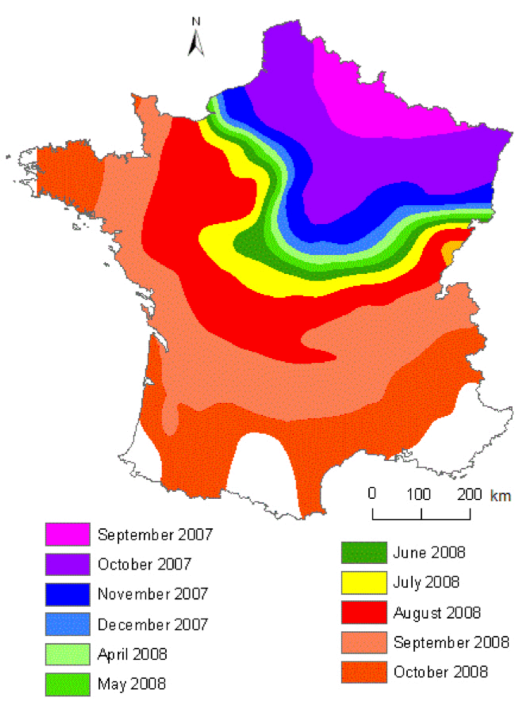
Source: Zoom Dosso/AFP/Getty Images

Epidemic curves 2014-2015



Velocity analysis

- Little is known about the direction and speed of EVD spread
- Velocity is not often calculated for human diseases but has been for several animal diseases
  - Animals: rabies, plague, bluetongue
  - Humans: sleeping sickness, Hanta virus



Source: Pioz et al, Estimating front-wave velocity of infectious diseases: a simple, efficient method applied to bluetongue

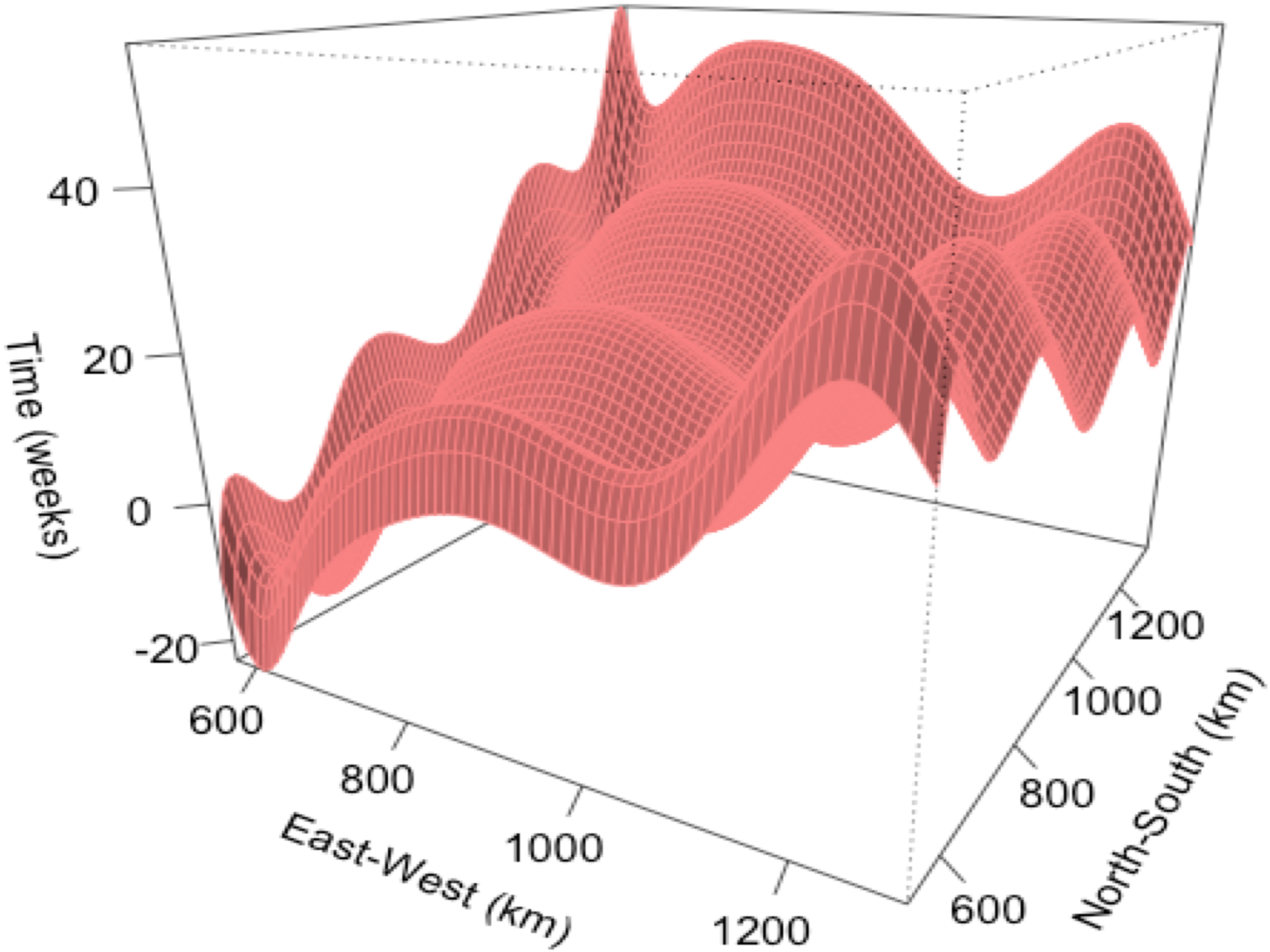
Source: Berrang-Ford L et al, Spatial analysis of sleeping sickness, southeastern Uganda, 1970-2003

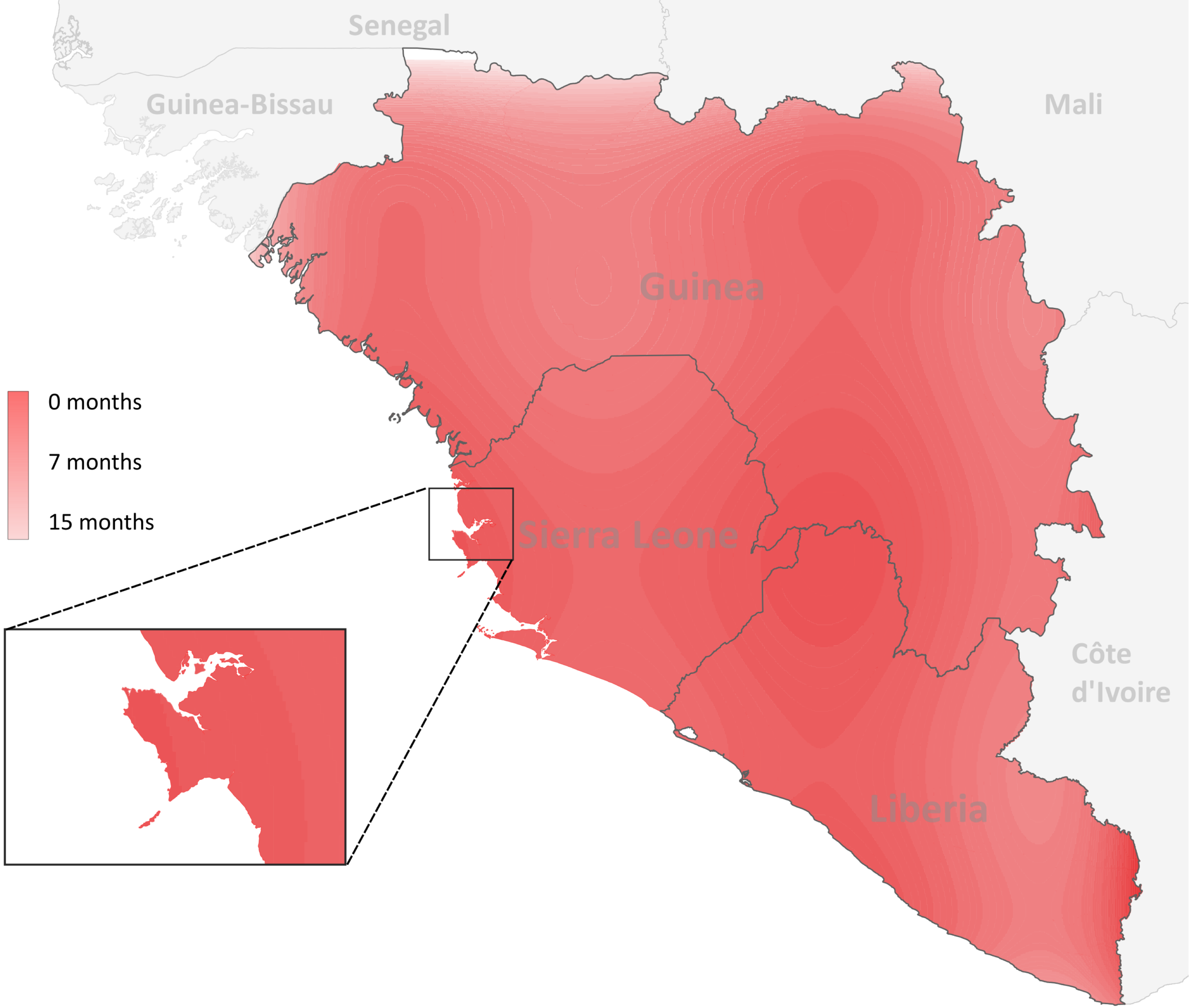
Methods

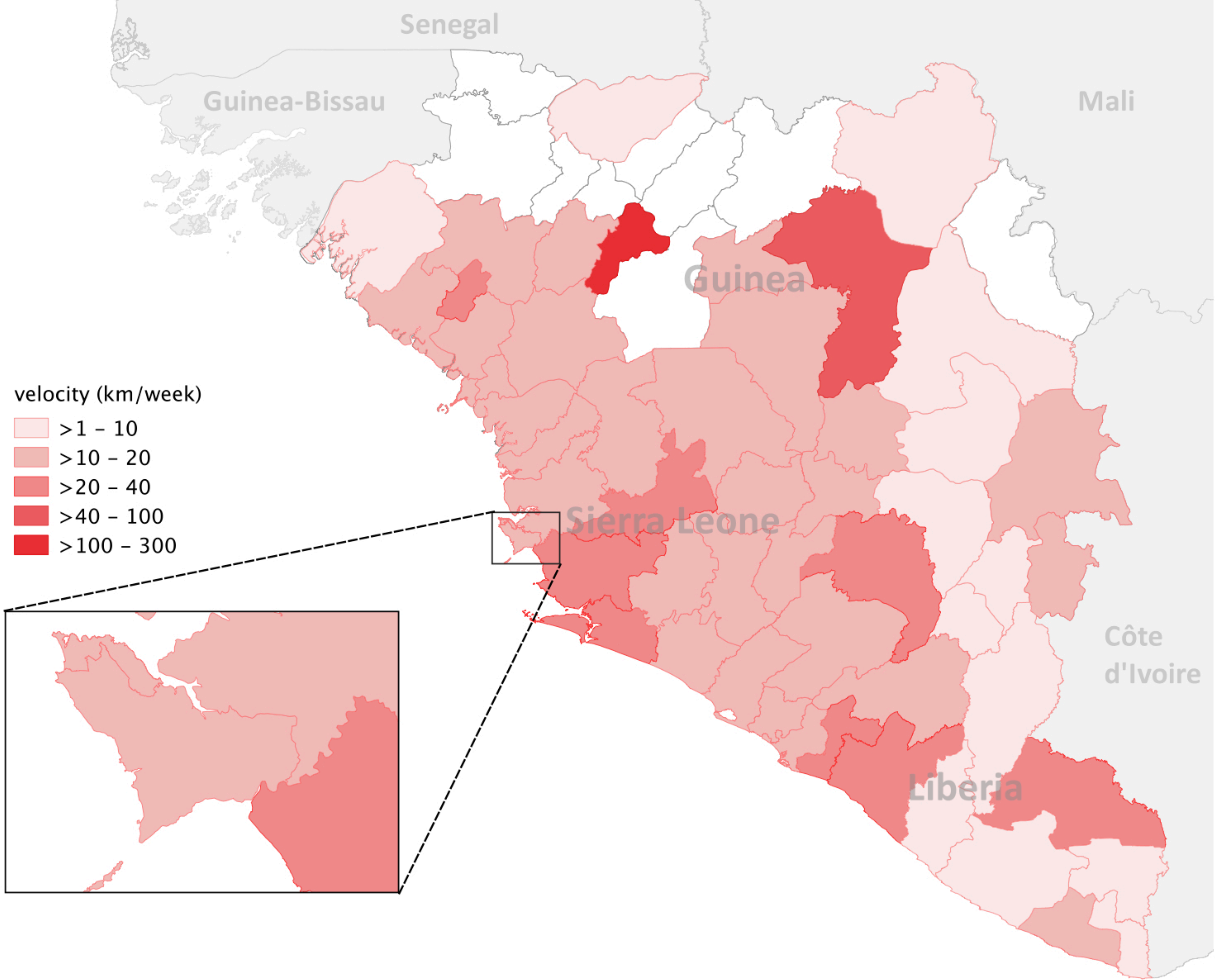
- Front-wave velocity, surface trend analysis
- Spatial interpolation method based on least squares regression to study diffusion in space and time
- Surface pattern constructed by mapping the specific timing of events at each (x,y) coordinate
- Shape and flexibility are determined by the polynomial order chosen (increasing order increases local curvature of fitted surface)

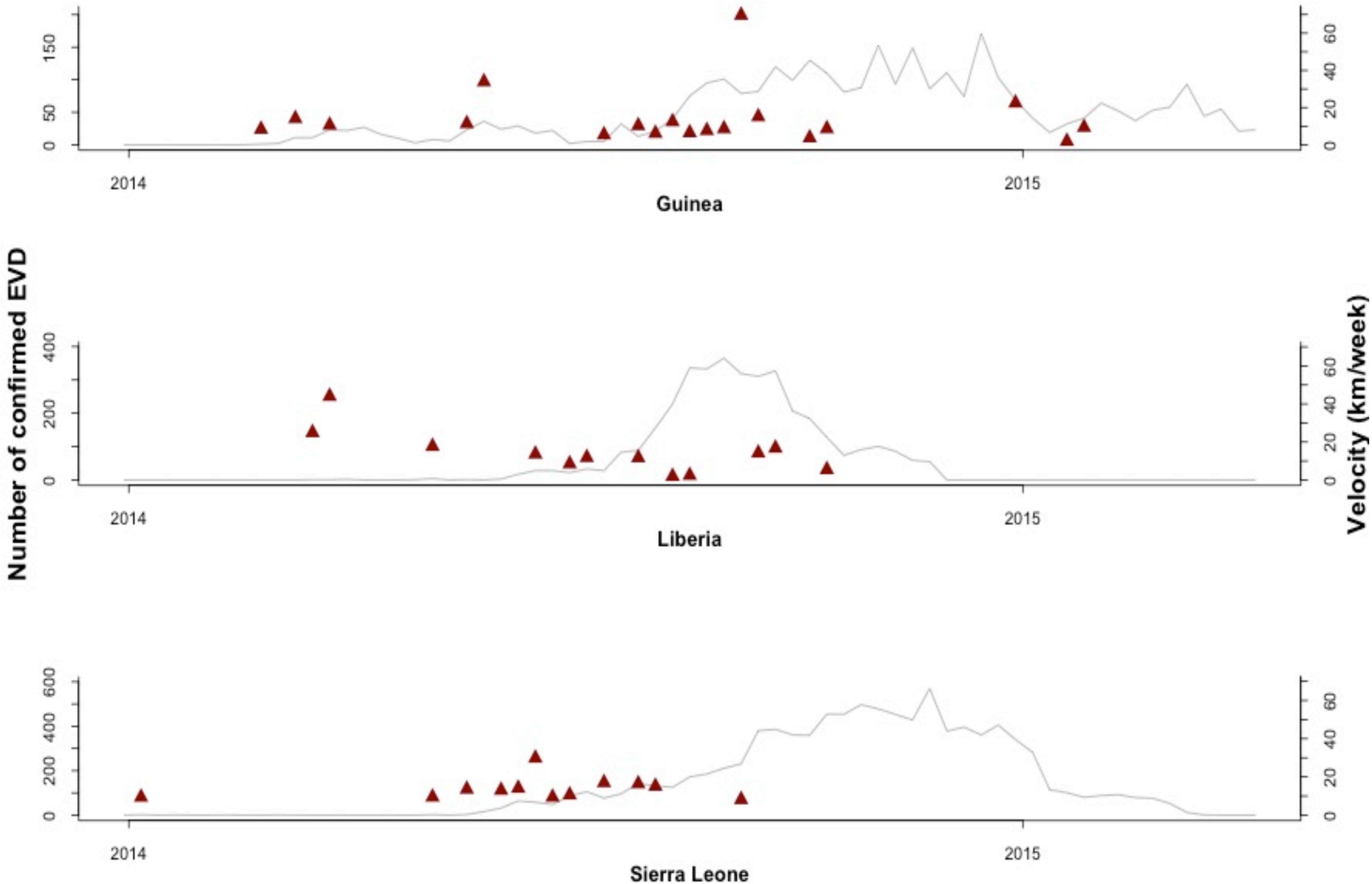
Model

- $f(t|x,y) = \beta_0 + \beta_1 X + \beta_2 Y + \beta_3 X^2 + \beta_4 Y^2 + \beta_5 X^3 + \beta_6 Y^3 + \beta_7 X^4 + \beta_8 Y^4 + \beta_9 X^5 + \beta_{10} Y^5 + \beta_{11} X^6 + \beta_{12} Y^6 + \beta_{13} XY$ (1)
- $\partial f(t|x,y) / \partial x = \beta_1 + 2\beta_3 X + 3\beta_5 X^2 + 4\beta_7 X^3 + 5\beta_9 X^4 + 6\beta_{11} X^5 + \beta_{13} Y$ (2)
- $\partial f(t|x,y) / \partial y = \beta_2 + 2\beta_4 Y + 3\beta_6 Y^2 + 4\beta_8 Y^3 + 5\beta_{10} Y^4 + 6\beta_{12} Y^5 + \beta_{13} X$ (3)
- Partial derivatives (2) and (3) provide expressions for a slope vector at a given location *X,Y*
- Magnitude and direction of rate of change (in weeks per km) was estimated by the inner product of the vector, where magnitude $||xy|| = \sqrt{(x^2 + y^2)}$ and the direction $\boldsymbol{\theta} = \tan^{-1}(y/x)$
- Residuals assessed for spatial autocorrelation

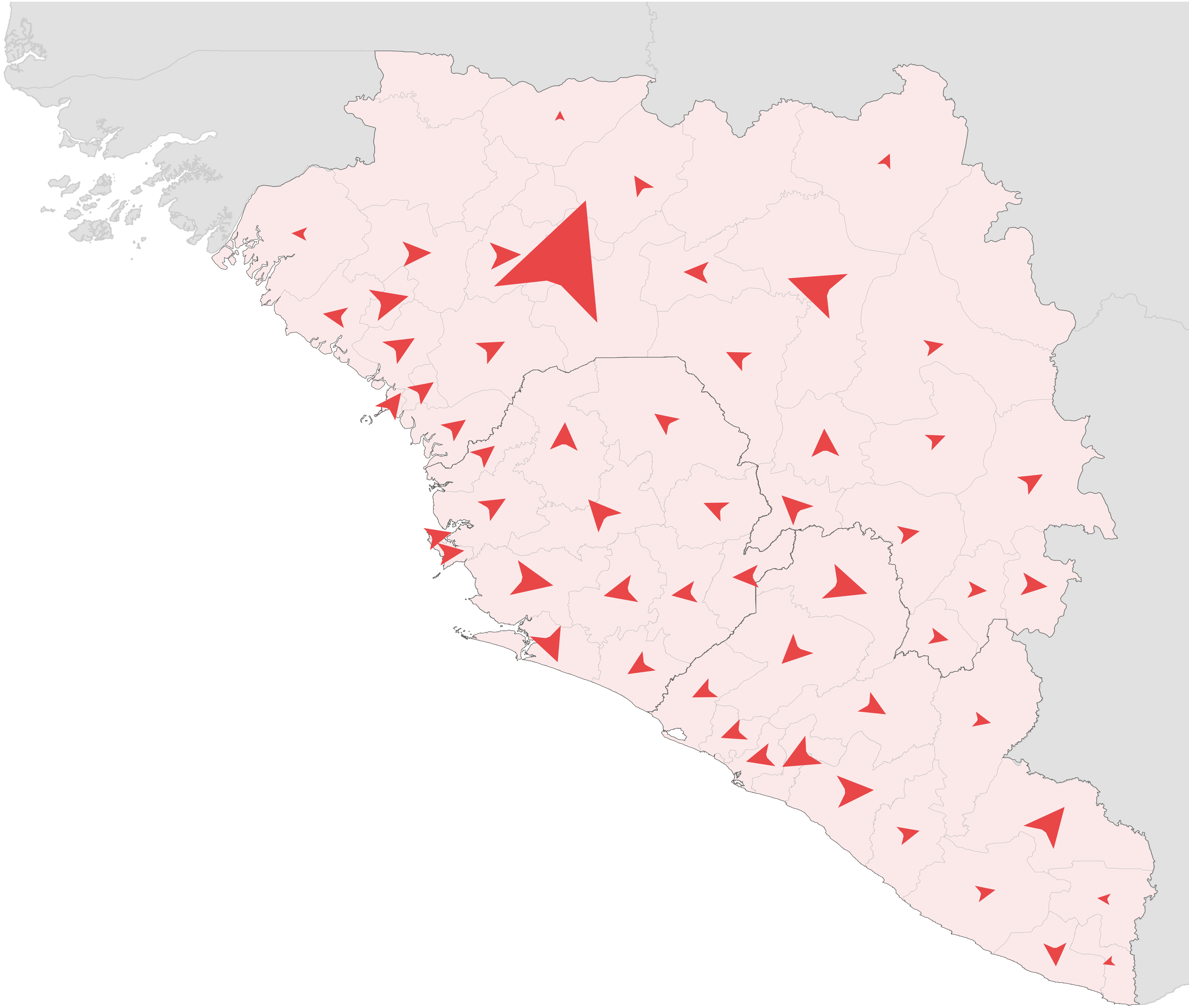

40
20
0
-20
Time (weeks)
600
800
1000
1200
East-West (km)
600
800
1000
1200
North-South (km)

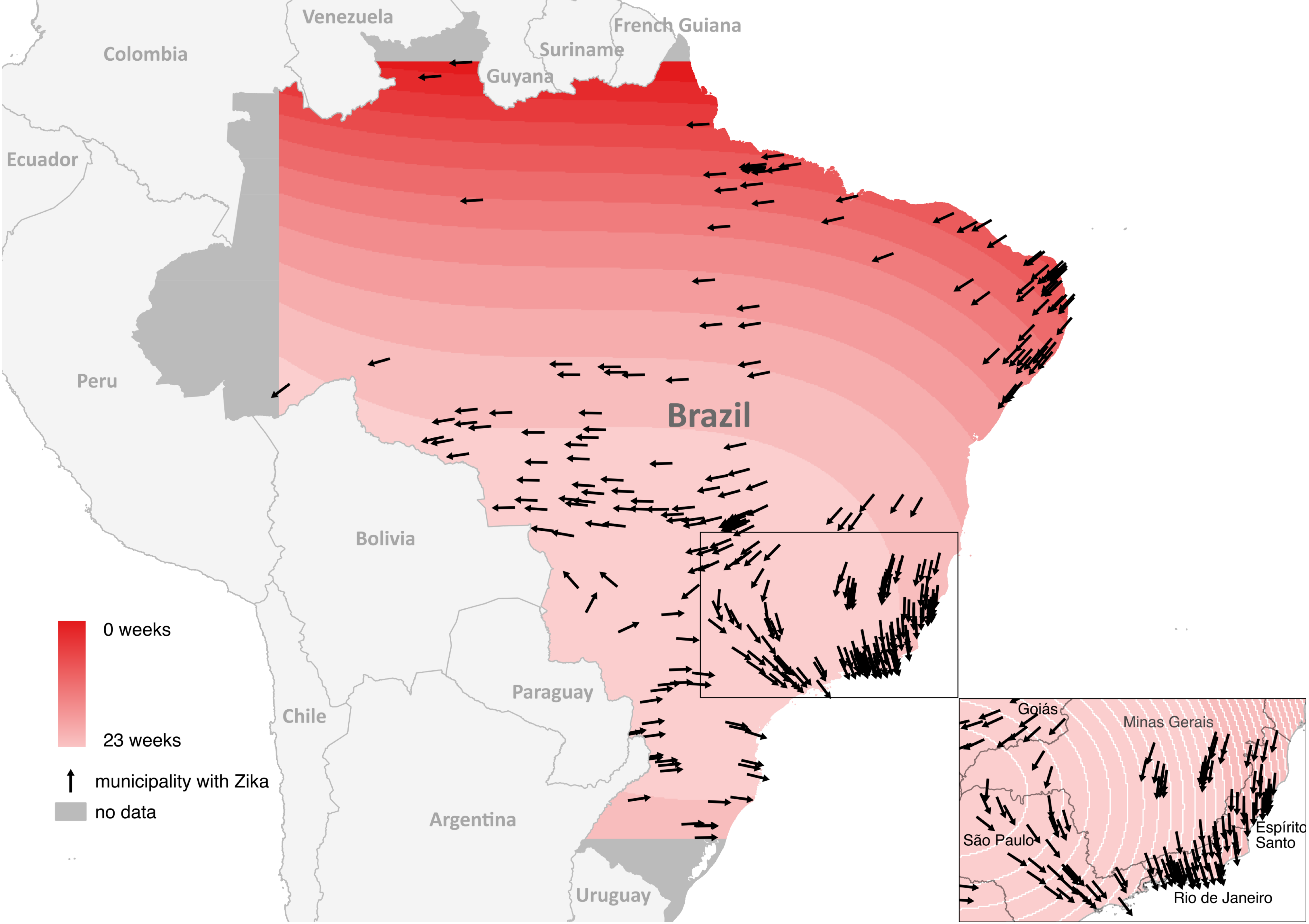

Senegal
Guinea-Bissau
Mali
Guinea
Sierra Leone
Côte d'Ivoire
Liberia
0 months
7 months
15 months


Senegal
Guinea-Bissau
Mali
Guinea
Sierra Leone
Liberia
Côte d'Ivoire
velocity (km/week)
>1 – 10
>10 – 20
>20 – 40
>40 – 100
>100 – 300



Number of confirmed EVD
Velocity (km/week)
Guinea
Liberia
Sierra Leone
2014
2015
0
50
150
200
400
600
20
40
60




Venezuela
French Guiana
Suriname
Guyana
Colombia
Ecuador
Peru
Brazil
Bolivia
Paraguay
Chile
Argentina
Uruguay
0 weeks
23 weeks
municipality with Zika
no data
Goiás
Minas Gerais
São Paulo
Espírito Santo
Rio de Janeiro

Study limitations

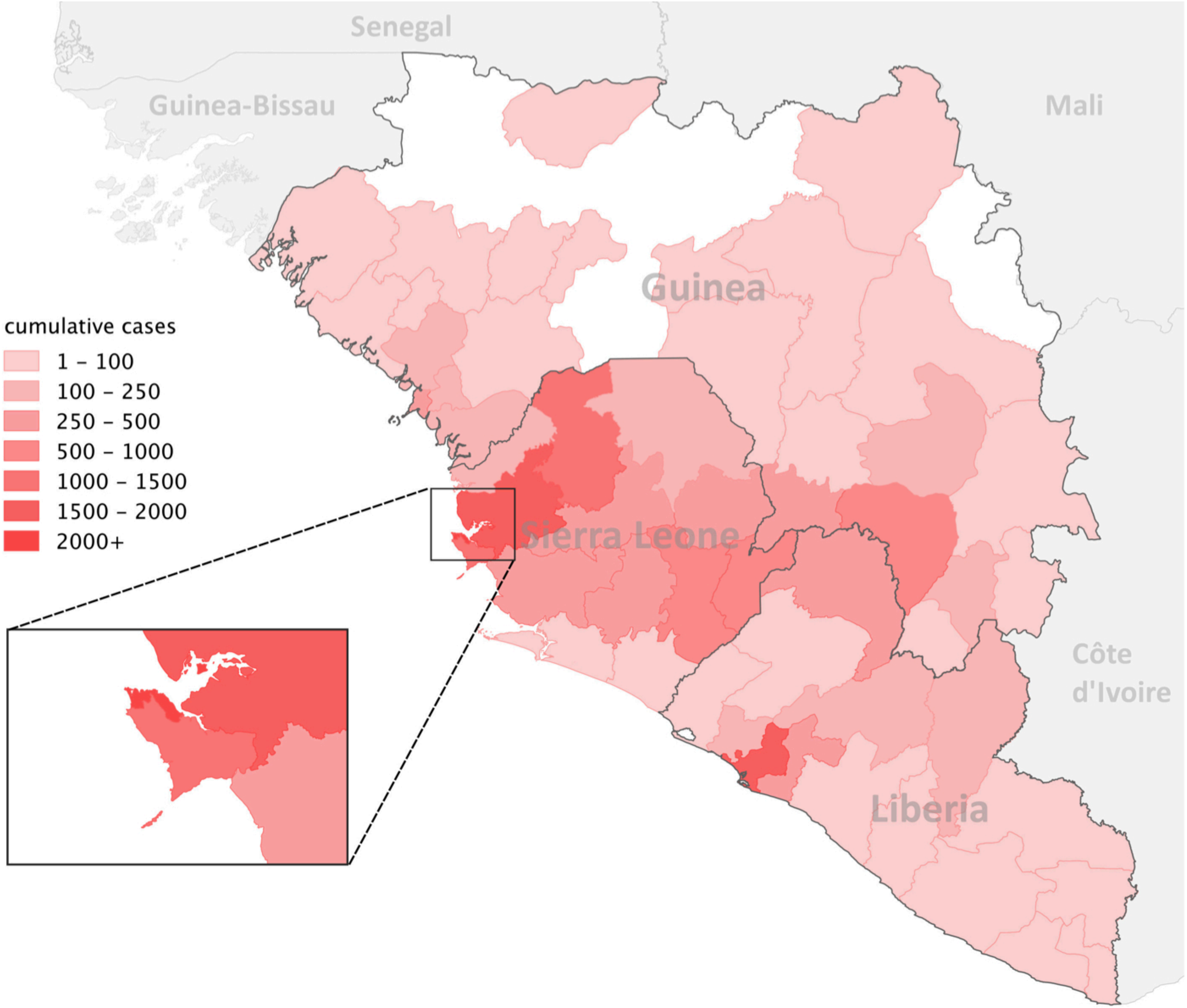
- WHO data subject to error including accuarcy and completeness
- Week of first confirmed EVD case may have been based on different dates including date of symptom onset or date of laboratory report
- Could have been earlier introductions of EVD that were not captured by surveillance system
- Data based on large geographic areas, increasing uncertainty associated with velocity estimates including edge effects

Conclusions

- Predicting disease movement is useful for identifying critical locations and corridors for containment efforts
- These methods should be applied to other diseases
- Extended to prediction and other predictors

Next analysis…understanding why

- Predictors of Ebola ecological niches, spillover events, or the onset of EVD outbreaks
  - EVD-related deaths in primates, deforestation, human forest activities, and population density
  - Precipitation, humidity, transition seasons, elevation, temperature, vegetation and vegetation density
- Several mathematical modelling studies estimate the size, speed, and patterns
- Few spatial studies based on empirical data
  - Social vulnerability was associated with spatial EVD transmission
  - Population, cases, and distance was associated with spatial risk of EVD infection



Senegal
Guinea-Bissau
Mali
Guinea
Sierra Leone
Liberia
Côte d'Ivoire
cumulative cases
1 – 100
100 – 250
250 – 500
500 – 1000
1000 – 1500
1500 – 2000
2000+

Objective & Methods

- Identify environmental and population-level demographic spatial predictors of human EVD risk
- Potential predictors
  - Environmental data, elevation, land area, roadway and waterway density
  - Population density
  - National DHS – household education, wealth, occupation, household structure, possessions and amenities
- Regressed cumulative total EVD cases on selected covariates
  - Selected model with best AIC
- Quantified amount of variation of EVD cases by using a spatial autoregressive modelling approach

Model

- Two random effects (uncorrelated residual variation and spatially correlated residual variation)
- INLA used to estimate marginal posterior distributions

$$
\begin{aligned}
&Y_i \sim Poisson(\mu_i)\\
&log(\frac{Y_i}{pop_i}) = \alpha_0 + \beta_1 x_1 + \beta_2 x_2 + ... + \beta_{12} x_{12} + u_i + \nu_i\\
&u_i \sim N(0, \frac{1}{\tau_u})\\
&\nu_i | \tau_\nu, \nu_j, i \neq j, \sim N(\frac{1}{n_i} \sum i \sim j \nu_j, \frac{1}{n_i \tau_\nu})\\
&\alpha_0, \beta_1, \cdot \cdot \cdot, \beta_j \sim N(0,1000)
\end{aligned}
$$

where *i* and *j* refer to two distinct regions in the study area, *i ~ j* refers to two neighboring regions, and n_i refers to the number of neighboring regions for region *i*.

Results

Table 1: Country-level summaries for selected covariates

Covariate	Guinea	Liberia	Sierra Leone
Total confirmed EVD cases	3,144	3,339	9,394
Average rainfall accumulation (cm)	3.2	3.6	4.8
Average elevation (m)	435.3	172.1	166.4
Roadway density (km/100 km^2)	10.0	11.2	16.8
Waterway density (km/100 km^2)	11.2	9.0	15.7
Cropland (%)	9.5%	5.1%	13.3%
Female headed households (%)	17.3%	35.2%	28.0%
Secondary education (%)	1.5%	10.5%	4.8%
Households (%) without toilet facilities	19.5%	45.2%	21.4%
Households (%) with electricity	26.2%	9.8%	13.5%
Households (%) with radio	61.5%	58.9%	58.8%

Results

Covariates	Rate ratio (95% credible interval)
Weekly rainfall accumulation (cm)	
<3.22	1.00
3.22-4.18	2.18 (0.66, 7.20)
>4.18	5.34 (1.20, 23.90)
Roadway density	
<0.09	1.00
0.09-0.11	0.61 (0.19, 1.96)
>0.11	1.22 (0.35, 4.26)
Population density	
<33.6	1.00
33.6-68.0	0.64 (0.18, 2.23)
>68.0	0.98 (0.22, 4.35)
Urban land cover (%)	
<0.02	1.00
0.02-0.09	4.87 (1.56, 15.40)
>0.09	5.74 (1.68, 19.67)
Household not possessing radios (%)	
<38.1	1.00
38.1-47.6	2.79 (0.90, 8.78)
>47.6	4.23 (1.16, 15.93)

Discussion

- Lack of radio ownership a strong predictor of EVD risk at district level
  - Serial dramas and popular music used to disseminate risk communication
  - Requires further study
- Rainfall and EVD transmission risk
  - Roads become impassable with higher rainfall
  - Time series approach may be helpful
- Roadway and waterway densities as proxies for population mobility
  - High roadway density could decrease risk by improving accessibility
  - Artifact of measurement error?
- Slight protective association with population density
- Increased risk in more urban areas could reflect population mobility

Limitations & Conclusions

- Missing important predictors
- Measurement error
  - Remote sensing data
  - DHS estimates at regional level for Guinea
  - Mismatch of time period for different data sources
- Our work has shed new light on population-level factors for EVD transmission risk
  - Future work should examine causality
  - Role of radio requires further study and modifiable risk factor for future outbreaks
- Need higher spatial resolution data and other important predictors

Summary

- Need for quick analysis to inform public health action in EID situations
  - Balance of data and methodological quality
- Need for enhanced TSA applied to different diseases (or other methods?)
- Understand when spatial confounding could be an issue
- Causality…the goal but difficult to achieve with surveillance data
- Need more (bio)statisticians on editorial boards of public health journals

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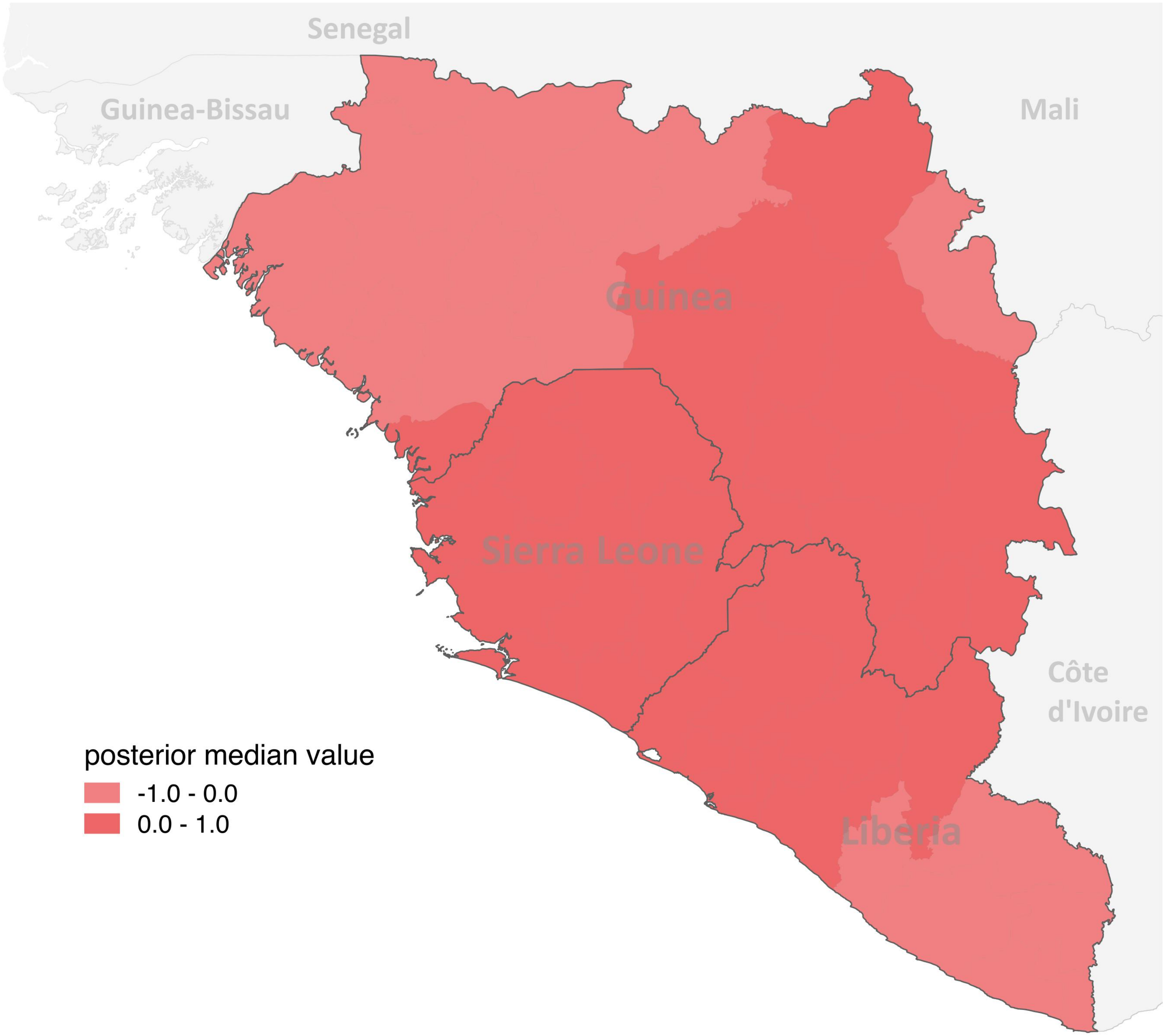
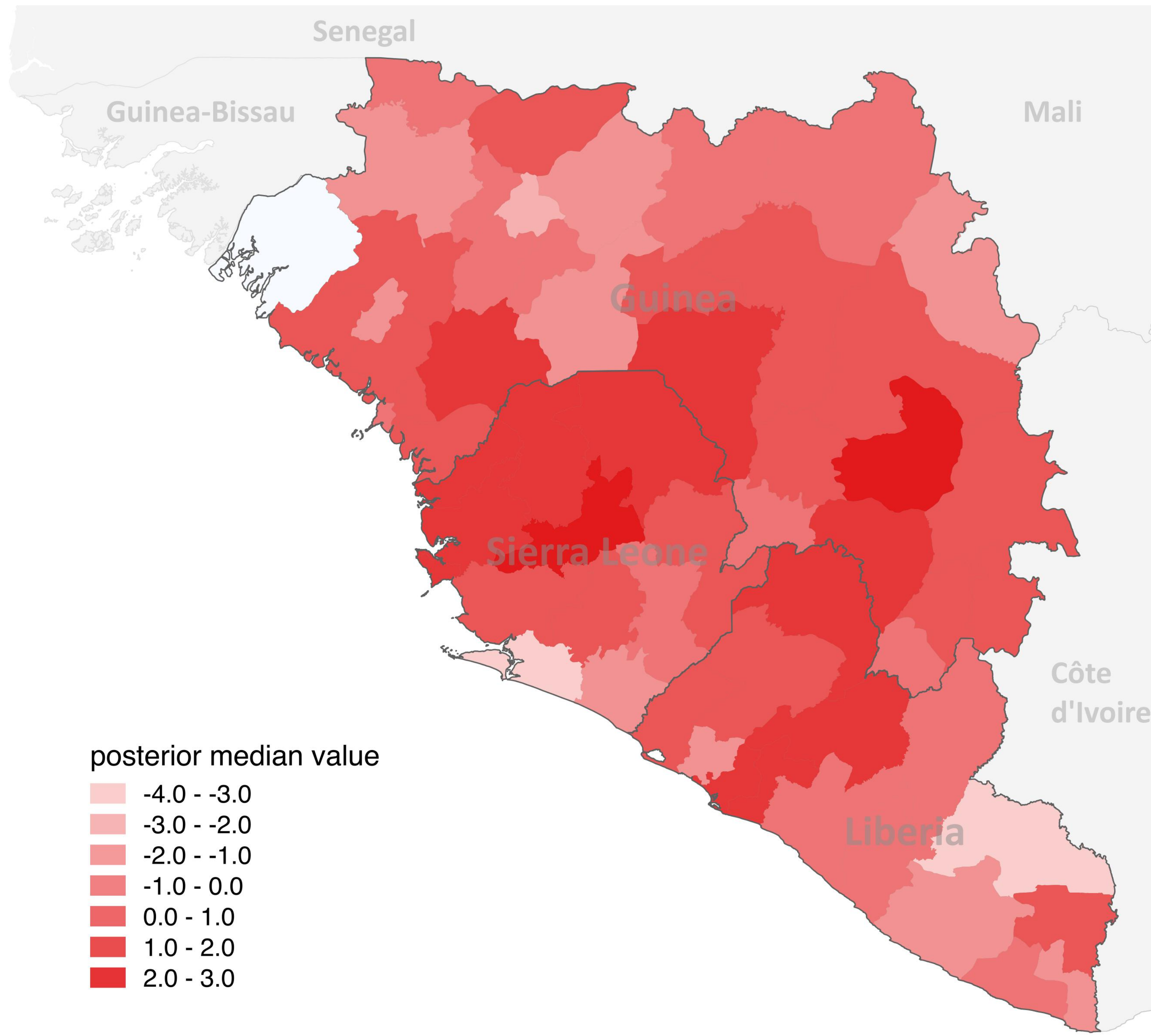
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

Photo credits from title slide

MSF staff carrying body of EVD victim: Seyllou/AFP/Getty Images
Ebola vaccine: Borgen magazine
Ebola virus: CDC



Senegal
Guinea-Bissau
Mali
Guinea
Sierra Leone
Côte d'Ivoire
Liberia
posterior median value
-1.0 - 0.0
0.0 - 1.0


Senegal
Guinea-Bissau
Mali
Guinea
Sierra Leone
Côte d'Ivoire
Liberia
posterior median value
-4.0 - -3.0
-3.0 - -2.0
-2.0 - -1.0
-1.0 - 0.0
0.0 - 1.0
1.0 - 2.0
2.0 - 3.0