Bayesian Spatio-Temporal Modelling of Disease Incidence with Nonignorable Missingness

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Oregon State University

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The Motivating Principle

CDC's CORE Commitment to Health Equity

CDC works to ensure health equity is embedded in an all-of-public health approach.

Learn More >

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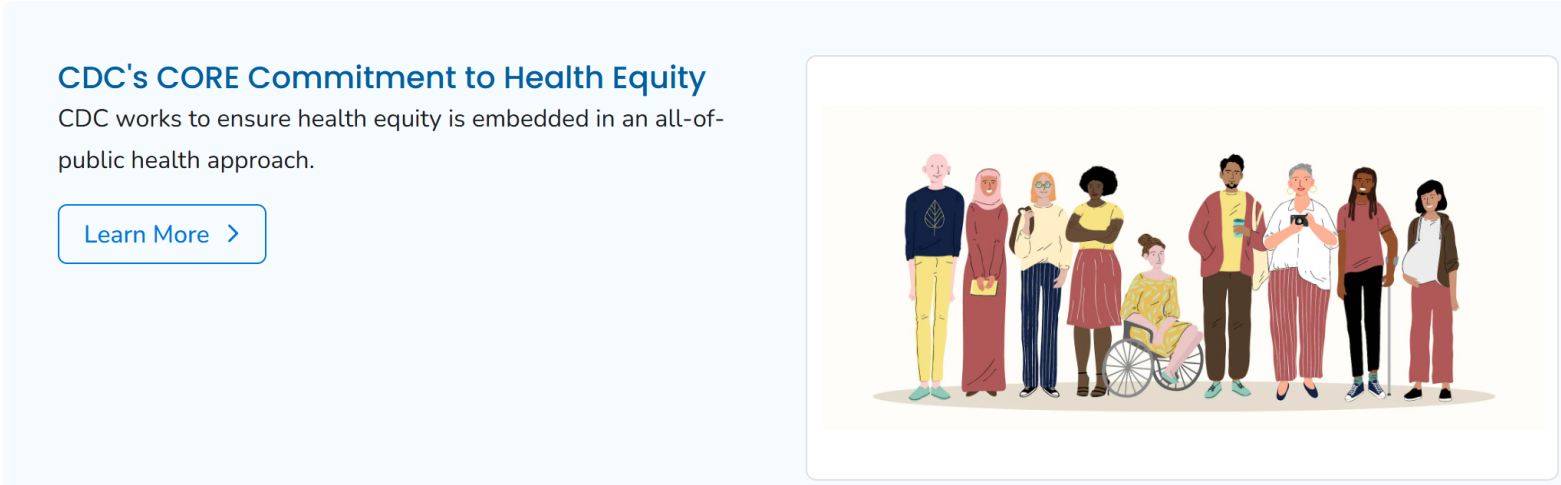

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- **O**ptimizing interventions
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Definition: MNAR Data

With $p = \Pr(\text{race is observed})$, we say that the race variable is Missing Not-at-Random (MNAR) if p depends on race itself or on other *un*observed variables

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  - *If* these covariates are Missing Not-at-Random (MNAR), then models fit with imputed data (or complete-cases-only) will yield biased parameter estimates
  - For many vulnerable or marginalized subpopulations, we can *expect* demographic membership to impact missingness ($\therefore$ MNAR)

Our Research Goals

- Develop a spatio-temporal model for the joint distribution of

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- Deterministic Models: ODE-based, cts. in time. With infection rate β and recovery rate γ, under frequency-dependent transmission:

$$\begin{aligned}
\frac{dX(t)}{dt} &= -\frac{\beta X(t)Y(t)}{N} \\
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- Working with surveillance (i.e. population-level) data, We want a *stochastic*, *discrete-time* analog to this SIR model, e.g.

$$\begin{aligned}X_t &= X_{t-1} + B_{t-d} - Y_t \\ Y_t &\sim F(\cdots)\end{aligned}$$

Brief History of Relevant Stochastic Models

(1) Time-Series SIR ("TSIR") Models:

- Kendall (1949) *Stochastic Processes and Population Growth.*
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(3) Zelner Contact-Heterogeneity Models:
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(4) Following the properties of the Negative Binomial distribution,

$$(\underbrace{Y_t - y_0}_{\text{\# failures}}) = \Big(\textstyle\sum_{i=1}^{y_0} T_i\Big) \sim \text{NB}\Big(\underbrace{y_0}_{\text{\# successes}}, \underbrace{e^{-\lambda t}}_{\text{success prob}} \Big) \sim \text{NB}\Big(\underbrace{y_0(e^{\lambda t} - 1)}_{\text{mean}}, \underbrace{y_0}_{\text{dispersion}} \Big)$$

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(5) Generalizing this formulation from the interval $(0, t)$ to our discretized intervals $(t-1, t)$, we can write

$$(Y_t - y_{t-1} \mid Y_{t-1} = y_{t-1}) \sim \mathrm{NB}\Big(y_{t-1}(e^{\lambda} - 1), y_{t-1}\Big)$$

and, if we make the simplifying assumption that prevalence = incidence (i.e. all infections recover before the next time period), then just

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(6) At this point, there's room for creativity in describing the hazard rate λ. Based on mass-action, we could take, e.g., $\lambda = \frac{\beta x_{t-1}}{N}$. so that

$$\begin{aligned} \mathrm{E}\left(Y_t \mid Y_{t-1} = y_{t-1}, X_{t-1} = x_{t-1}\right) &= y_{t-1} e^{\frac{\beta x_{t-1}}{N}} - y_{t-1} \\ &\approx \frac{\beta x_{t-1} y_{t-1}}{N} - y_{t-1} \qquad \text{for small } \beta x_{t-1}/N \end{aligned}$$

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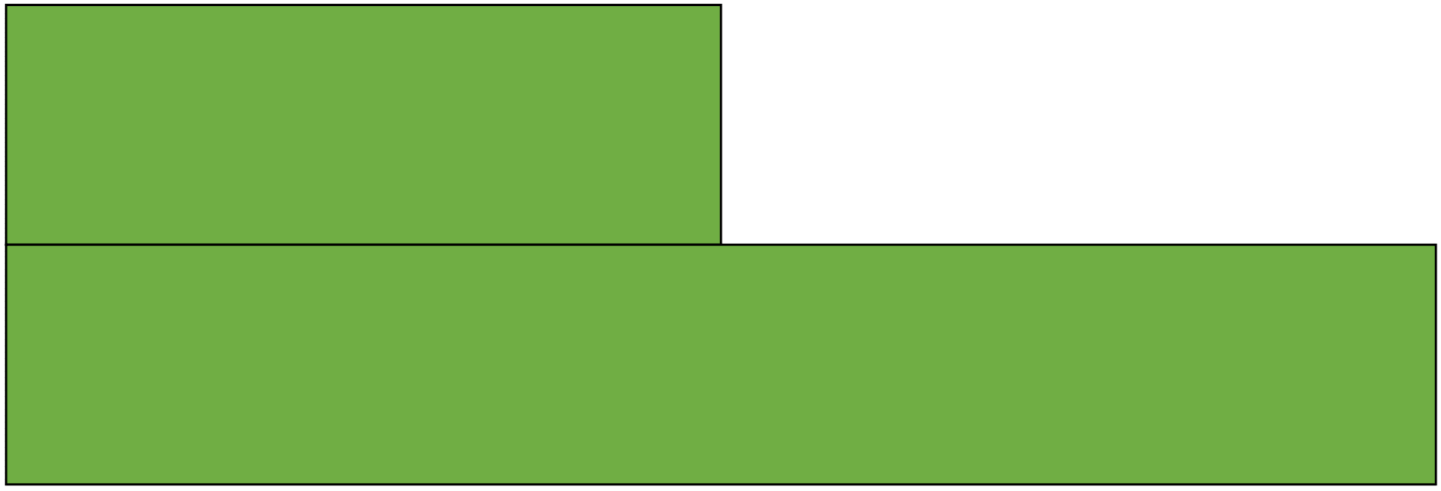
Missingness in the Simplest Case

Black population:
500 people



White population:
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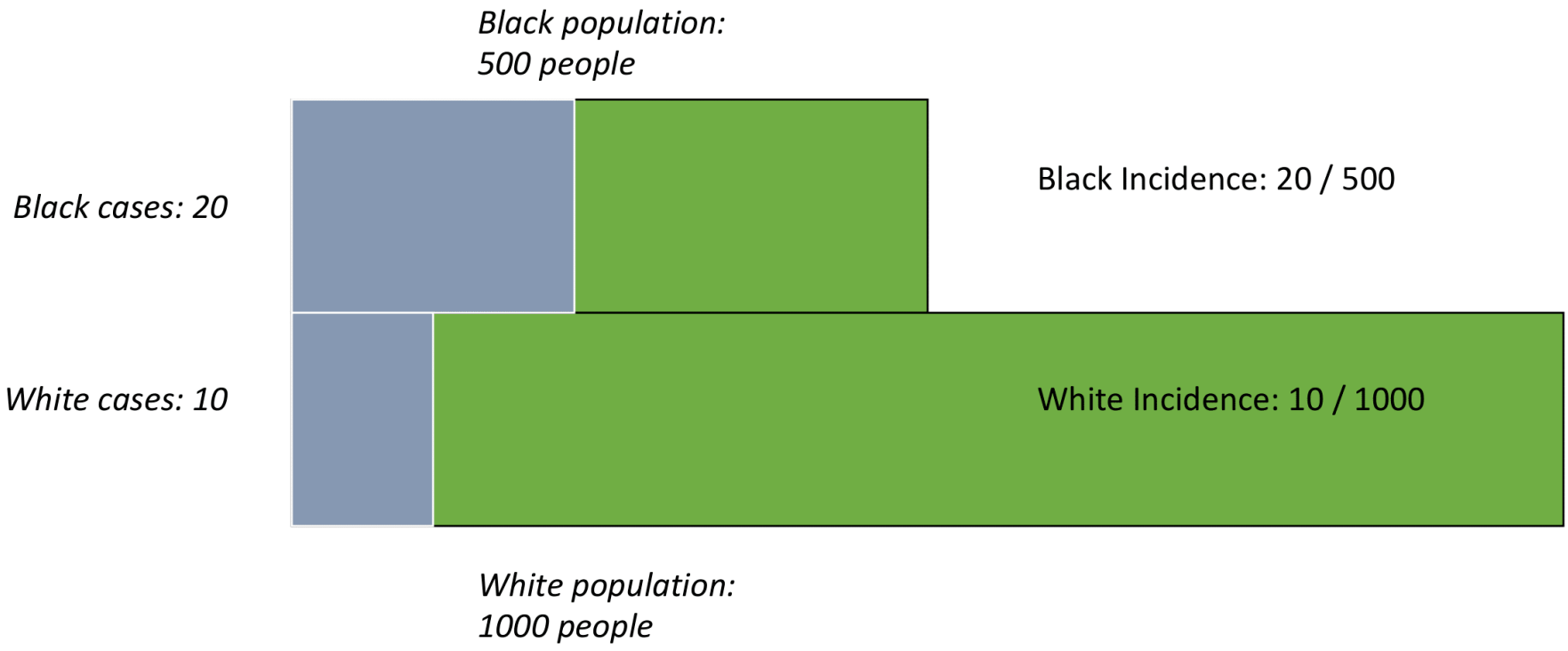

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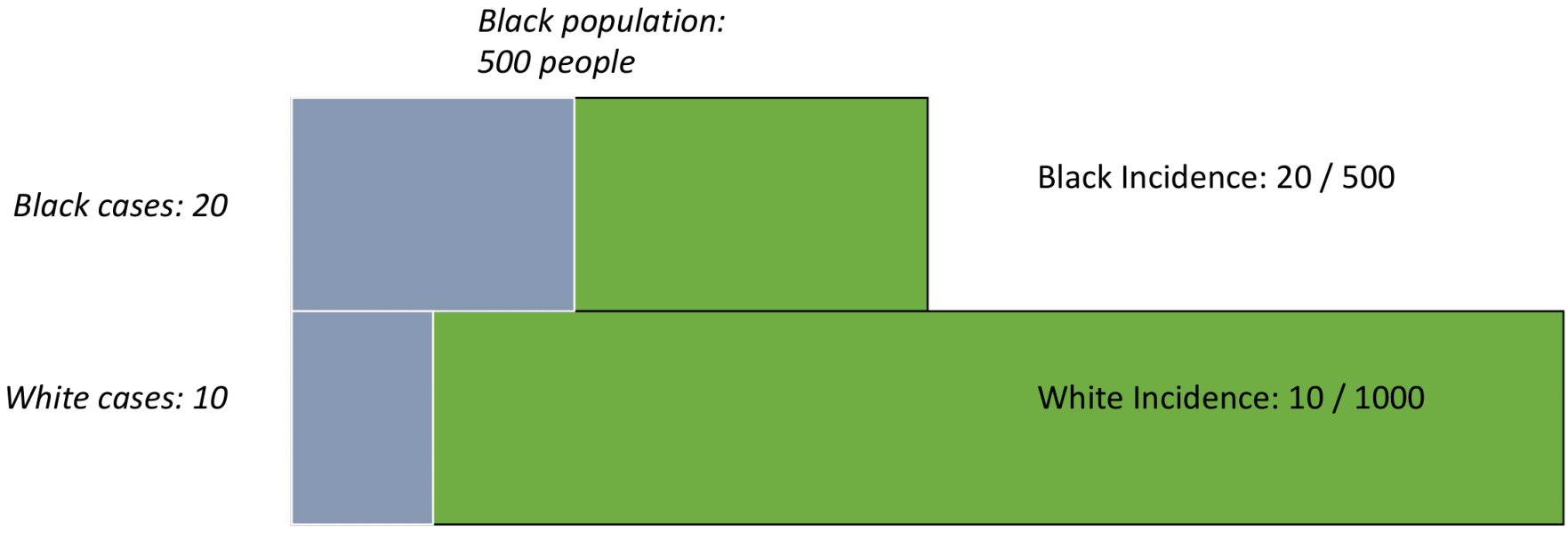

True risk of Black residents relative to White residents:

20 / 500 / (10 / 1000) = 4

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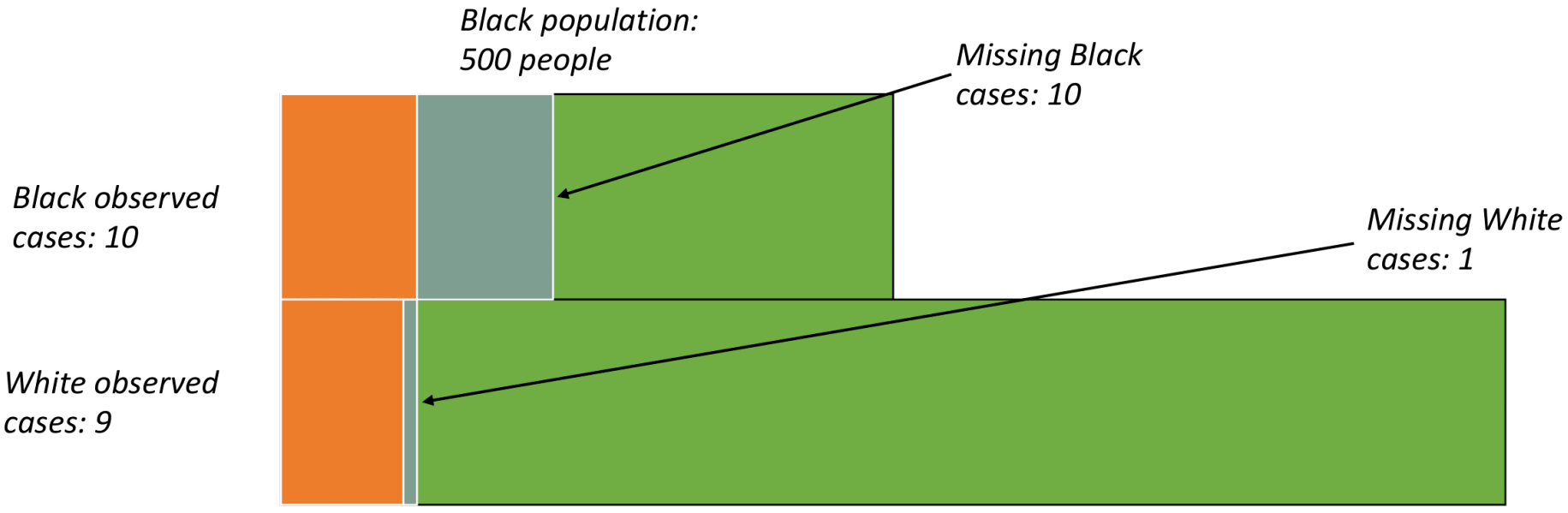

Observed risk of Black residents relative to White residents:

$10 / 500 / (9 / 1000) \cong 2$

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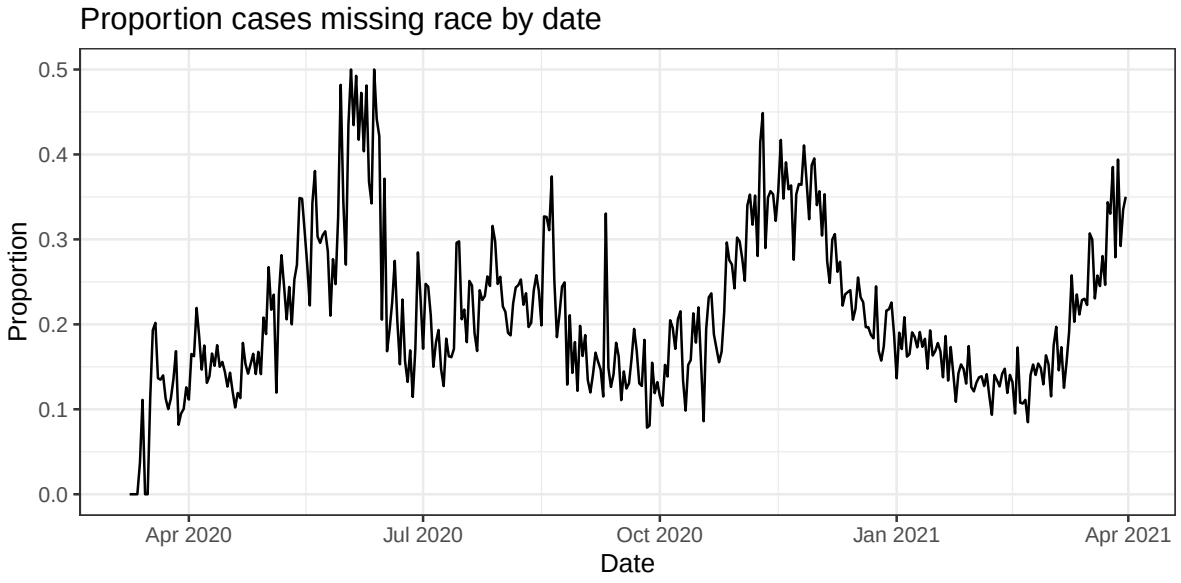
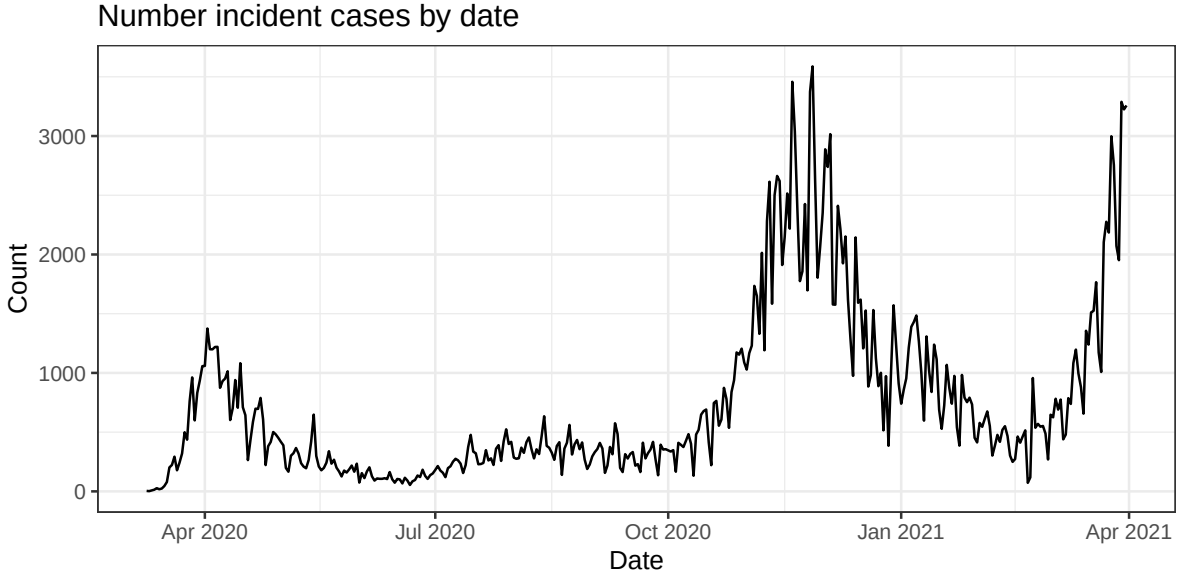
Missingness in Real Life





Overview: Missingness Process Models

- At time t, for individual k from race j, let
  - Y_{tjk} denote presence/absence of infection (binary)
  - M_{tjk} denote missingness (binary)

  so that Y_{tjk} is observed only when $M_{tjk} = 1$

- A model for data subject to missingness is just a specification of $f(\mathbf{y}, \mathbf{m})$, which is done through some kind of decomposition:

Selection Factorization: $f(\mathbf{y}, \mathbf{m}) = f_1(\mathbf{y}) f_2(\mathbf{m}|\mathbf{y})$

Pattern-Mixture Factorization: $f(\mathbf{y}, \mathbf{m}) = g_1(\mathbf{m}) g_2(\mathbf{y}|\mathbf{m})$

Random Effects: $f(\mathbf{y}, \mathbf{m}) = \int h_1(\mathbf{y}|\mathbf{u}) h_2(\mathbf{m}|\mathbf{u}) h_3(\mathbf{u}) d\mathbf{u}$

Derivation #3: Missingness in a TSIR-like Model

(1) Model *true* incidence-by-race with a discrete-time 1st-order Markov model, i.e. $(Y_{tgij}|\mathbf{Y}_{(t-1)}) \sim \text{Pois}\left(\lambda^{\text{TOT}}_{tgij}\right)$

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(3) Marginalize over Y_{tgij} to obtain the *observational* model:

$$\left\{ \begin{array}{l} X_{tgij} \sim \text{Pois}\left(\lambda^{\text{TOT}}_{tgij} p_{tgij}\right) \\ M_{tgi} = Y_{tgi\bullet} - \sum_{j=1}^{J} X_{tgij} \\ \qquad\quad \sim \text{Pois}\left(\sum_{j=1}^{J} \lambda^{\text{TOT}}_{tgij}(1 - p_{tgij})\right) \end{array} \right\}$$

EE-Like Observational Model Specification

$$(X_{tgij}|\mathbf{Y}_{(t-1)gi\bullet}) \sim \text{Pois}\left(\lambda^{\text{TOT}}_{tgij} p_{tgj}\right)$$
$$(M_{tgi}|\mathbf{Y}_{(t-1)gi\bullet}) \sim \text{Pois}\left(\sum_{j=1}^{J} \lambda^{\text{TOT}}_{tgij}(1-p_{tgj})\right)$$
$$\lambda^{\text{TOT}}_{tgij} = \lambda^{\text{AR}}_{tgj} Y_{(t-1)gi\bullet} + \lambda^{\text{NE}}_{tgj} \sum_{g'=1}^{G} w_{gg'} Y_{(t-1)g'\bullet\bullet} + \lambda^{\text{EN}}_{tgj} E_{gij}$$

$$\log\left(\lambda^{\text{AR}}_{tgj}\right) = \mu^{\text{AR}} + \alpha^{\text{AR}}_{j} + \beta^{\text{AR}}_{g}$$
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The Data (Part 1)

$(t, g, i, j) = (\textit{time},\ \textit{location},\ \textit{stratum},\ \textit{race})$

X_{tgij} = number of cases from (t, g, i) observed with race j

M_{tgi} = number of cases from (t, g, i) missing race

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The Data (Part 2)

$Y_{tgi\bullet}$ = *true* number of cases from (t, g, i)

$Y_{tg\bullet\bullet}$ = *true* number of cases from (t, g)

$\mathbf{Y}_{tgi\bullet} = (Y_{tg1\bullet}, Y_{tg2\bullet}, ..., Y_{tgI\bullet})$

Note: $Y_{tgi\bullet}, Y_{tg\bullet\bullet}$ are observed, but Y_{tgij} aren't

EE-Like Observational Model Specification

$$(X_{tgij}|\mathbf{Y}_{(t-1)gi\bullet}) \sim \text{Pois}\left(\lambda^{\text{TOT}}_{tgij} p_{tgj}\right)$$

$$(M_{tgi}|\mathbf{Y}_{(t-1)gi\bullet}) \sim \text{Pois}\left(\sum_{j=1}^{J} \lambda^{\text{TOT}}_{tgij}(1-p_{tgj})\right)$$

$$\lambda^{\text{TOT}}_{tgij} = \lambda^{\text{AR}}_{tgj} Y_{(t-1)gi\bullet} + \lambda^{\text{NE}}_{tgj} \sum_{g'=1}^{G} w_{gg'} Y_{(t-1)g'\bullet\bullet} + \lambda^{\text{EN}}_{tgj} E_{gij}$$

$$\log\left(\lambda^{\text{AR}}_{t\cdot j}\right) = \mu^{\text{AR}} + \alpha^{\text{AR}}_{\cdot} + \beta^{\text{AR}}$$

$$\log\left(\lambda^{\text{NE}}_{t\cdot j}\right)$$

$$\log\left(\lambda^{\text{EN}}_{t\cdot j}\right)$$

$$\text{logit}\left(p_{\cdot}\right)$$

The Data (Part 3)

$w_{gg'}$ = distance weight between locations g and g'

$$= \begin{cases} \frac{1}{(\#\text{ neighbors})_g} & \text{if } g \text{ adjacent to } g' \\ 0 & \text{if } g \textit{ not} \text{ adjacent to } g' (\text{or } g = g') \end{cases}$$

E_{gij} = population count from (g, i, j)

EE-Like Observational Model Specification

$$(X_{tgij}|\mathbf{Y}_{(t-1)gi\bullet}) \sim \text{Pois}\left(\lambda^{\text{TOT}}_{tgij} p_{tgj}\right)$$

$$(M_{tgi}|\mathbf{Y}_{(t-1)gi\bullet}) \sim \text{Pois}\left(\sum_{j=1}^{J} \lambda^{\text{TOT}}_{tgij}(1-p_{tgj})\right)$$

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$$\log\left(\lambda^{\text{AR}}_{tgi}\right) = \mu^{\text{AR}} + \alpha^{\text{AR}}_{i} + \beta^{\text{AR}}_{g}$$

The Disease Process (Competing Risks Framework)

$\lambda^{\text{TOT}}_{tgij}$ = hazard rate from all sources

$\lambda^{\text{AR}}_{tgj}$ = hazard rate of self-area/"autoregressive" infections

$\lambda^{\text{NE}}_{tgj}$ = hazard rate of neighboring-area infections

$\lambda^{\text{EN}}_{tgj}$ = hazard rate of background/"environmental" infection

EE-Like Observational Model Specification

$$(X_{tgij}|\mathbf{Y}_{(t-1)gi\bullet}) \sim \text{Pois}\left(\lambda^{\text{TOT}}_{tgij} p_{tgj}\right)$$
$$(M_{tgi}|\mathbf{Y}_{(t-1)gi\bullet}) \sim \text{Pois}\left(\sum_{j=1}^{J} \lambda^{\text{TOT}}_{tgij}(1-p_{tgj})\right)$$
$$\lambda^{\text{TOT}}_{tgij} = \lambda^{\text{AR}}_{tgj} Y_{(t-1)gi\bullet} + \lambda^{\text{NE}}_{tgj} \sum_{g'=1}^{G} w_{gg'} Y_{(t-1)g'\bullet\bullet} + \lambda^{\text{EN}}_{tgj} E_{gij}$$

$$\log\left(\lambda^{\text{AR}}_{tgj}\right) = \mu^{\text{AR}} + \alpha^{\text{AR}}_{j} + \beta^{\text{AR}}_{g}$$
$$\log\left(\lambda^{\text{NE}}_{tgj}\right) = \mu^{\text{NE}} + \alpha^{\text{NE}}_{j} + \beta^{\text{NE}}_{g}$$
$$\log\left(\lambda^{\text{EN}}_{tgj}\right) = \mu^{\text{EN}} + \alpha^{\text{EN}}_{j} + \beta^{\text{EN}}_{g} + \gamma^{\text{EN}} t + \delta^{\text{EN}} \sin(\tfrac{t}{52} 2\pi) + \varepsilon^{\text{EN}} \cos(\tfrac{t}{52} 2\pi)$$

The Missingness Process

p_{tgj} = probability that a case from (t, g, j) reports their race

EE-Like Observational Model Specification

$$(X_{tgij}|\mathbf{Y}_{(t-1)gi\bullet}) \sim \text{Pois}\left(\lambda^{\text{TOT}}_{tgij} p_{tgj}\right)$$
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$$\lambda^{\text{TOT}}_{tgij} = \lambda^{\text{AR}}_{tgj} Y_{(t-1)gi\bullet} + \lambda^{\text{NE}}_{tgj} \sum_{g'=1}^{G} w_{gg'} Y_{(t-1)g'\bullet\bullet} + \lambda^{\text{EN}}_{tgj} E_{gij}$$

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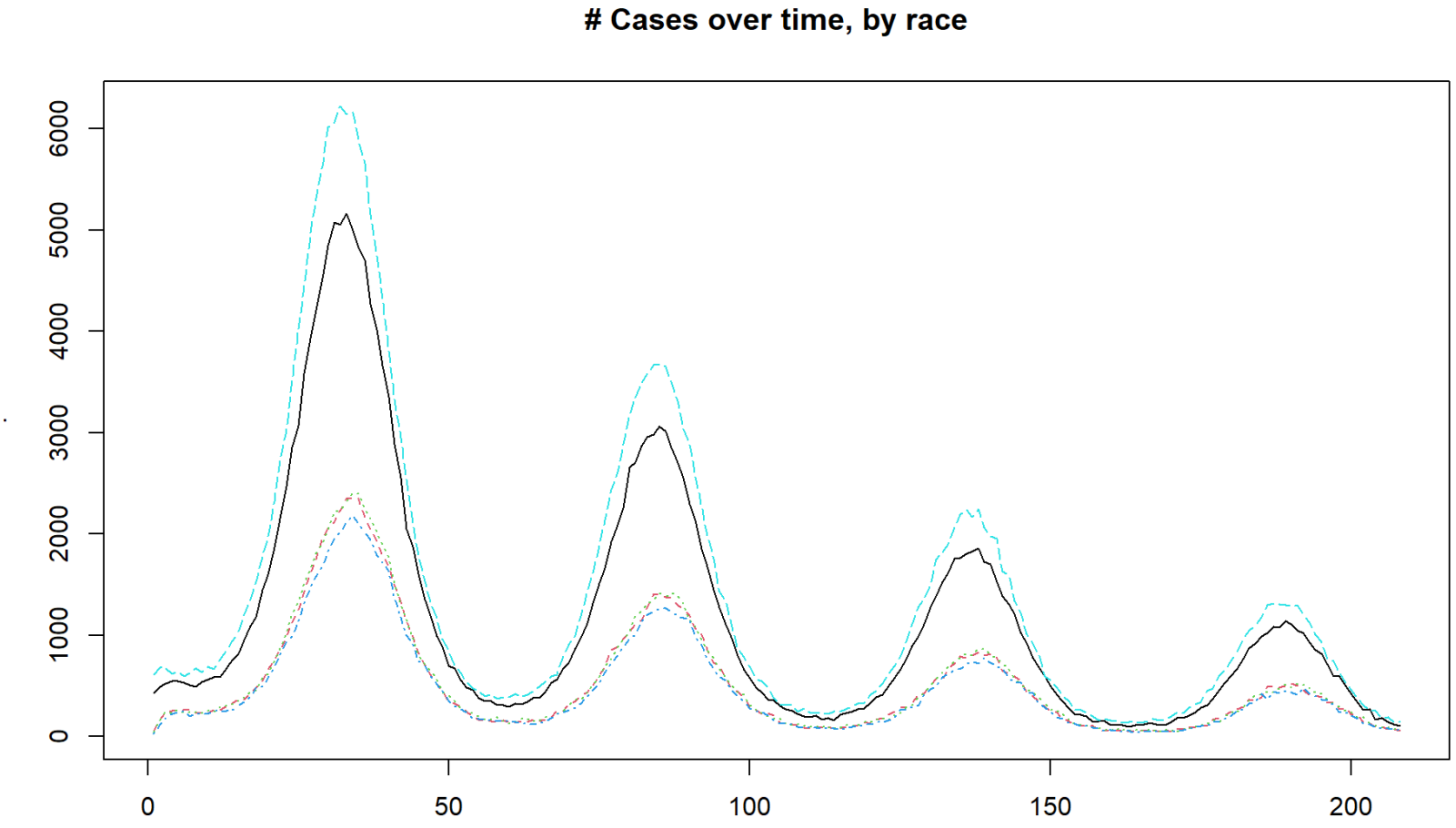
$$\text{logit}\left(p_{tgj}\right) = \mu^{(\text{p})} + \alpha^{(\text{p})}_{j} + \beta^{(\text{p})}_{g}$$

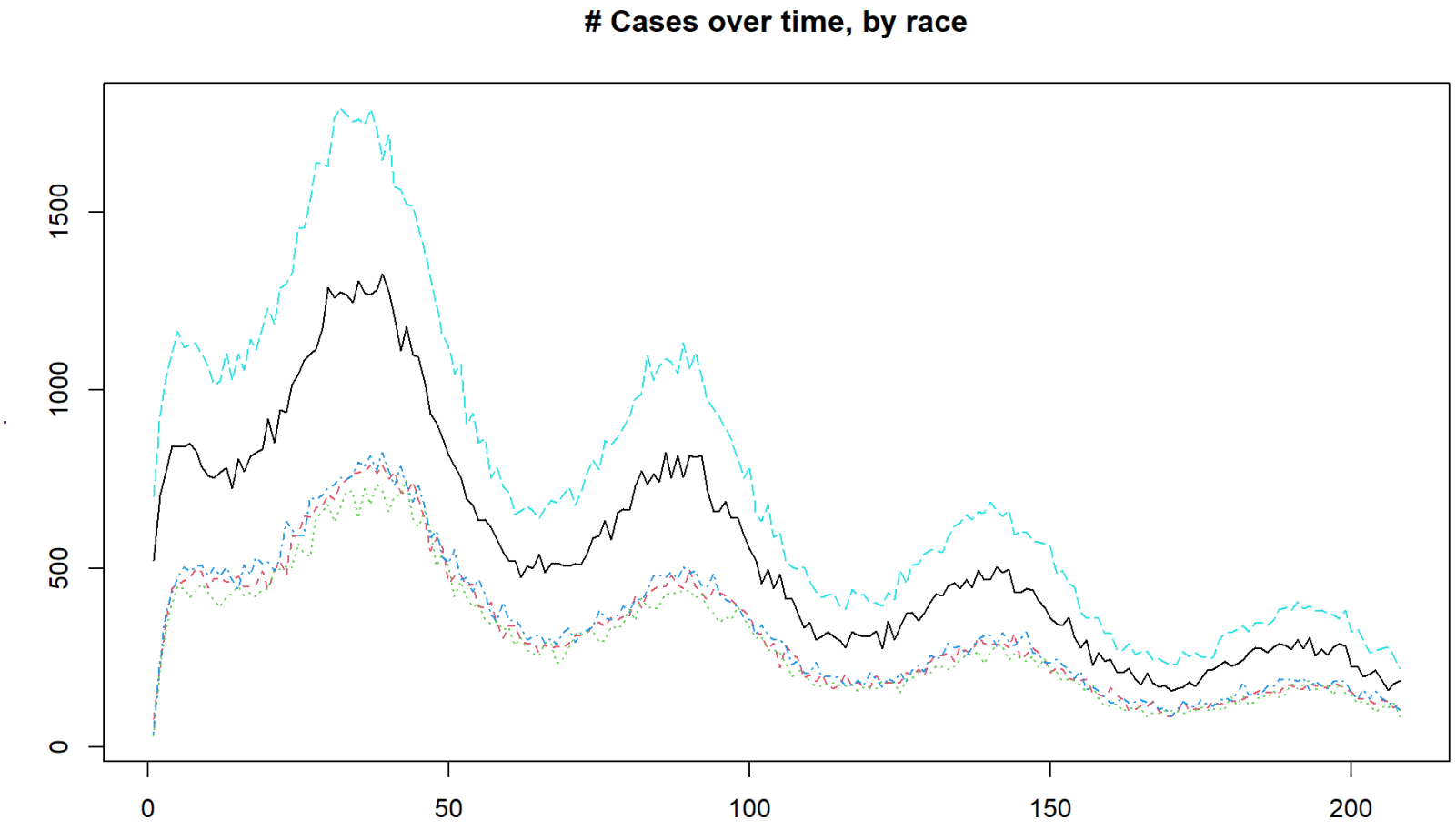
Simulation Study Overview (Work-In-Progress)

- Data generated according to the Latent Model in R
- Model fitting performed via HMC with Stan
- Scenarios to Consider:
  - Similar EE-type model, ignoring missingness entirely
  - Similar EE-type model, imputation via statistical model
  - Similar EE-type model, imputation via ML or MICE
  - TSIR models (i.e. Neg. Bin. likelihood) for each of the above

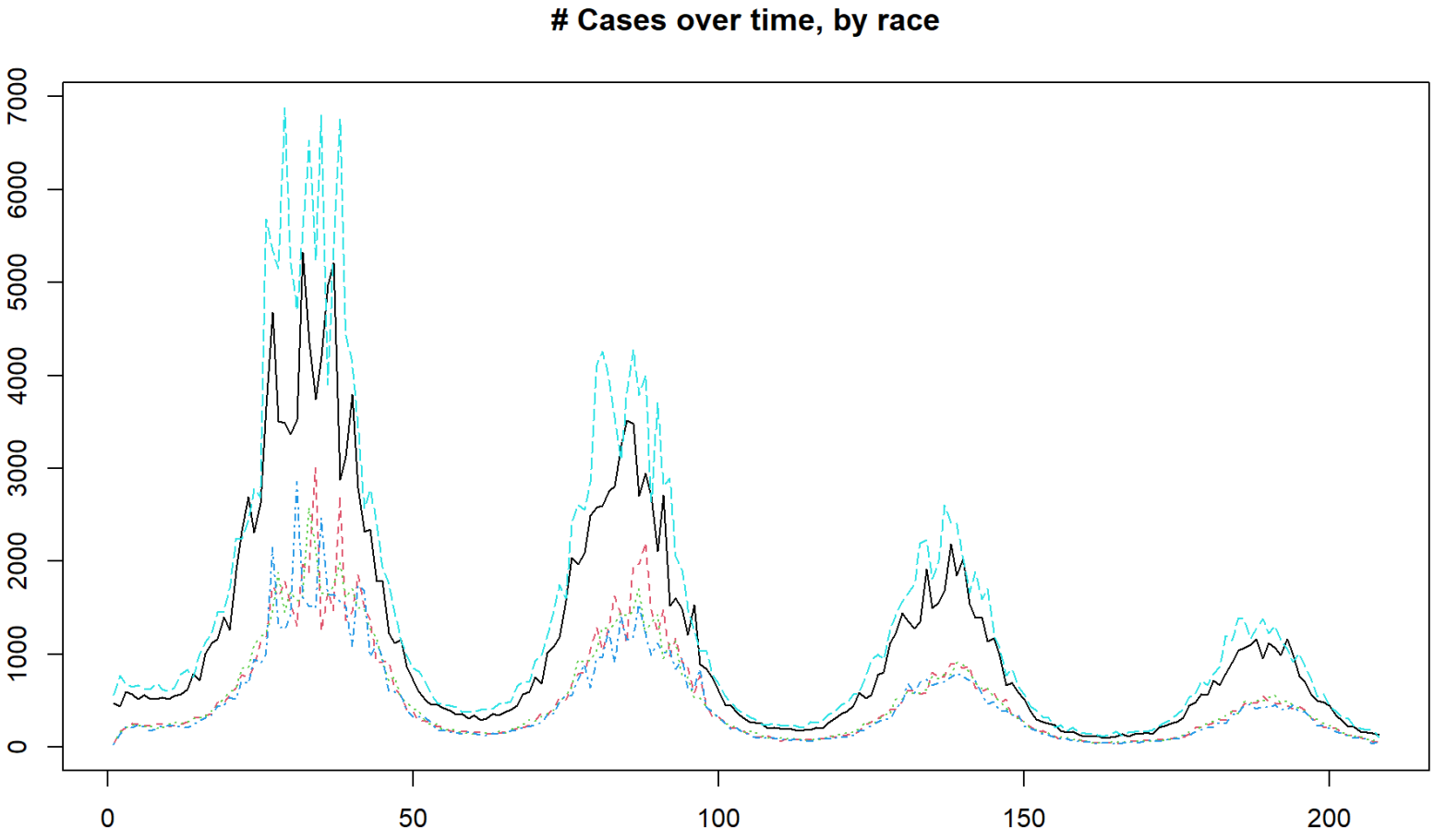
Simulated Data (Poisson)



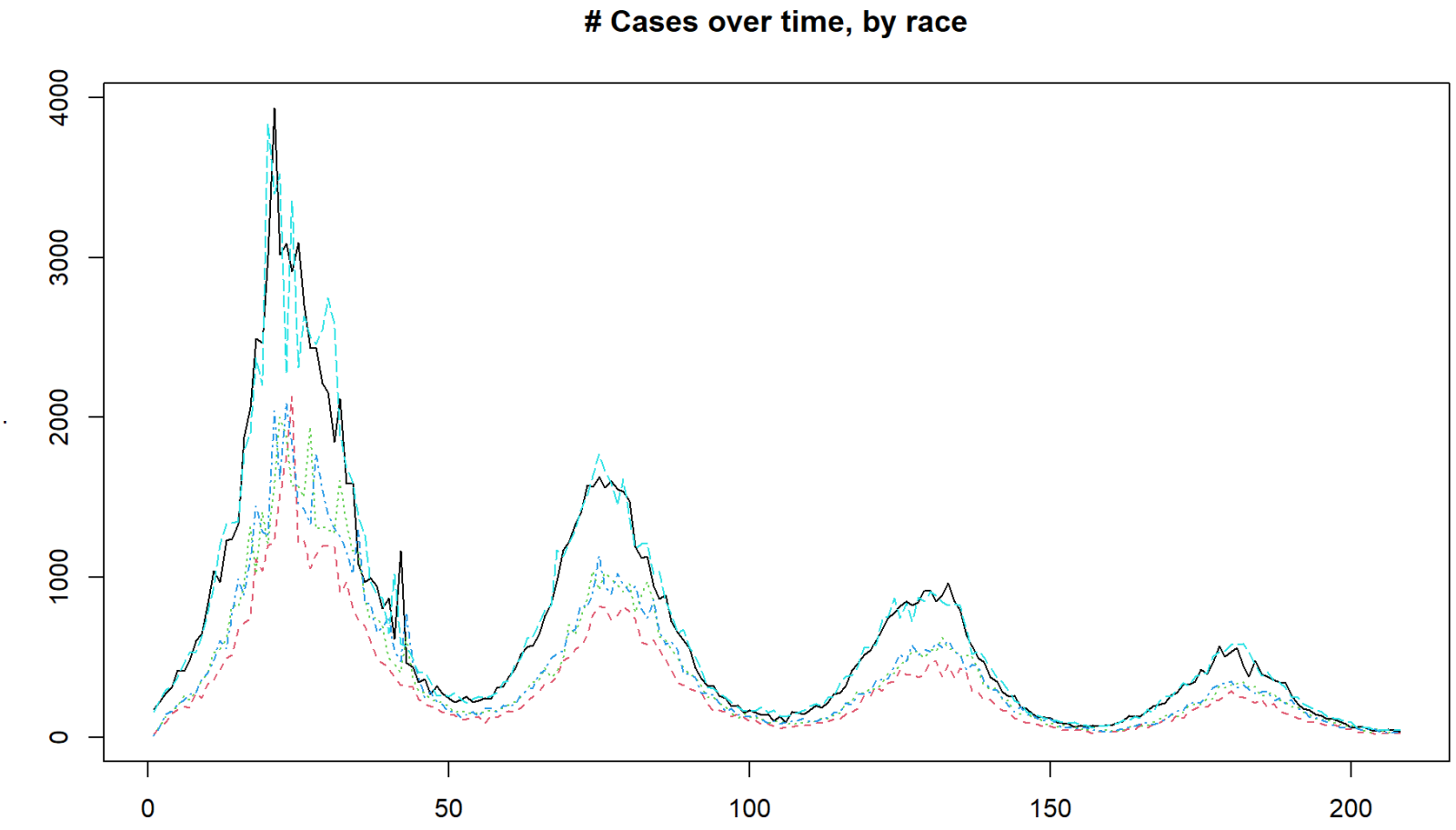
Simulated Data (Poisson)



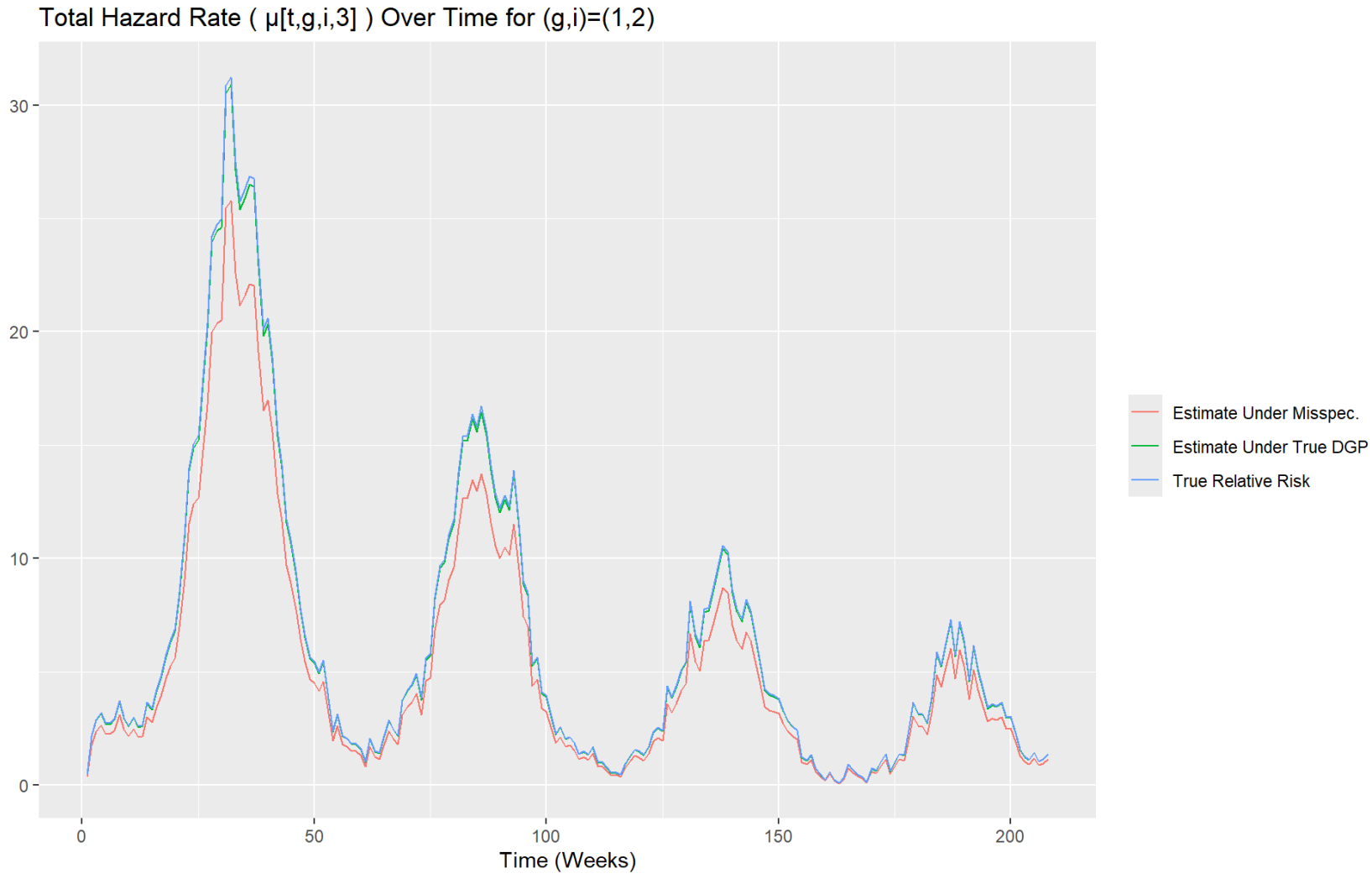
Simulated Data (Negative Binomial)



Simulated Data (Negative Binomial)



Preliminary Results (Idealized Scenario)



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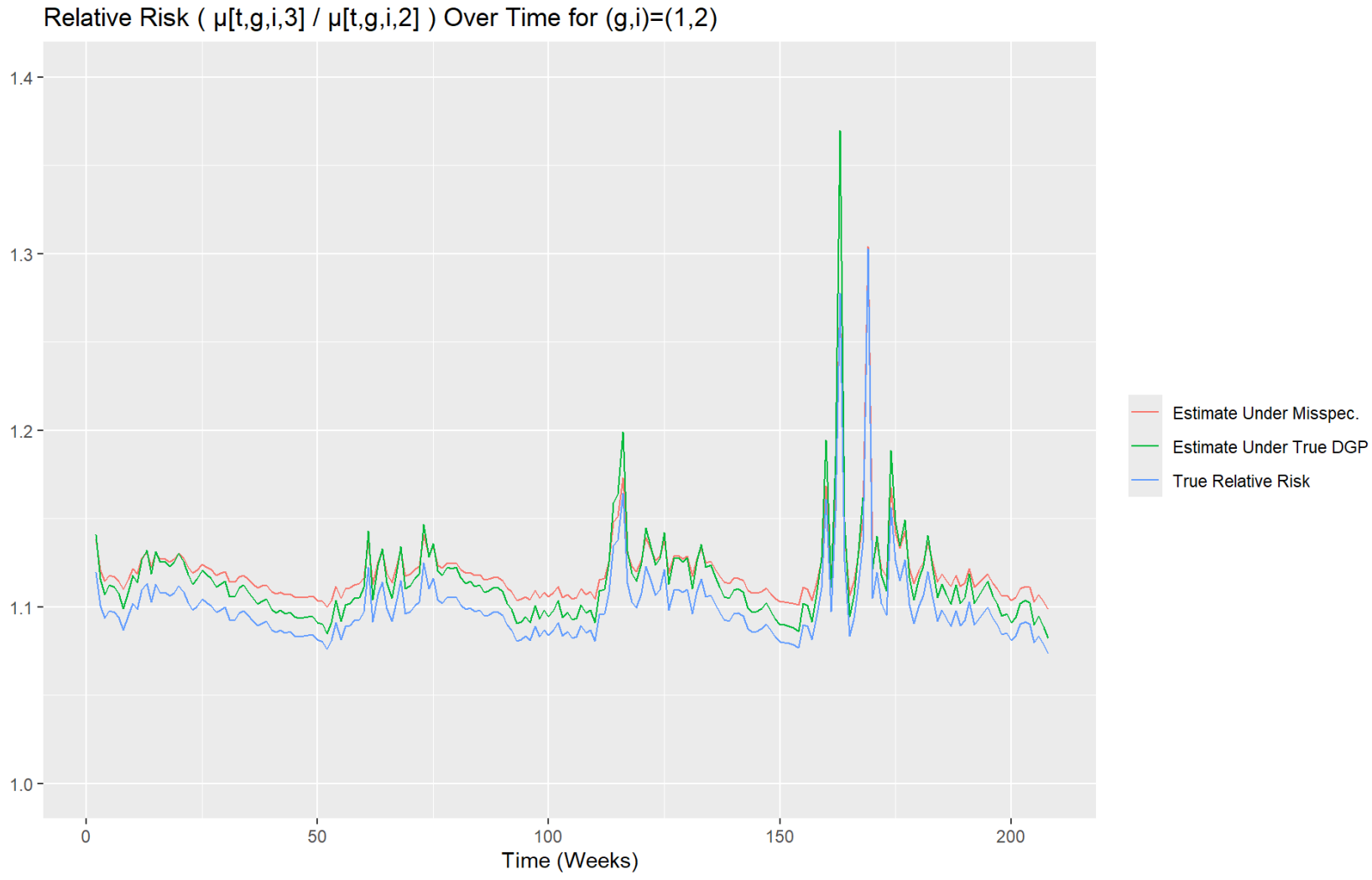
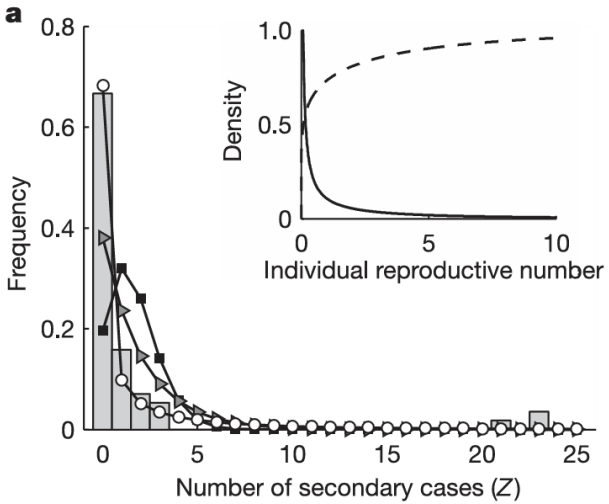


Motivation for Zelner Contact-Heterogeneity Model

- Observation: Individual-level contact-tracing data seems to suggest the average number of secondary-infections caused by an individual (i.e. R_0) exhibits individual-level heterogeneity (see Lloyd-Smith et al. 2005)



- Observation: If we wish to stratify a disease model by geography and demography, there is no obvious way in the aforementioned frameworks to specify how new infections are doled-out *across* strata

Derivation #4: Zelner Contact-Heterogeneity Model

(1) Suppose the (latent) individual R_0 of infected i in geography g during the interval $(t-1, t)$ is given by

$$r_{tgi} \overset{\text{iid}}{\sim} \text{Gamma}\Big(\underbrace{\tfrac{R_0}{\theta}}_{\text{shape}}, \underbrace{\theta}_{\text{scale}} \Big)$$

(2) The total (latent) infectiousness at time t for geography g becomes

$$(r_{tg\bullet} \mid Y_{tg} = y_{tg}) = \Big(\textstyle\sum_{i=1}^{y_{tg}} r_{ti}\Big) \sim \text{Gamma}\Big(\tfrac{R_0}{\theta} y_{tg}, \theta\Big)$$

(3) Assume homogeneous mixing, and that all of the latent infectiousness is deposited in the single time period after infection. Then the force of infection is

$$\lambda_{tg} = \zeta \frac{r_{(t-1)g}}{n_g} + (1-\zeta) \sum_{g' \neq g} \frac{r_{(t-1)g'}}{N - n_{g'}}$$

(4) Following a process almost identical to the EE model framework:

$$(Y_{tg} \mid \mathbf{r}_{(t-1)}) \sim \text{Pois}\left(n_g \lambda_{tg}\right)$$

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  - Determining conditions for local and global identifiability
  - Determining validity of rare-disease assumption and consequences of violation

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