Detecting changes in dispersion in COVID-19 case counts using a negative binomial model

JSM 2024

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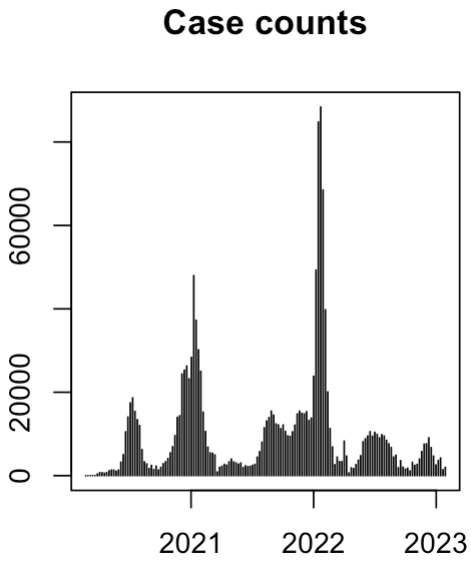
Why study variability?



- Highly variable case count time series suggest transmission heterogeneity or changes in R

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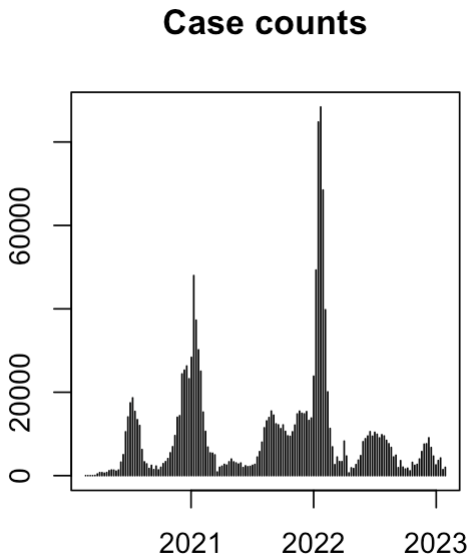

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- Metrics of variability are overlooked: "How is variability related to different phases of an epidemic?" [2]

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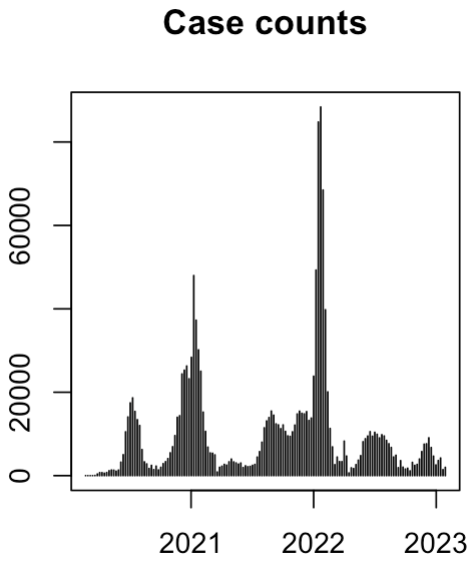

- Highly variable case count time series suggest transmission heterogeneity or changes in R
- Metrics of variability are overlooked: "How is variability related to different phases of an epidemic?" [2]
- Adam et al.[1] found that COVID-19 transmission heterogeneity decreased over time

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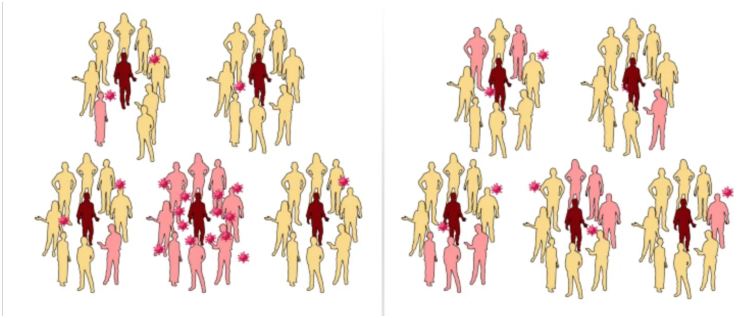
Why study variability?

- Dispersion of a case count time series may be a useful metric–part of a framework that models variance flexibly



[5]

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Why study variability?

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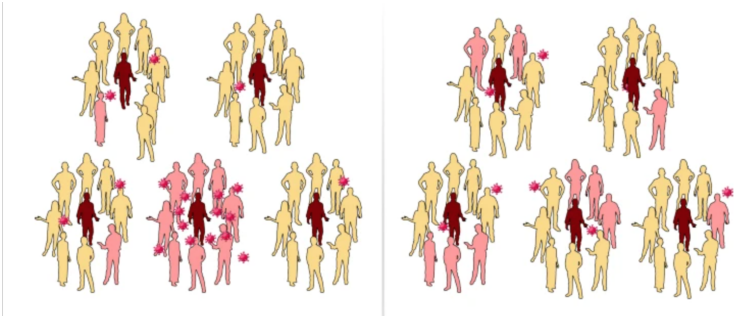

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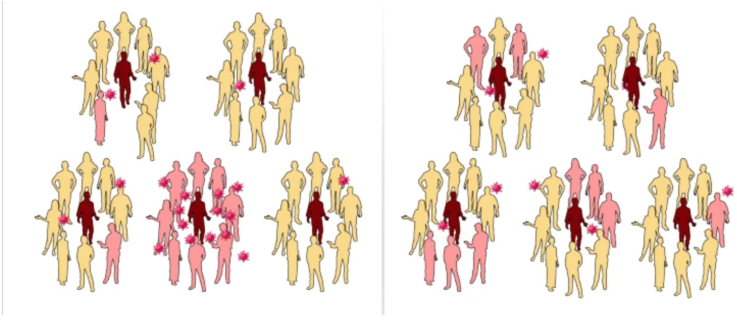
- Useful way to think about dispersion in case count time series, degree of dispersion is degree of clustering/crowding of cases



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- Let λ_t be epidemic intensity at time t, I_t be incidence at time t, and θ_t be dispersion at time t

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- Linear predictor includes a natural spline in time to account for autocorrelation in case counts

$$log(E[Y_i]/n_i) = \beta_1 h_1(t_i) + \beta_2 h_2(t_i) + \beta_3 h_3(t_i) \quad (2)$$

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- Model fit on a rolling basis to each time series

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Negative binomial model

- $$f_t(I) = \binom{I + \theta - 1}{I} \left(\frac{\mu}{\mu + \theta}\right)^I \left(\frac{\theta}{\mu + \theta}\right)^\theta \quad (5)$$

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Negative binomial model

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- $$E(I) = \mu \tag{6}$$
$$Var(I) = \mu + \frac{\mu^2}{\theta} \tag{7}$$

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- LRT framework: at each time step along a time series, fit null model and θ change model, conduct LRT to produce p-value

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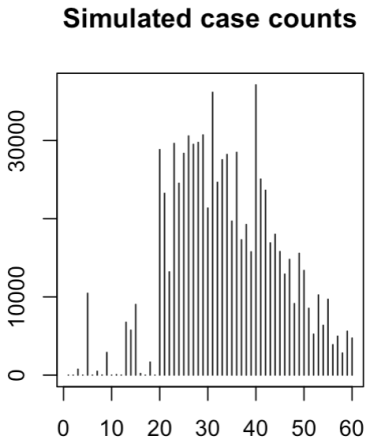
Simulated time series data set



- Validity/power simulations: Gaussian and uniform epidemic curves with an attack rate of 0.1

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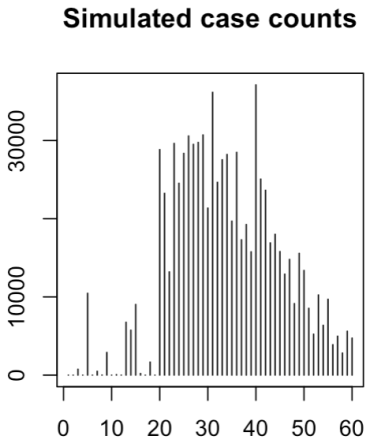

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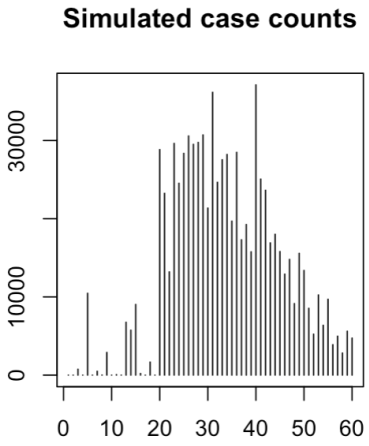

- Validity/power simulations: Gaussian and uniform epidemic curves with an attack rate of 0.1
- Varied magnitude of θ change, location of the change, underlying population size, and epidemic curve shape
- Epidemic curves over 60 time steps each were produced, and the LRT procedure was applied to each

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Performance: simulated data

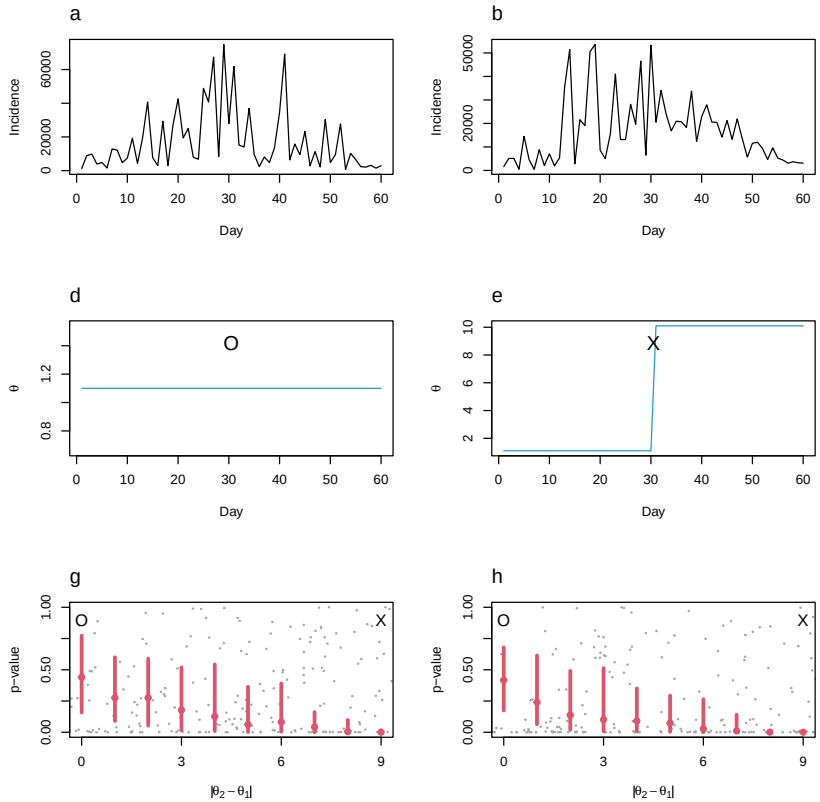

Figure 1: Detecting dispersion changes in incidence time series. A/B: Simulated incidence when dispersion is constant/changes. C/D: Constant/changing dispersion used above. E: Performance of LRT with simulated data that has different absolute differences in theta (x-axis of each pane) illustrates p-value distribution across different population sizes. O and X mark the null and alternative hypotheses indicated in panels C and D.

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Application to empirical data

- Weekly case counts from US counties between 2020-01-04 and 2023-03-18

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- Weekly case counts from US counties between 2020-01-04 and 2023-03-18
- Estimated θ_t for 154 time steps for 144 US counties (IRLS procedure implemented via the NBPSeq package[7] and from Di et al.[6])

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Application to empirical data

- Weekly case counts from US counties between 2020-01-04 and 2023-03-18
- Estimated θ_t for 154 time steps for 144 US counties (IRLS procedure implemented via the NBPSeq package[7] and from Di et al.[6])
- Investigated large counties (largest three counties in each state)

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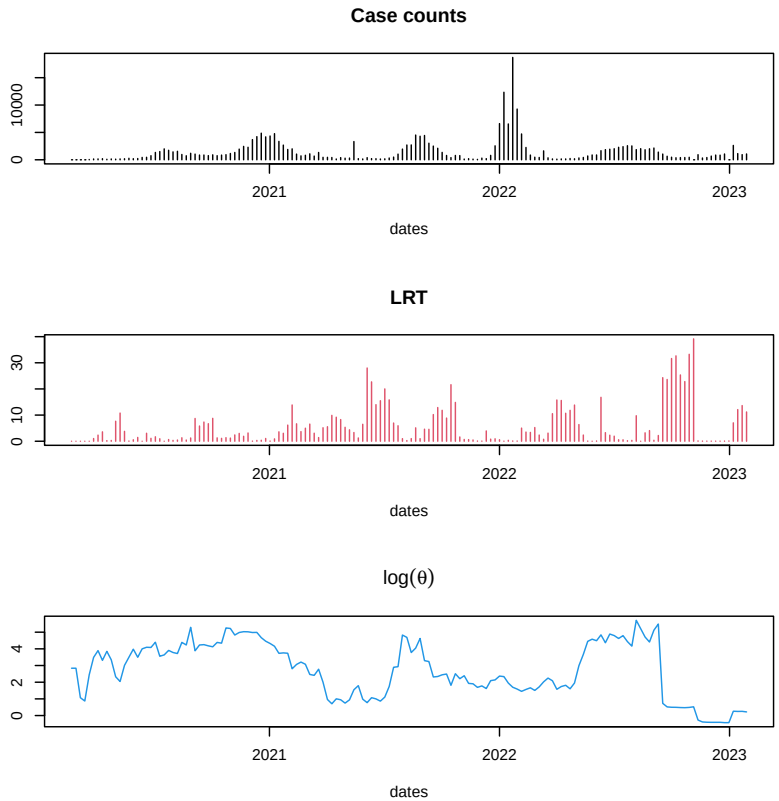

Figure 2: Method applied to case counts between 2020-01-04 and 2023-03-18 for Jefferson County, AL. A: Case counts . B: LRT statistic C: Log dispersion parameter.

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Results: empirical data

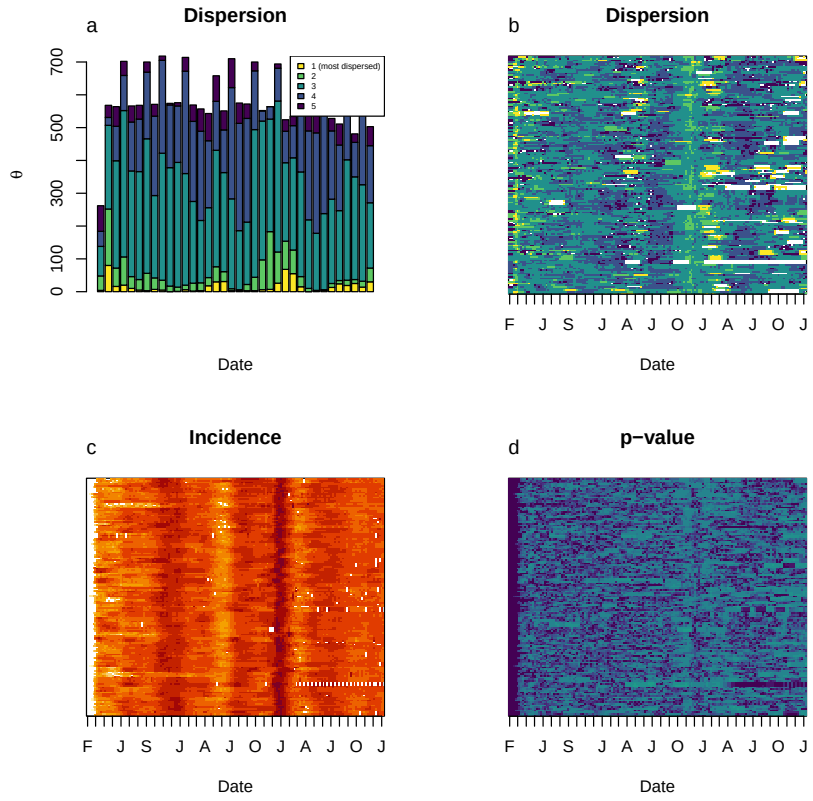

Figure 3: Incidence and dispersion in large counties in the US. A: Binned log of the dispersion parameter. B: Log of the dispersion parameter for each of the large counties (y-axis). C: Log incidence for each of the large counties (y-axis). D: LRT p-values for each of the large counties (y-axis).

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Concluding remarks

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- LRT procedure performed well for relevant range of population sizes
- Dispersion is high at unexpected times (near peak incidence)
- Concentration of changes in dispersion parameter near peak incidence
- Methods that use population-level data are important: timing/allocation of public health resources can be achieved with limited resources

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[1] Dillon Adam et al. *Time-varying transmission heterogeneity of SARS and COVID-19 in Hong Kong*. Tech. rep. ISSN: 2693-5015 Type: article. Mar. 2022.

[2] Matthew Graham et al. "Measles and the canonical path to elimination". en. In: *Science* 364.6440 (May 2019), pp. 584–587. ISSN: 0036-8075, 1095-9203.

[3] Bryan T. Grenfell, Ottar N. Bjørnstad, and Bärbel F. Finkenstädt. "Dynamics of Measles Epidemics: Scaling Noise, Determinism, and Predictability with the TSIR Model". In: *Ecological Monographs* 72.2 (2002). Publisher: Ecological Society of America, pp. 185–202. ISSN: 0012-9615.

[4] Monte Lloyd. "'Mean Crowding'". In: *The Journal of Animal Ecology* 36.1 (Feb. 1967), p. 1. ISSN: 00218790.

[5] Bjarke Frost Nielsen, Kim Sneppen, and Lone Simonsen. "The counterintuitive implications of superspreading diseases". en. In: *Nature Communications* 14.1 (Oct. 2023), p. 6954. ISSN: 2041-1723.

[6] Di Yanming et al. "The NBP Negative Binomial Model for Assessing Differential Gene Expression from RNA-Seq". In: *Statistical Applications in*

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Thanks!

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