Bayesian Spatial Analysis of Infectious diseases: models and metrics

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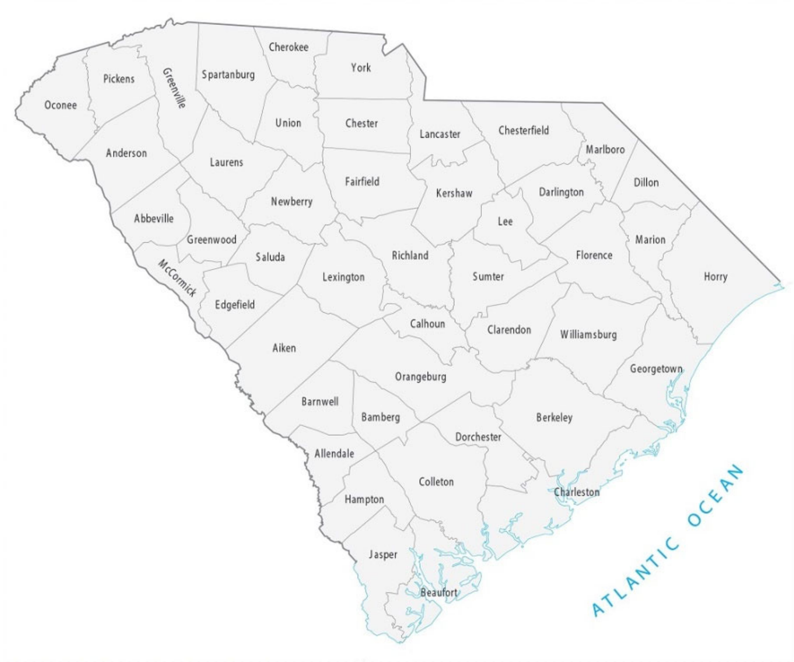
Acknowledgement

- Including collaborative work with Joanne Kim MUSC

Motivation: location

- SC state in USA
- 46 counties



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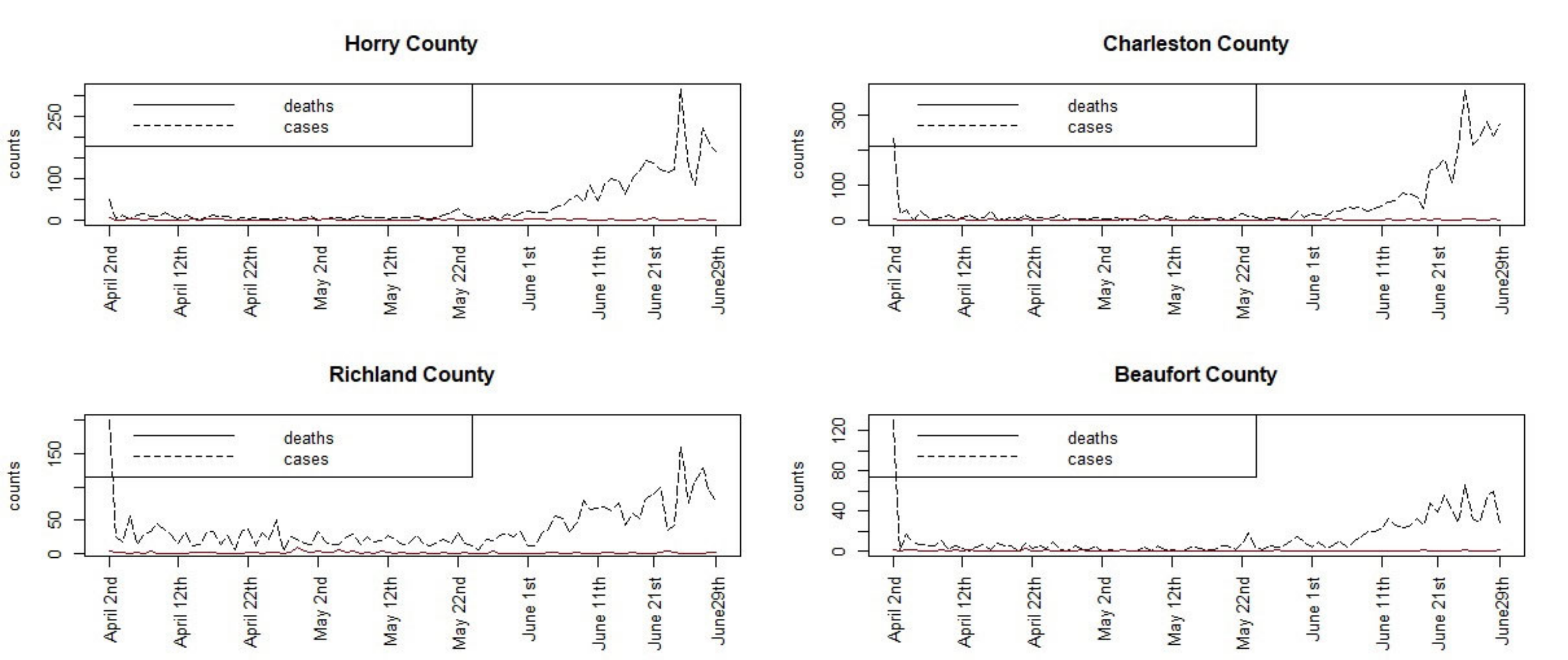
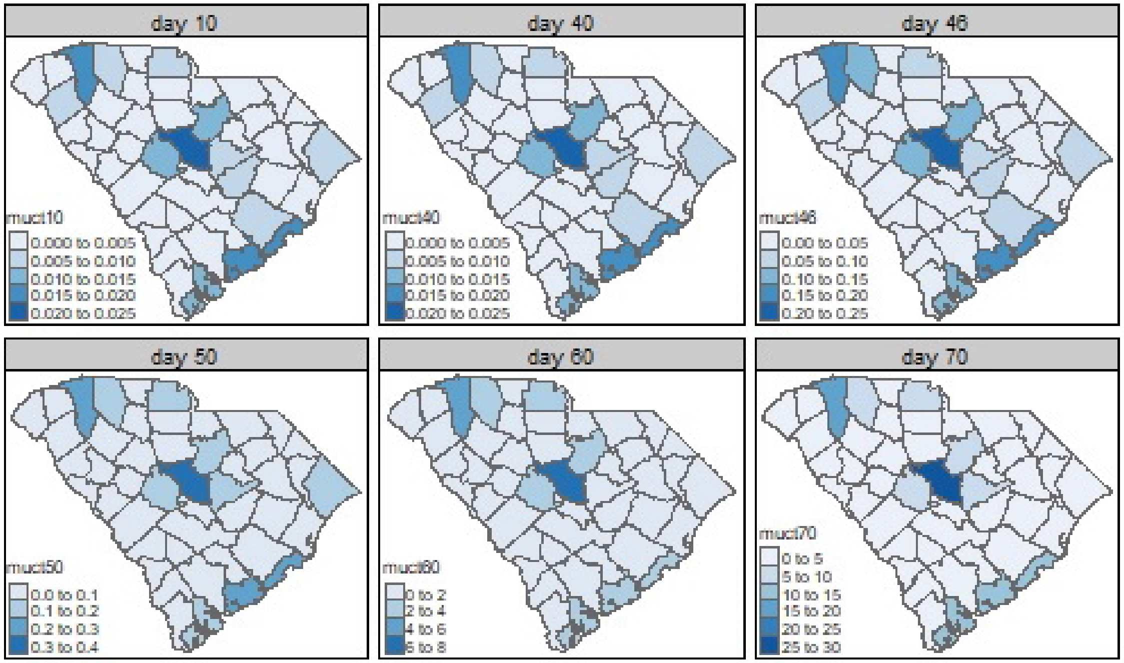
Motivation: Covid-19 in SC counties 2020: April 2nd – June 29th

- Dynamic Profiles
- 4 selected counties



Spatial background

- Modelled estimates of risk



Background

- Infectious disease models:
  - Descriptive
  - Mechanistic
- Descriptive models are usually random effect based
- Mechanistic models deal with transmission and are typically compartment models such as SIR or SEIR. They can be agent-based also.
- Individual or aggregate?

Individual models

- Classic susceptible-Infected-removed (SIR) models
- Differential equation models
- Difference versions can lead to lagged models
- R_0 is a function of coupled ODEs
- Often data is not available at the individual level in that observing all infected/removed could be problematic: under-ascertainment is common
- Very few epidemics where the complete realisation of the process is observed. (Hagelloch measles epidemic, **1861** is an exception)

Some assumptions

- Each person has independent risk of being infected

at *i* th location and time *j* with probability

$$p_{ij} = 1 - \exp\{-\lambda_{ij}\}$$
$$\lambda_{ij} = f(\text{susceptibility}, \text{closeness of infectives}, \text{contextual effects})$$

- Models for this probability can be constructed with likelihoods and hence the Bayesian paradigm is available.
- Usually models are based on contact distances in some way.
- Can also be contextual
- Examples are found in Deardon et al (2010) and elsewhere.

Aggregate count models

- Often counts of new infectives are more readily available.
    - Due to confidentiality concerns in human populations
    - Also stability concerns.
- Typical models assumed are:
    - Poisson in large populations with low probability of infection
    - binomial in finite populations
    - Poisson approximation is often adequate for SIR models
    - Negative binomial models are sometimes assumed to accommodated overdispersion. However these are not needed when using BHMs with a Poisson data model and random effects

SIR time series count models

- Morton and Finkenstädt (2005) Discrete time modelling of disease incidence time series by using Markov chain Monte Carlo methods. *Journal of the Royal Statistical Society* C, 54, 575-594 (M&F)
- A good example of time series modeling of measles outbreaks in London, UK. Assumes a SIR model where infective counts depend on previous infectives and susceptible pool.

Modelling constructs

- Transmission model
  - Observed new infectives at *i* th location and time *j* : y_{ij}
  - True infective count at *i* th location and time *j*: I_{ij}
  - Susceptible pool at *i* th location and time *j* : S_{ij}
  - Removal at *i* th location and time *j* : R_{ij}
- Accounting equation
  - Idealised

$$S_{ij} = S_{i,j-1} - I_{i,j-1} - R_{i,j-1}$$

Under-ascertainment

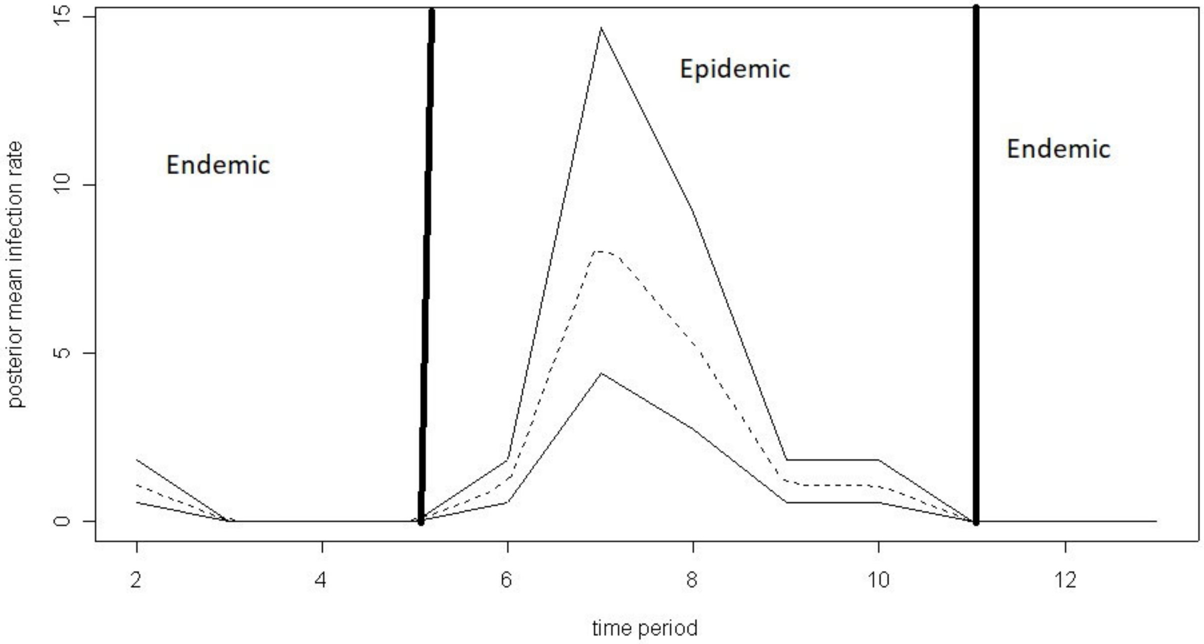
- Both true case count and true removal count could be under-ascertained
- The whole epidemic is seldom observed
- What to do?
  - Treat observed as the modelled data
    - Treat the true as a scaled version (simplest option)
  - Model the observed but estimate the true as a latent component (more complex and computationally difficult)
  - M&F assumed $y_{ij} \sim bin(\rho, I_{ij})$

Endemicity/Epidemicity

- For some disease there could be endemic behavior as well as epidemic.
- Endemicity occurs when a disease remains in the population but is not in an epidemic state
- Seasonal flu is slightly endemic (as some cases occur outside the main seasons)
- Outbreaks in the winter months represent an epidemic phase
- Models can be constructed where we have

$$E(y_{ij}) = \mu_{ij} = En_{ij} + Ep_{ij}$$

Endemic-Epidemic



Asymptomatic/Symptomatic

- With some viruses there can be asymptomatic and symptomatic cases (e.g. Covid19, typhoid)
- Confirmed tests of those with symptoms establish symptomatic case counts. Of course the degree of testing undertaken determines how many are found.
- Asymptomatic cases can infect others.
  - It is not clear how to assess these cases as they are not observed
  - Surveys of populations can yield proportions of asymptomatics, but these need to be repeated frequently. This is why wide spread testing in the Covid19 pandemic is important
  - In models the proportion of asymptomatics can be assumed known (but varied to assess effects).

Spatio-temporal modeling

- Mechanistic models are relevant
- SIR models are possible
- Here I describe an spatial extension of the M&F time series model, which allows for the spatial correlation and also neighborhood direct effects

Model structure I

$$y_{ij} \sim Poiss(\mu_{ij})$$

$$\mu_{ij} = S_{ij} f(y_{i,j-1};\boldsymbol{\theta})$$

S_{ij} are current susceptibles at start of time priod

$$\mathrm{S}_{ij} = S_{i,j-1} - I_{i,j-1} - R_{i,j-1}$$

Should $I_{i,j-1}$ be replaced by $y_{i,j-1}$?

- Can also use a binomial model if the sparseness is not too great

Model Structure II

- How is $f(y_{i,j-1};\boldsymbol{\theta})$ parameterised?
- Different models could be envisaged
  - Direct dependence on previous counts
  - Neighborhood dependence
  - Also dependence on predictors such as population density or % under the poverty line
  - Addition of spatially-structured noise? ICAR ?

SC Flu season county data

- Some previous work on the 2004 Flu season in SC led to an extension of the M&F model with spatial structure.
- Lawson and Song (2010) Bayesian hierarchical modeling of the dynamics of spatio-temporal influenza season outbreaks *Spatial and Spatio-temporal Epidemiology*, 1, 187-195 (L&S)
- Data: biweekly influenza C+ lab notifications
  - 13 periods
  - Iceberg effect

Flu models: Model I

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

- Model assumes that the observed count is a proportion of the true infectives
- The true infectives depend on the previous true infective count

Flu models: Model II

- Accounting model

$$
\begin{aligned}
&I_{ij} \sim Pois(S_{ij} f(I_{ij-1})) \\
&S_{ij+1} \sim N(\mu_{ij+1}, \sigma_s{}^2) \\
&\mu_{ij+1} = S_{ij} - I_{ij} - R_{ij} \\
&R_{ij} \sim N(\beta I_{ij}, \sigma_R{}^2)
\end{aligned}
$$

Simpler version: Model 2

$$
\begin{aligned}
&I_{ij} \sim Pois(\pi_{ij}) \\
&\pi_{ij} = S_{ij} f(I_{ij-1})) \\
&S_{ij+1} = \mu_{ij+1} \\
&\mu_{ij+1} = S_{ij} - I_{ij} - R_{ij} \\
&R_{ij} = \beta I_{ij}
\end{aligned}
$$

Model 2

- How to parameterize the dependence on the previous infectives?

$$\log \pi_{ij} = \log S_{ij} + \log f(I_{ij-1})$$

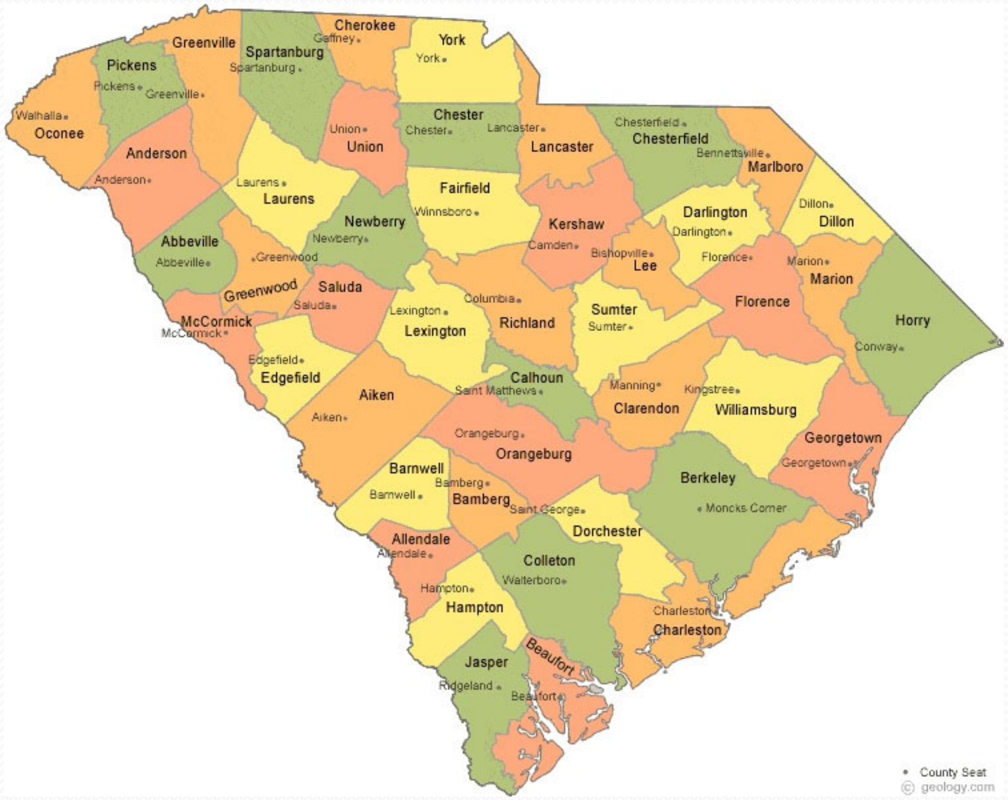
Dependencies

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

$$OR$$

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

SC counties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Chesterfield
Lancaster
Anderson
Bennettsville
Marlboro
Anderson
Laurens
Laurens
Fairfield
Winnsboro
Darlington
Darlington
Dillon
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Newberry
Newberry
Kershaw
Camden
Abbeville
Abbeville
Greenwood
Bishopville
Lee
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Marion
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Saluda
Saluda
Columbia
Lexington
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Richland
Sumter
Sumter
Florence
Horry
McCormick
McCormick
Conway
Edgefield
Edgefield
Calhoun
Saint Matthews
Manning
Clarendon
Kingstree
Williamsburg
Aiken
Aiken
Orangeburg
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Georgetown
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Barnwell
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Bamberg
Bamberg
Berkeley
Moncks Corner
Saint George
Dorchester
Allendale
Allendale
Colleton
Walterboro
Hampton
Hampton
Charleston
Charleston
Beaufort
Jasper
Ridgeland
Beaufort
County Seat
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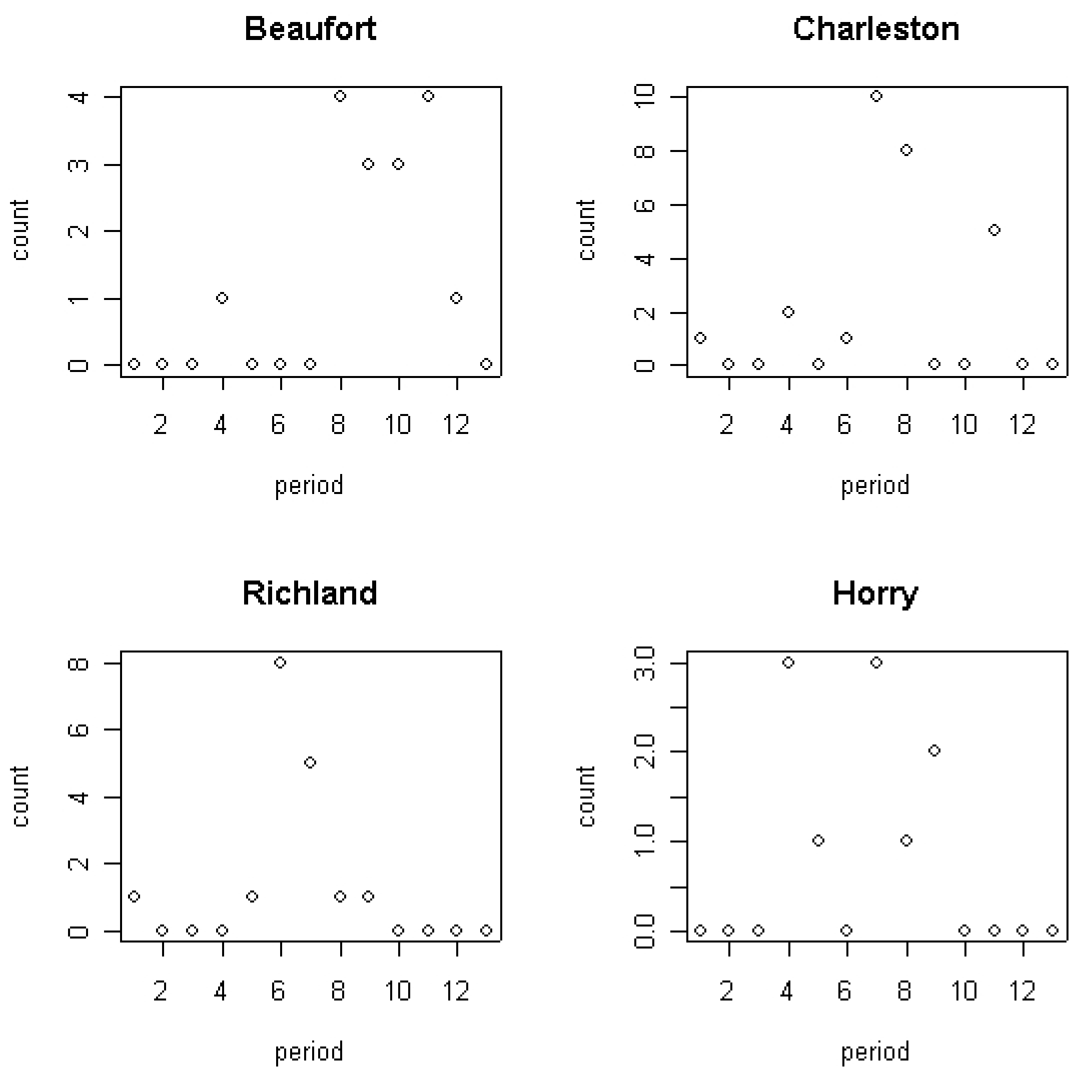
Data: 4 counties



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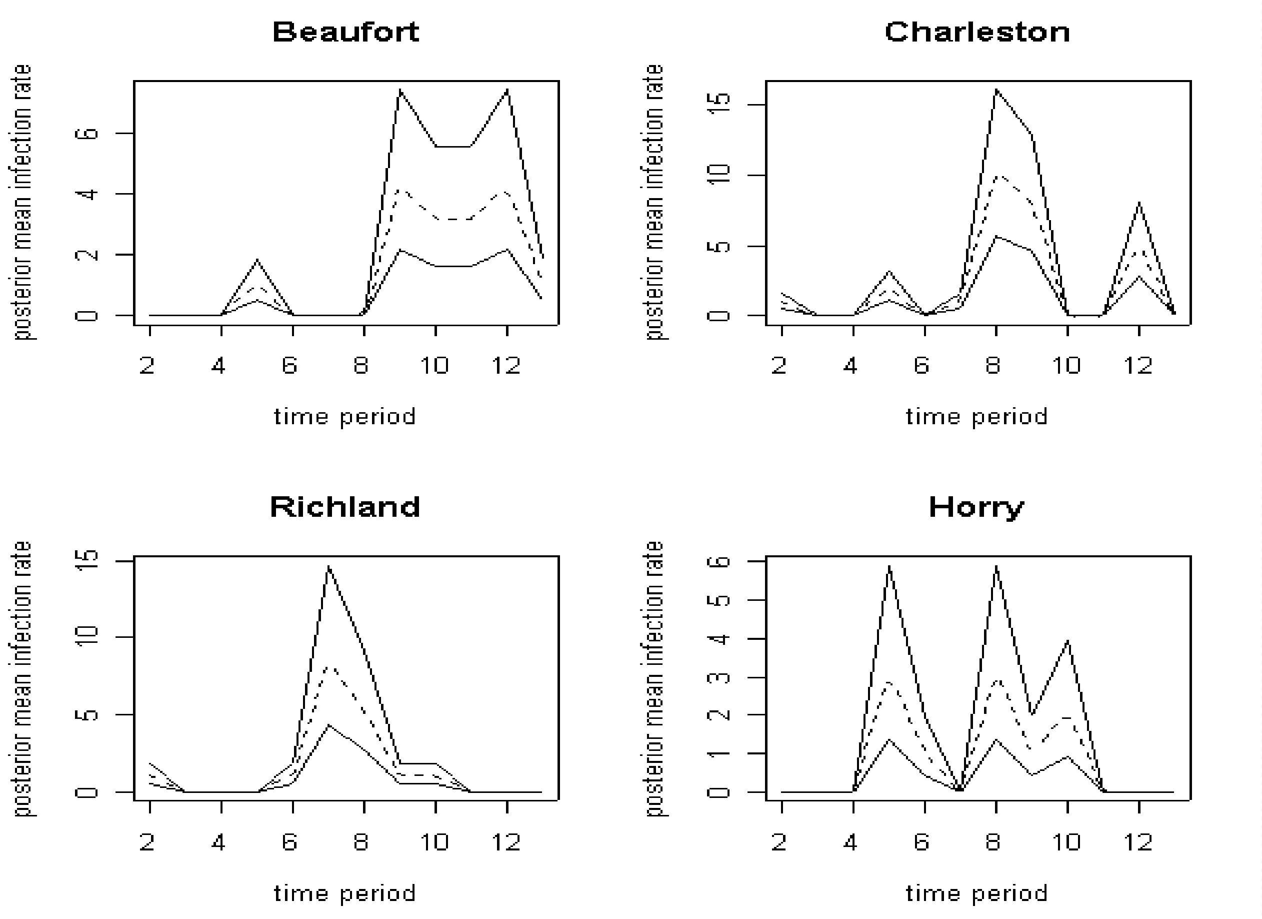
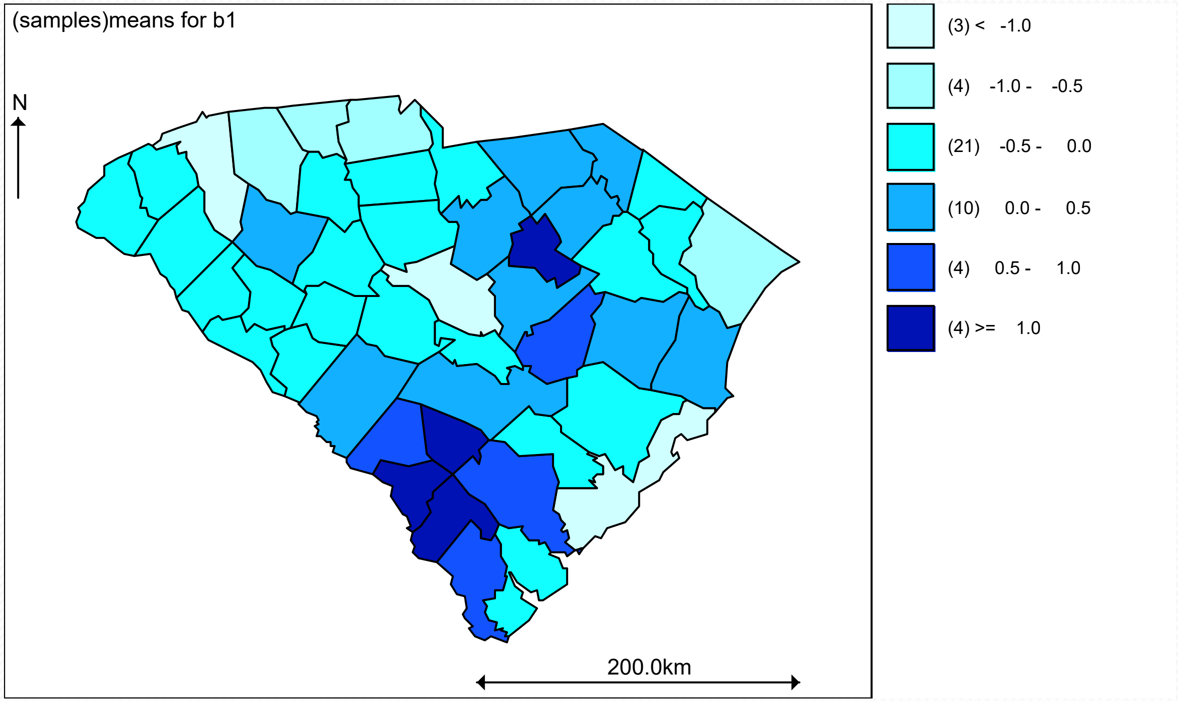
Results: posterior mean risk profiles



Spatial heterogeneity: model 1



Covid19 in South Carolina

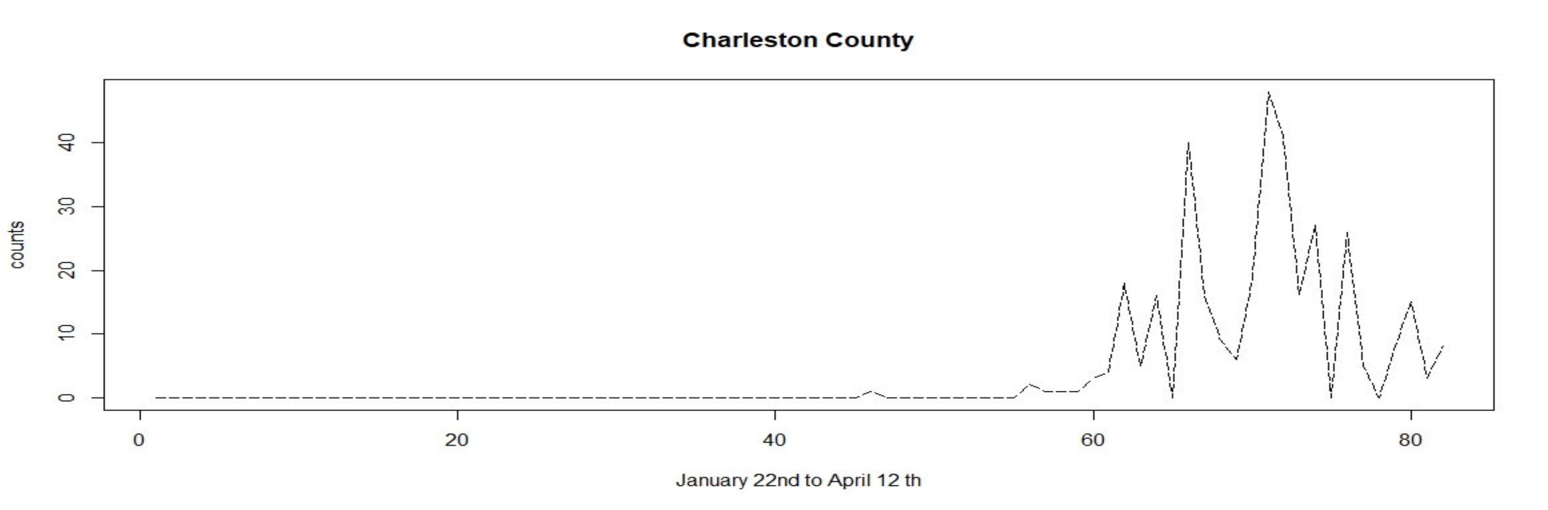
- Covid19 virus has gripped the world since late 2019.
- It is now a pandemic and few areas are unaffected
- Both cases and deaths are being recorded in various countries
- Scale is an issue: publicly available data is at province /state, county level but not below, although post codes are reported routinely on web sites.
- Individual level data is not publicly available right now

Aggregate data

- In the US both Johns Hopkins GitHub site and the New York Times site have county level daily cases and deaths.
- The JHU site is a amalgam of 10 different sources
- NYT site is based on National Center for Health Statistics (NCHS) US deaths data and case data from state health departments, and is well documented
- We have tried to use the JHU data but it is not well documented
- The NYT data seems to be more stable and well doucmented.

SC county level daily data

- Daily data on new cases
- Daily data on deaths
- Starting in January 2020
- Data from January 22nd to April 12th



Cases and Deaths

- Reporting issues
  - Cases: under-reporting as only severe symptoms in most cases are tested (symptomatic cases)
    - Asymptomatic not reported
    - Symptomatic under-ascertained
  - Cumulative count reporting errors:
    - Misallocation to wrong county
    - Testing
  - Deaths: only hospital Covid19 deaths recorded (initially) and also serious under-reporting especially in care homes.

Models

- Approach:
  - Assume that there is no endemic component (as yet!) and so we only have a propagator model coupled to accounting equation for symptomatic (*sym*) cases
  - Asymptomatics (*asym*) are largely unknown and so we either estimate the latent component or use scaling
  - As new infections must be a function of sym and asym

we must include both in any dependence model

Covid19 county level models

- Cases

$$sym_{ij} \sim Pois(\mu_{ij})$$

$$\mu_{ij} = S_{ij} f(sym_{i,j-1}, asym_{i,j-1}, \text{predictors, spatial confounding})$$

$$S_{ij} = S_{i,j-1} - I_{i,j-1} - R_{i,j-1}$$

where $I_{i,j-1}$ is the total case load

R_{ij} current removal (death, recovery)

- Asymptomatic assumed a proportion of symptomatic

Specific model components

- A variety of model variants have been run but the results cited here are for the following setup.
  - asym is 25% of sym
  - ICAR model assumed as spatial confounder
  - % under poverty line included as predictor
  - Removal consists recovered (0.1 of sym) and deaths
  - Best model found using DIC comparisons
  - Weakly informative gamma priors assumed for precisions

Models examined

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

$$2)\log f(I_{ij-1}) = b_0 + b_1 \log[I_{ij-1} + \sum_{l \in \delta_i} I_{lj-1}]$$

$$3)\log f(I_{ij-1}) = b_0 + b_1 \log I_{ij-1} + b_2[\%Pov] + b_i$$

$$4)\log f(I_{ij-1}) = b_{0j} + b_1 \log I_{ij-1} + b_2[\%Pov] + b_i$$

$$5)\log f(I_{ij-1}) = b_{0i} + b_1 \log I_{ij-1} + b_2[\%Pov]$$

DICs and a variant

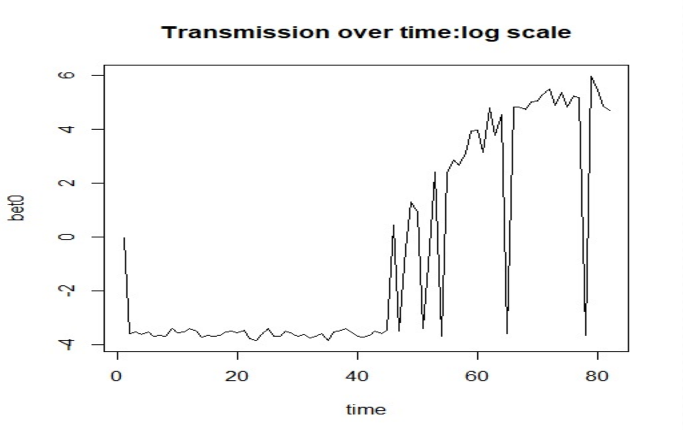
Model	DIC	pD (using SD(Dev)/2		
1	19449.2	72.16		
2	10,321,293.0	2499.6		
3	19431.0	55.99		
4	14327.2	122.74		*
4b	15057.6	36.97	minus ICAR	
5	19454.9	75.34		

Model 4 results

- Parameter estimates

Parameter	Posterior mean	SD
b1	-0.834	0.0088
b2	-0.699	0.0166

- b0



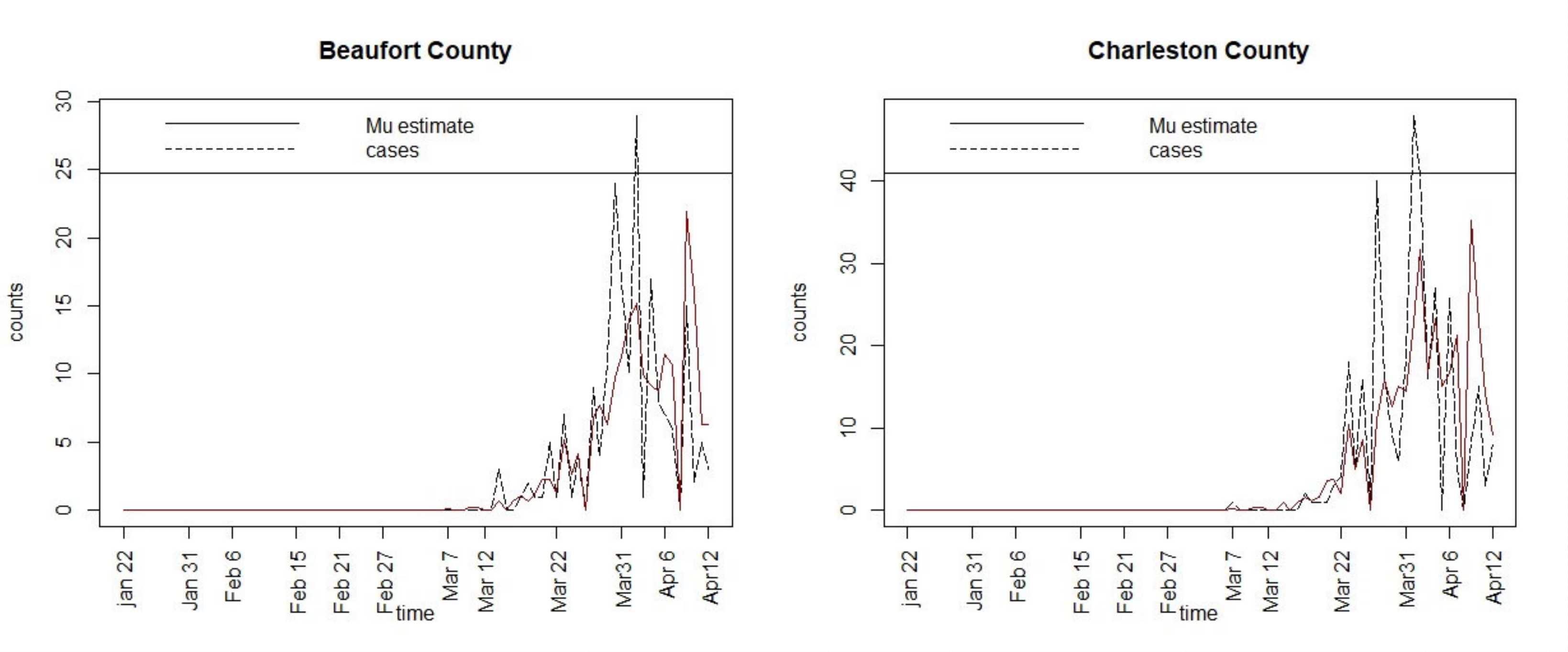
Key dates

- March 7th first case in Kershaw county SC
- March 12th WHO declares Pandemic
- March 13th SC state of emergency declared
- March 14th schools closed
- March 18th restaurants closed
- March 31st non essential businesses closed

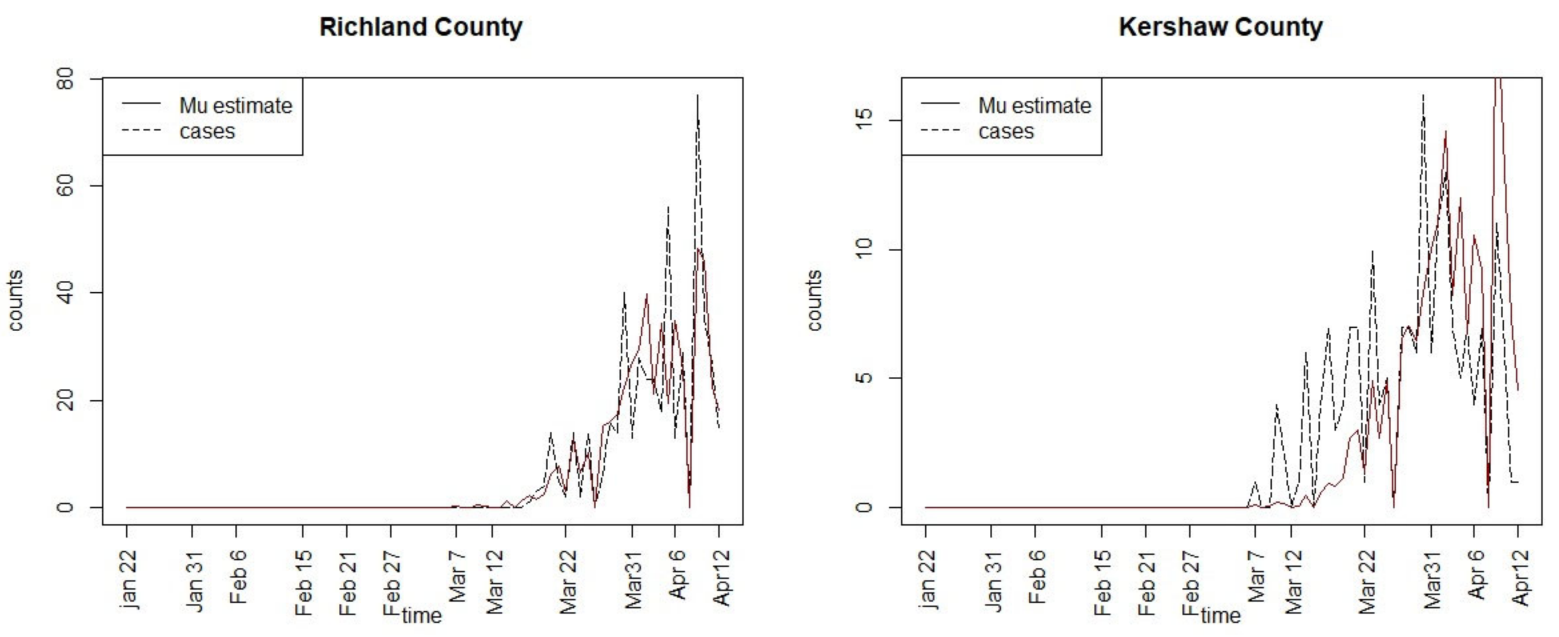
- April 6th stay at home order (lockdown)

- April 24th some lifting…some businesses opening
- May 1st lifted…open air restaurants open
- May 11th dining inside restaurants allowed
- May 12th stay at home order lifted

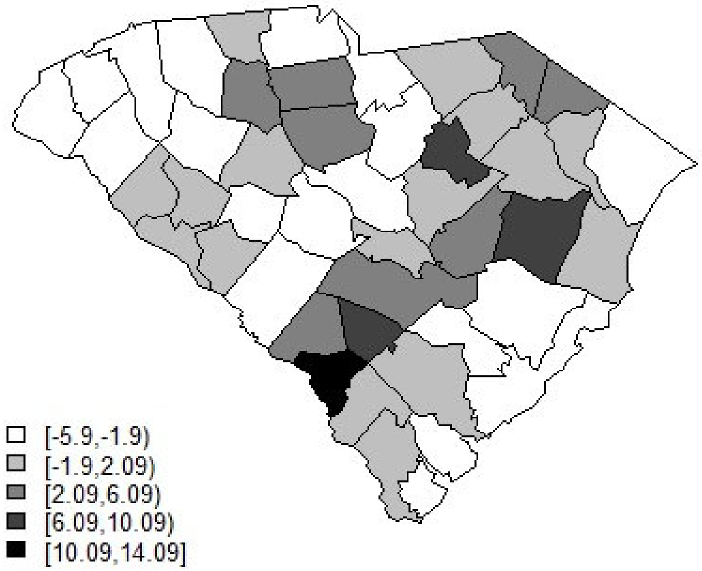
Posterior mean time profiles



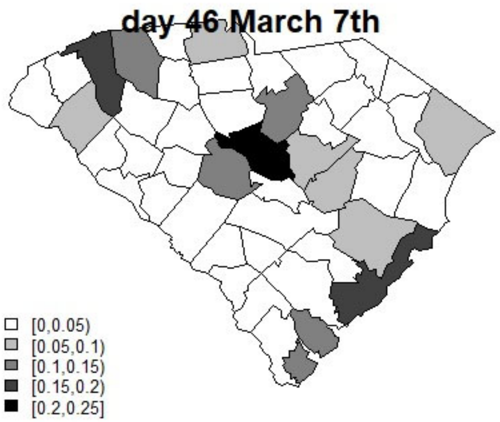
Posterior mean time profiles

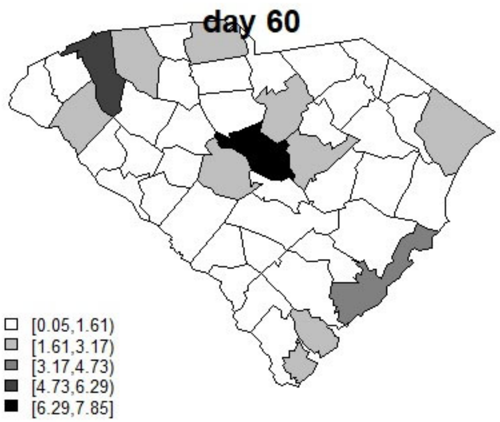


Spatial confounding: ICAR component

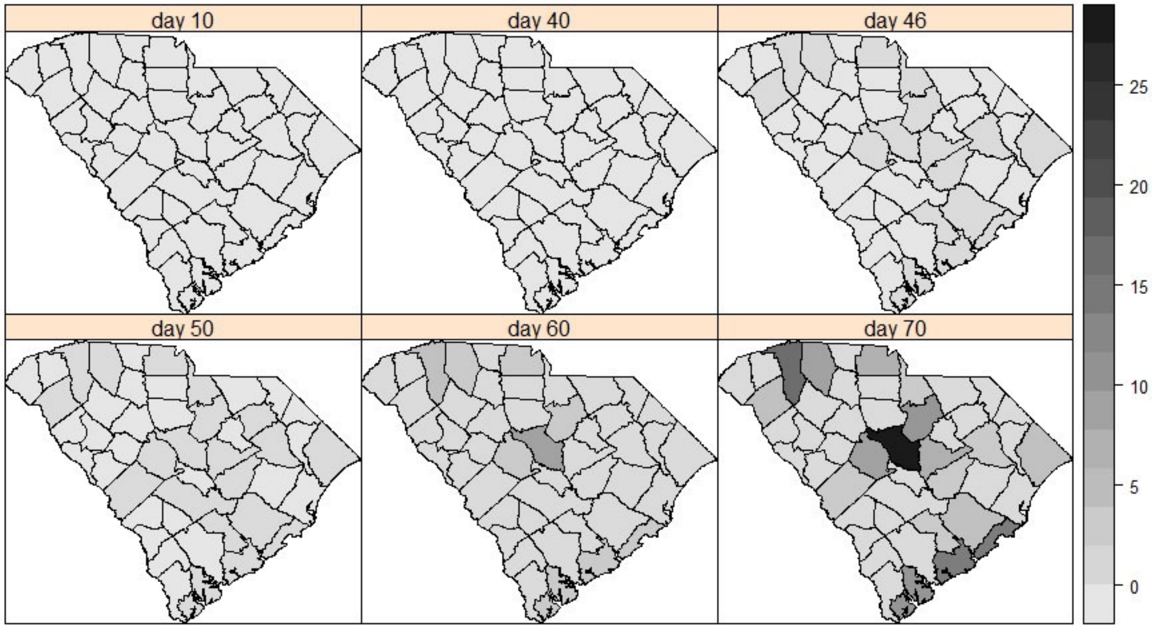


Posterior mean level maps: day 46 and 60





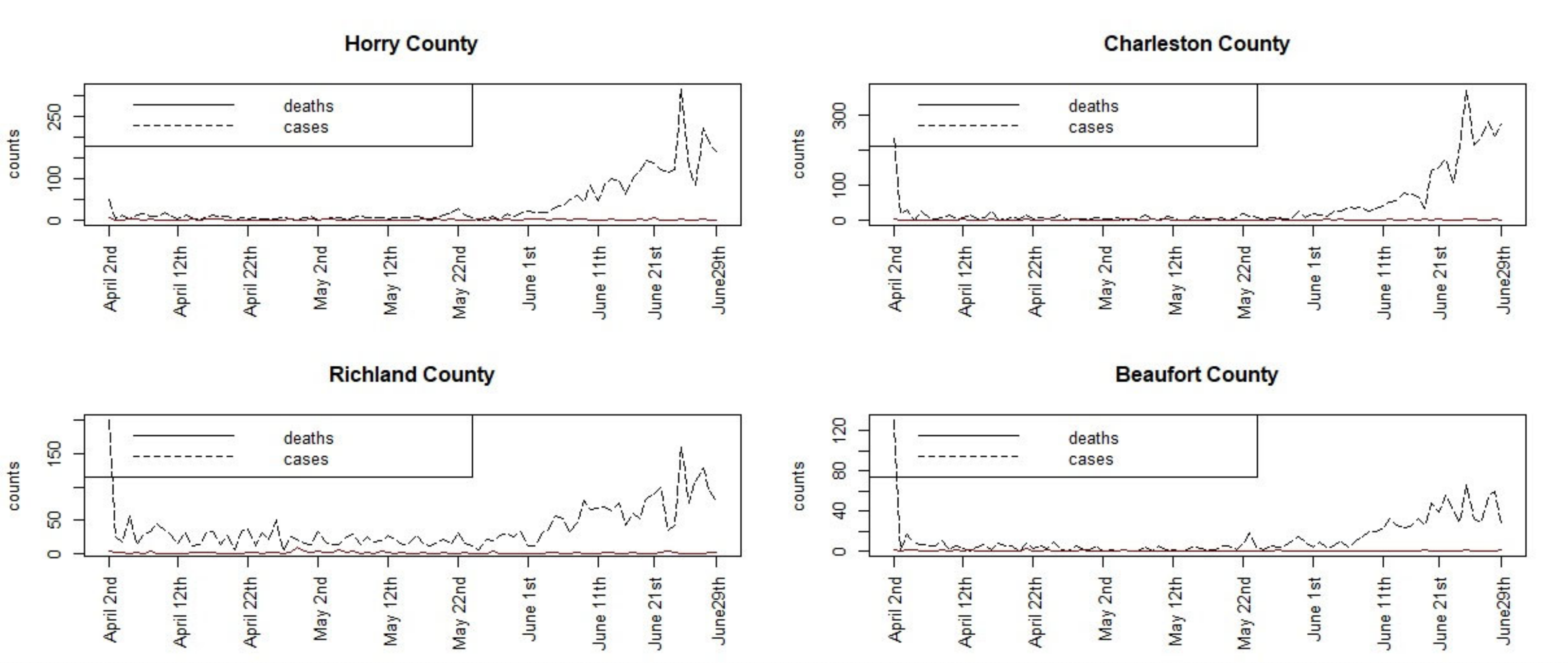
Sequence of posterior maps



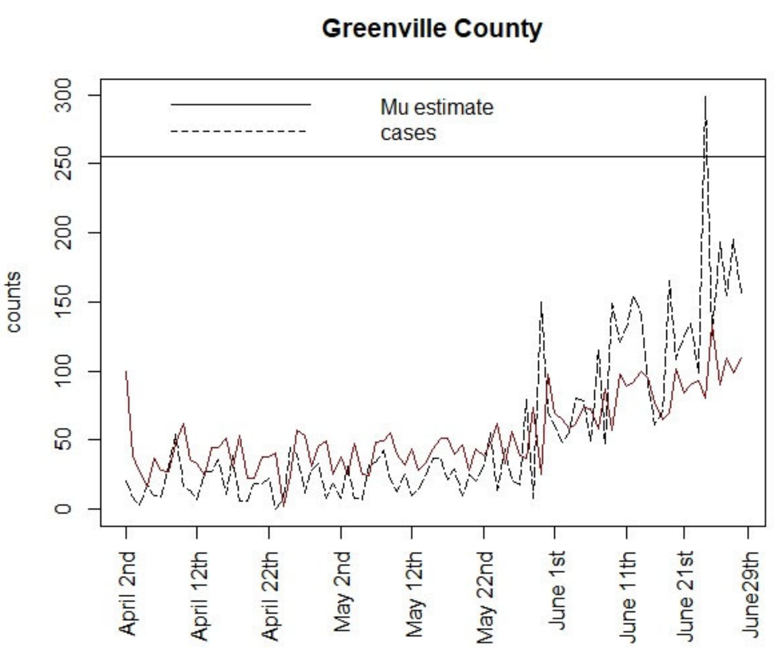
Later Periods and smoothed data

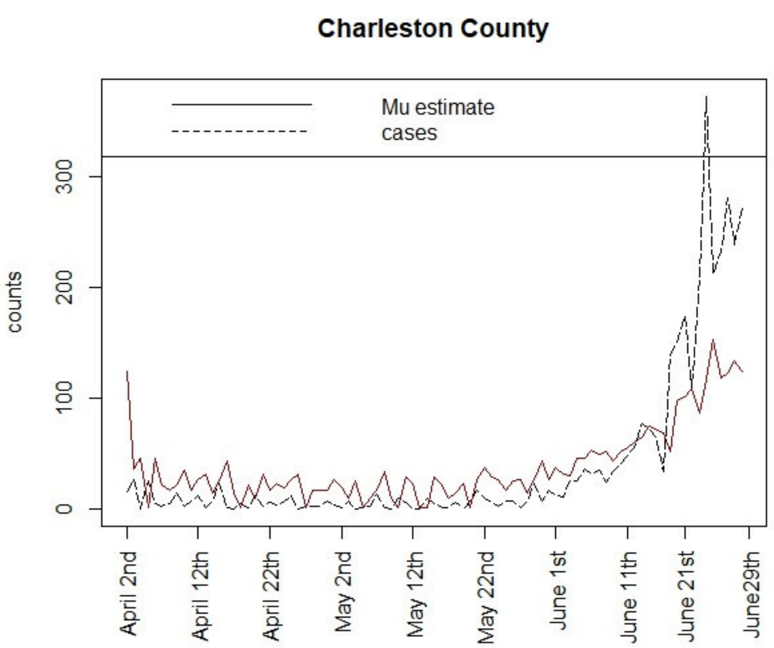
- A second period from April 2nd to June 29th was observed which included the second wave.
- Data for both periods were also subsequently smoothed using a 3 day smoothing.
- One step prediction was also enabled.
- Similar models were fitted to these additional data
- Model 3 with % poverty and spatial ICAR effect had best GOF

Second wave: April 2nd – June 29th

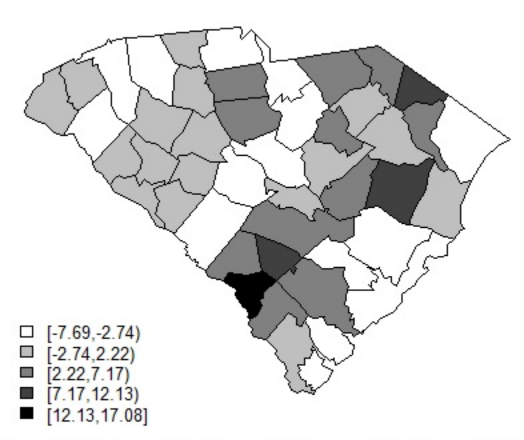


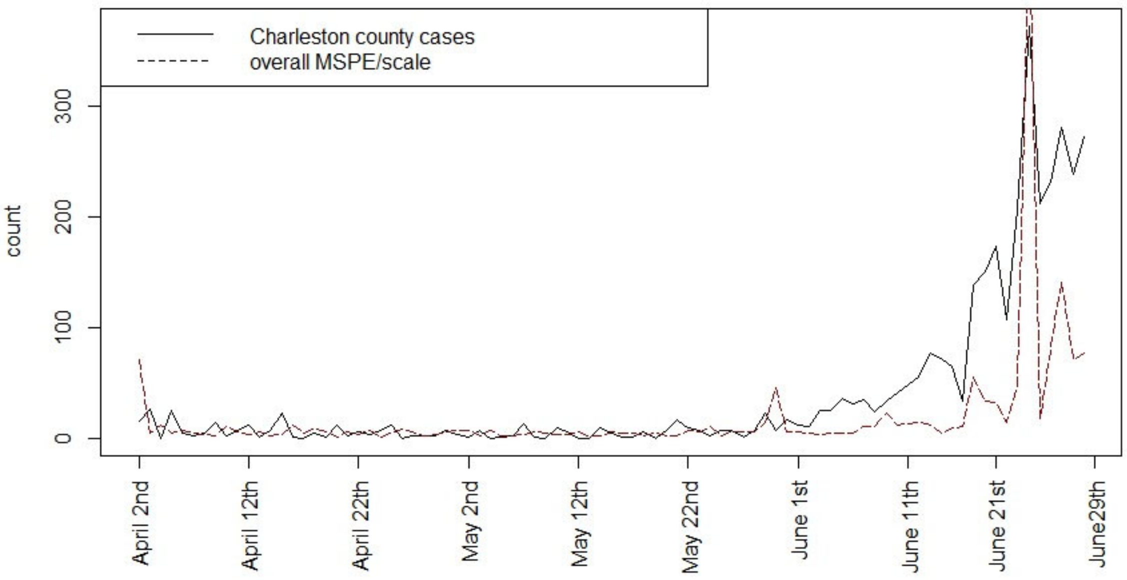
Model 3 estimates : second period



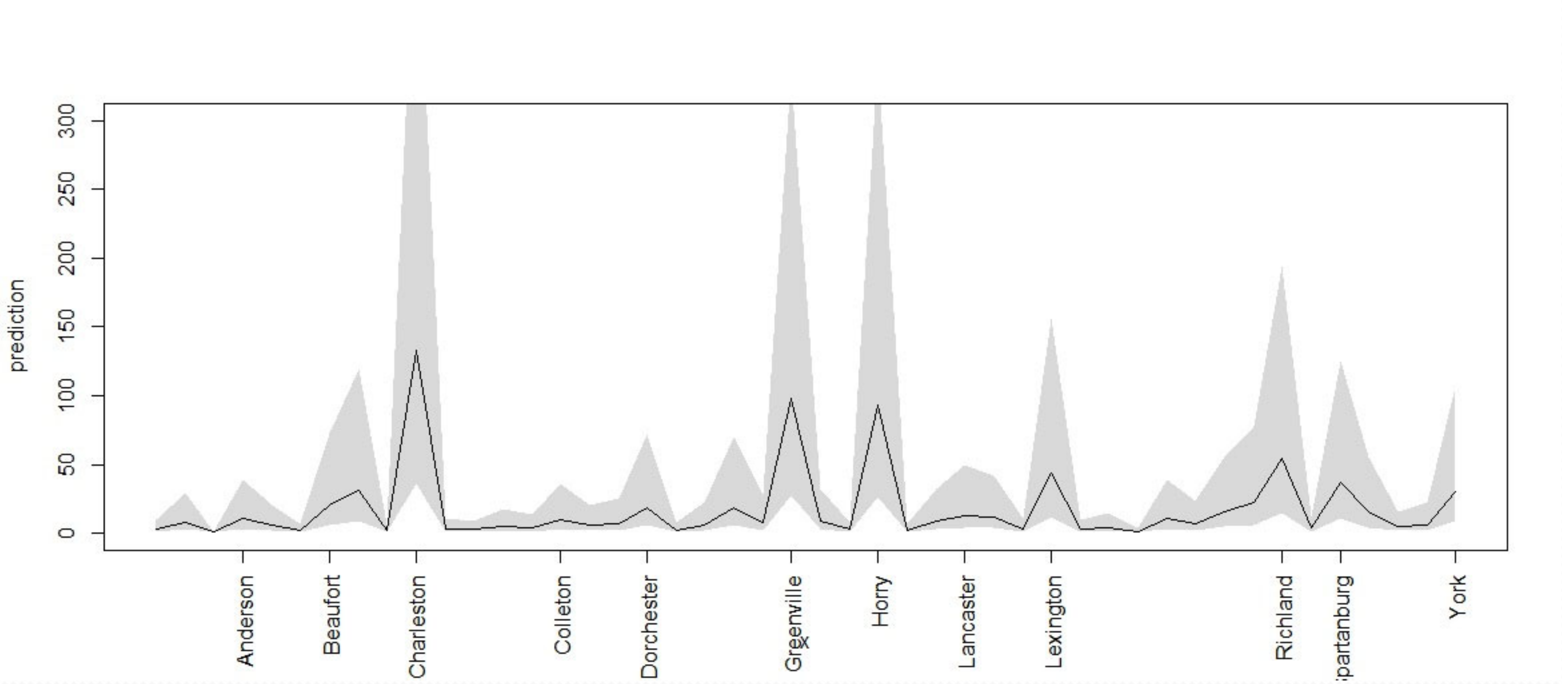


Spatial ICAR effect and MSPE for Charleston county

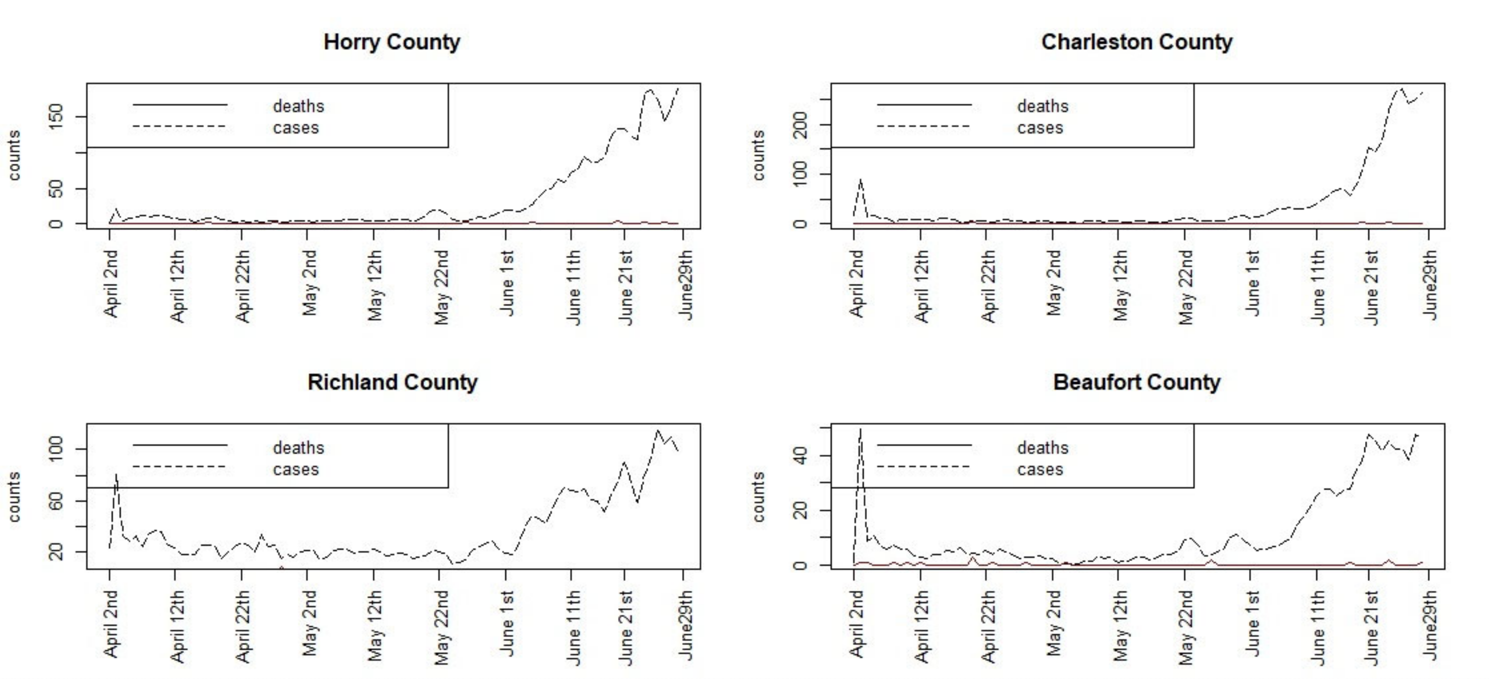




Prediction: one step June 30th



Smoothed Data (3-day average)



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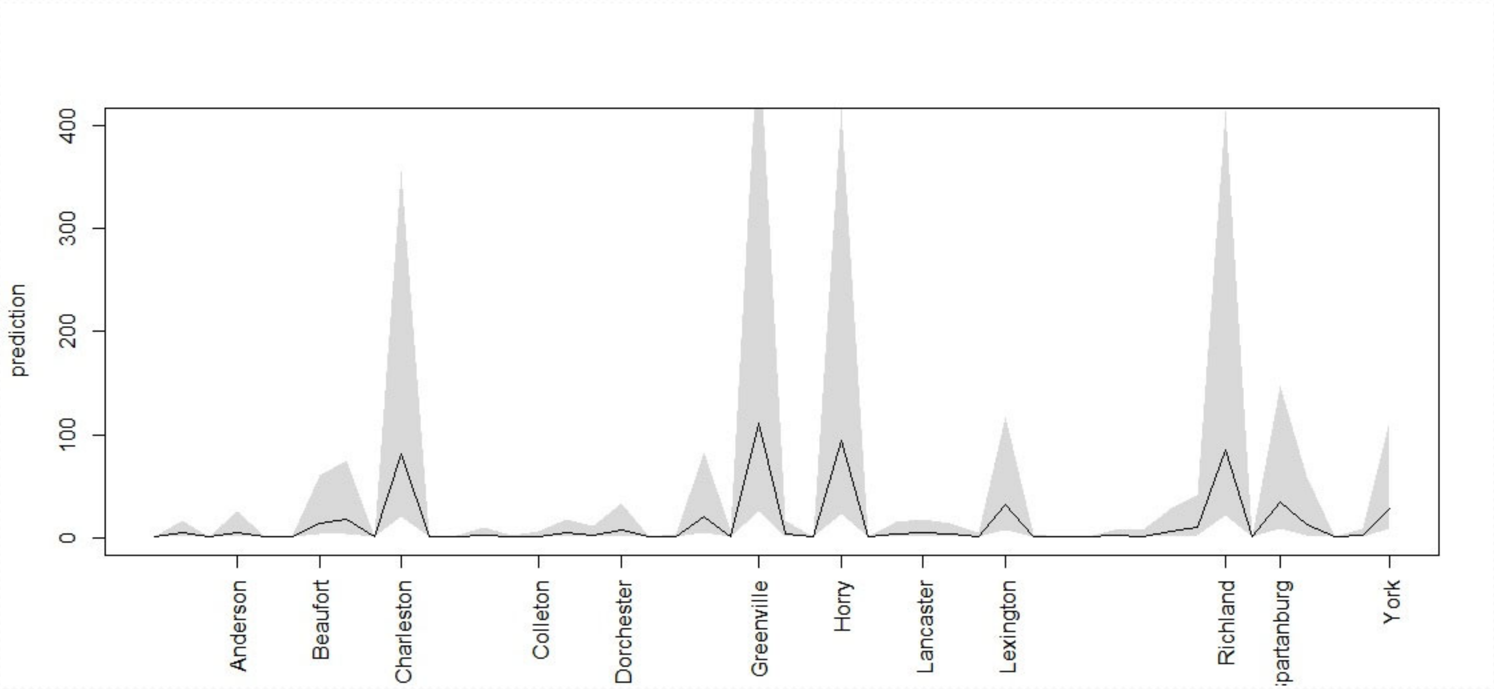
Model results smoothed data



Comments

- SIR/SEIR Bayesian models can be estimated retrospectively for epidemic situations
- Some accounting for biases (weekends, county switches, underascertainment, asymptomatics) can be made via smoothing, scaling and asymptomatic modeling
- Death modeling could also be added as a joint model with lags
- Predictions can also be made
- Deprivation is a major factor in all best Covid-19 models

Paper

- Lawson, A. B. and Kim, J. (2021) Space-time Covid-19 Bayesian SIR Modeling in South Carolina
- https://www.medrxiv.org/content/10.1101/2020.11.03.20225227v1
- https://doi.org/10.1101/2020.11.03.20225227
- Accepted for PlosOne

NYT site

- https://www.nytimes.com/interactive/2020/us/coronavirus-us-cases.html
- Github repository: https://github.com/nytimes/covid-19-data

Prediction and Surveillance

- A suitable retrospective model could be used for prediction but is not necessarily the best for surveillance
- Prediction is about getting close to true risk
- Surveillance is about detecting changes in risk

- Predictive distribution is useful for prediction within the observed data, and approximate prediction in the future
- However the confidence in prediction obviously decreases the further into the future moved.
- Better to have predictive evolving scenario so that data is incorporated as it arrives (prospectively)

Surveillance and metrics

- Surveillance models are often not optimal for retrospective studies
- Alternatively, the best fitting model for space-time retrospective data is not necessarily the best for detection of change.
- Imagine a situation where we have endemic and epidemic scenario, so that

$$E(y_{ij}) = En_{ij} + Ep_{ij}$$

where

$$Ep_{ij} = \alpha_0 + \alpha_1 p_{i,j-1}$$

and the propagator is $p_{i,j-1}$

Retrospective/Prospective

- A good retrospective model could have all the ingredients needed in En_{ij}
- For example we could have a descriptive RE ST model of the form

$$E(y_{ij}) = En_{ij} = \mu_{ij} = e_{ij}\lambda_{ij}$$

$$\log(\lambda_{ij}) = \alpha_0 + v_i + u_i + \gamma_j + \psi_{ij}$$

- However this could be too adaptive in time (!)
- We don’t want to model out the changes.

Detection of Change

- May want to detect $p_{i,j-1}$
- OR the existence of dependence via α_0, α_1
- One approach simply tests for positivity of these parameters
- Another approach uses metrics to detect changes
  - this is similar to the approach in quality control where processes are being monitored for compliance
  - In the disease case the monitoring has to be more sophisticated and account for at risk population.

Metrics

- A variety of measures are commonly employed to assess capabilities of models. E.g.
  - Predictive capability.....how well does the model predict the data and the future data (mspe, pmse,.......)
  - Residual deviation......using residuals to assess change
    - Bayesian predictive and surveillance residuals (see e.g. Vidal Rodeiro and Lawson (2006) Monitoring Changes in Spatio-temporal Maps of Disease. *Biometrical Journal*, 46,3,463-480)
- Metrics are posterior functionals that are intended to detect changes prospectively.

- Two different metrics have been proposed for Bayesian small area online monitoring
  - SCPO: Surveillance conditional Predictive Ordinate
  - SKL: Surveillance Kullback-Leibler measure

SCPO

- The SCPO is defined, for an MCMC sample of size G, as

$$SCPO_{ij} = \frac{1}{G}\sum_{g=1}^{G} Pois(y_{ij} \mid e_{ij}\lambda_{i,j-1}^{g})$$

- It is the average probability of the current data, given the previous time period's posterior sampled risk.
- If the SCPO is close to 1 then the data is closely predicted
- Often $1 - SCPO_{ij}$ is used for detection

SKL

- Kullback-Leibler divergence measures have two forms

and often the two are added together to give a total values: TSKL

- KL divergence is designed to assess differences in probabilities

$$p_1 = \sum_g Pois(y_{i,j}; e_{i,j}\lambda^{g}{}_{i,j-1}) / G$$

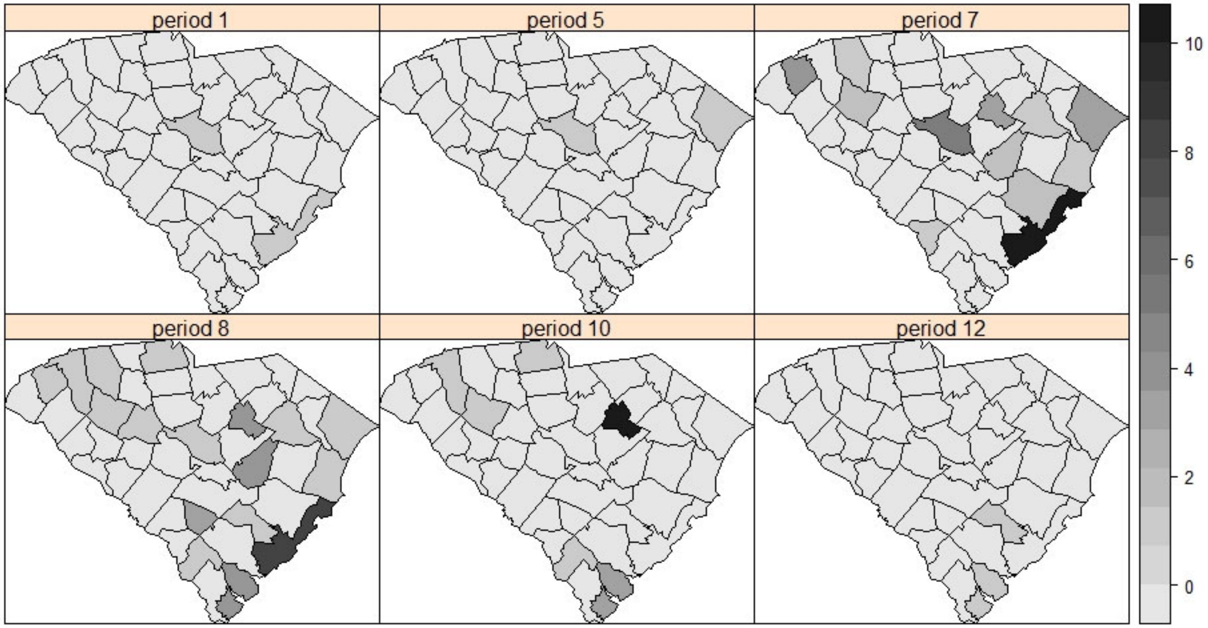
$$p_2 = \sum_g Pois(y_{i,j-1}; e_{i,j-1}\lambda^{g}{}_{i,j-1}) / G$$

$$skl_1 = p_1 \log\left(\frac{p_1}{p_2}\right);\ skl_2 = p_2 \log\left(\frac{p_2}{p_1}\right)$$

$$Tskl = skl_1 + skl_2$$

SC Flu season 2004-2005

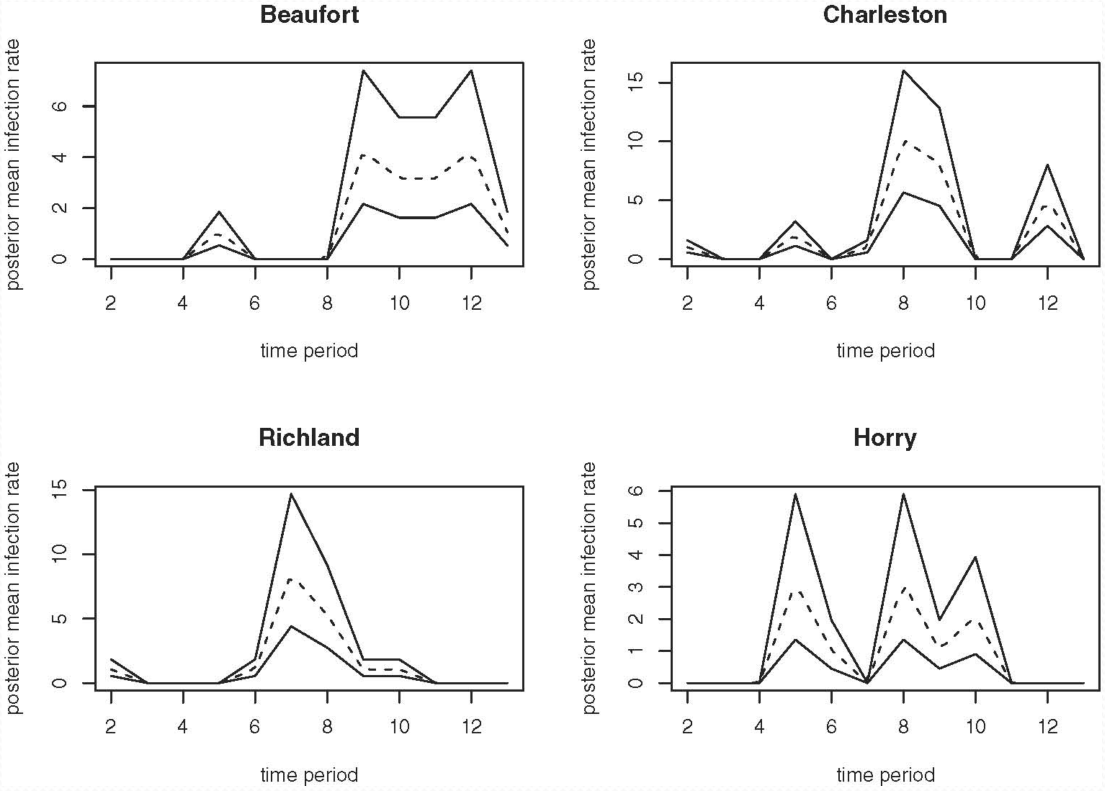
- County level C+ notifications (counts)
- 13 biweekly periods
- 46 counties



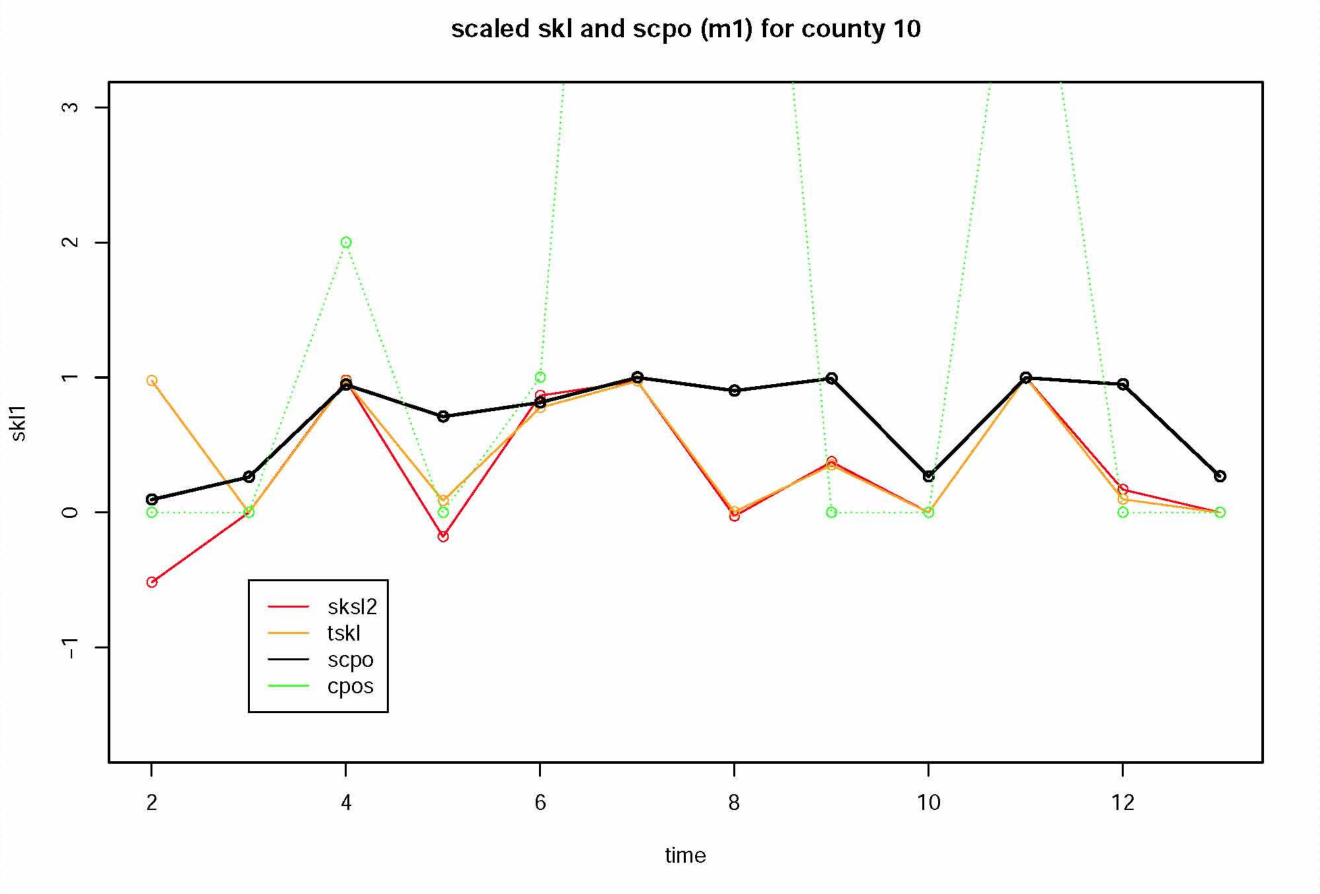
Some examples

- SC flu season 2004-2005
- County level
- Posterior mean risk

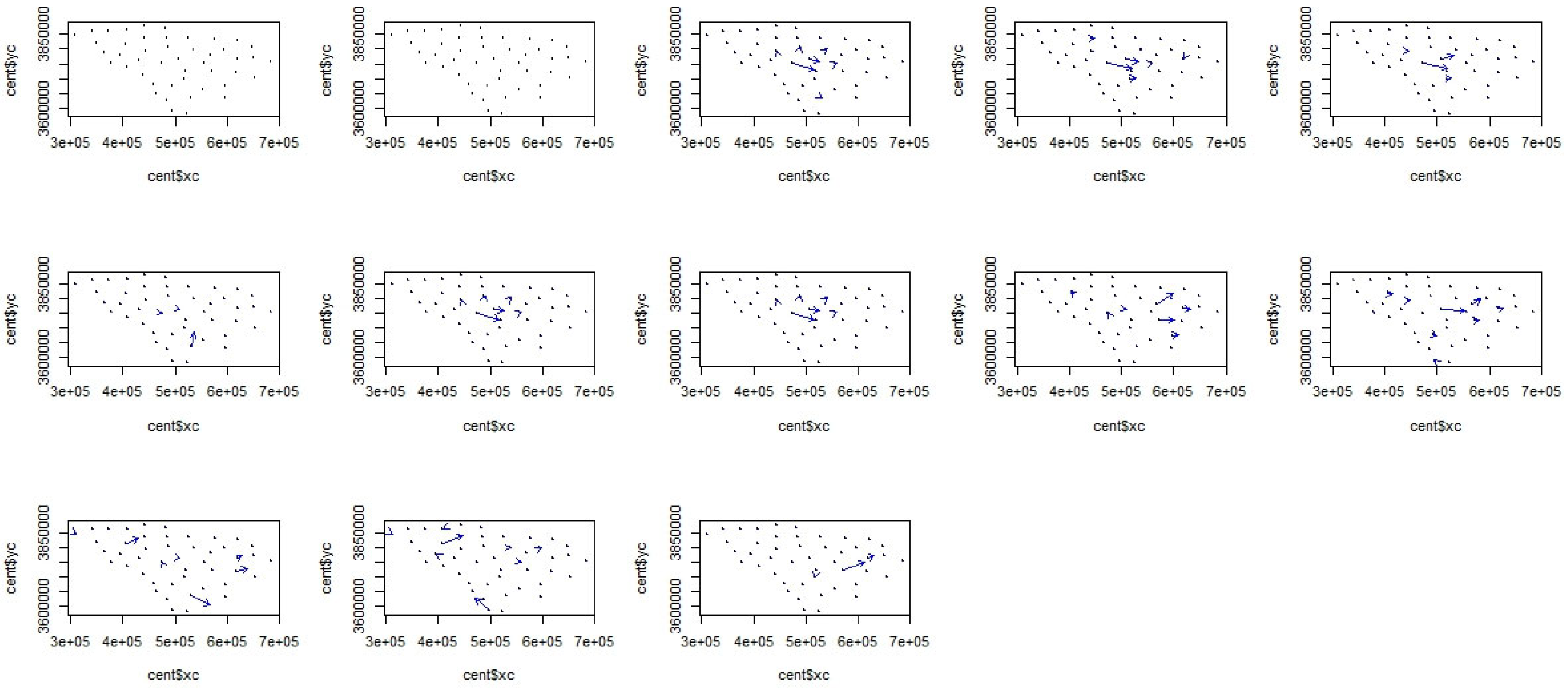
and 95 %credible intervals



Charleston county example



Directional potential modeling



Conclusions I

- Bayesian models can provide a range of tools for helping in the task of epidemic modeling and surveillance
- Descriptive models are limited in their predictive capabilities
- Endemic-epidemic models are a good avenue to pursue
- Lagged dependency models, which are approximations to difference equations, can fit reasonably well to daily respiratory infection data (e. g. Covid-19)

Conclusions II

- Infection rates can be estimated, neighborhood dependence and residual spatial effects can be included
- Predictors can be included also: % under poverty line was a significant correlate with infection risk.
- Metrics can be used to detect the start of epidemics and also their duration or termination
- Much work is needed in the calibration and tailoring of metrics for multivariate spatial data streams: a truly big BIG data application in public health.

References

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Thank you