Modeling the Dynamics of COVID-19

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SGLK15007U: Strategies for Health Promotion and Disease Prevention
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Table of Contents

Introduction

Mathematical Models

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Definition: A representation, in mathematical terms, of the behavior of real phenomena

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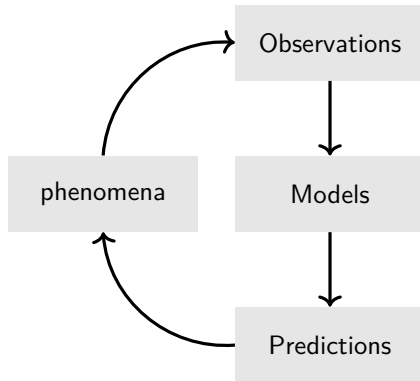

Figure 1: An elementary understanding of the scientific method (Dym and Ivey 1980).

Why use Models?

Policy decisions must be based on incomplete data:

- Vaccination strategies
- Interventions to achieve control
- Amount and distribution of healthcare resources

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Parameters with well understood interpretations

- Formal framework highlights their role and interactions
- Estimate using statistical inference

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Why use Models?

Models are used to answer a variety of scientific questions. Including:

- Quantify epidemic risk
- Forecasting
- Estimate time-varying reproduction numbers
- Quantify effects of mitigation efforts
- Counterfactuals: what would have happened?

Spectrum of Infectious Disease Models

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Quantitative methods are used very widely in epidemiology

- e.g. infer epidemiological quantities
  - Latency, infectious period, generation time, IFR

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Many terms used to characterize such models:

- mechanistic vs statistical
- deterministic vs stochastic
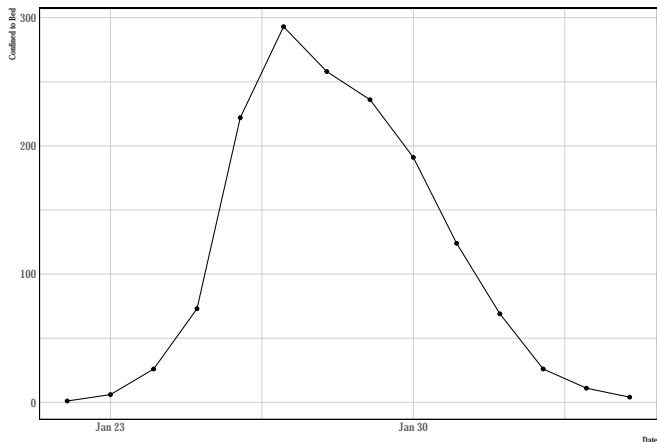- agent-based, compartmental
- spatial, temporal

Compartmental Models

Boarding School Influenza Outbreak

Influenza outbreak at a boy's boarding school in 1978

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(Example inspired by Robin Thompson Lecture *"How do mathematicians model infectious disease outbreaks?"*)

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$$i_t = R^t \qquad (1)$$

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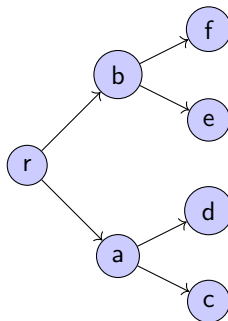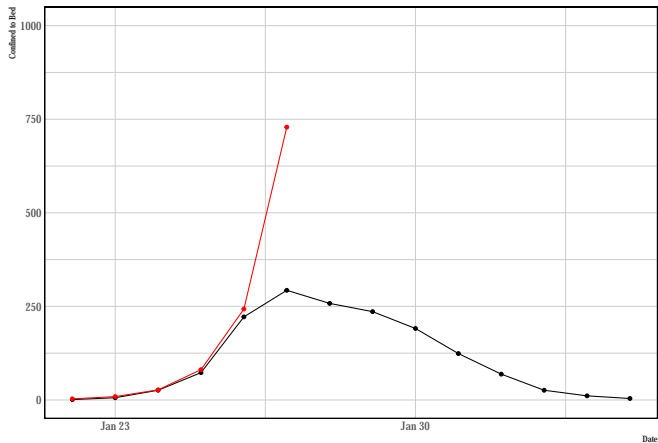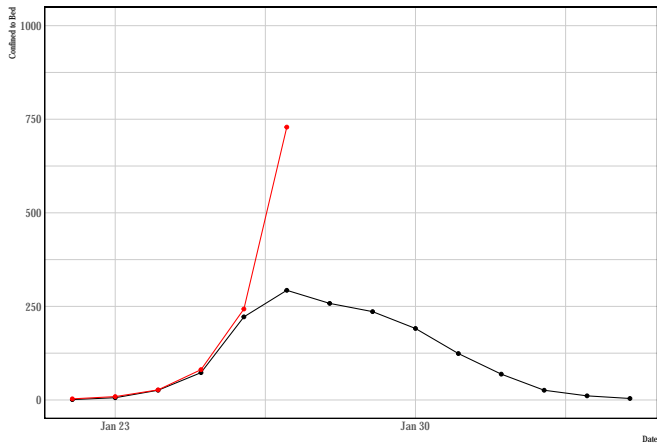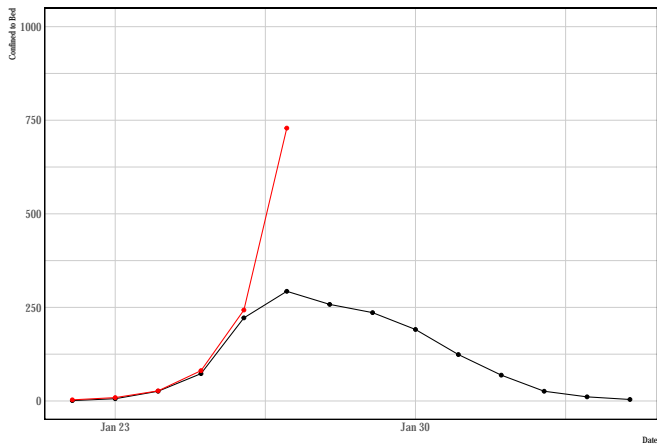
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Exponential Growth: How does it do?

Used $R = 3$ here. Early growth appears exponential
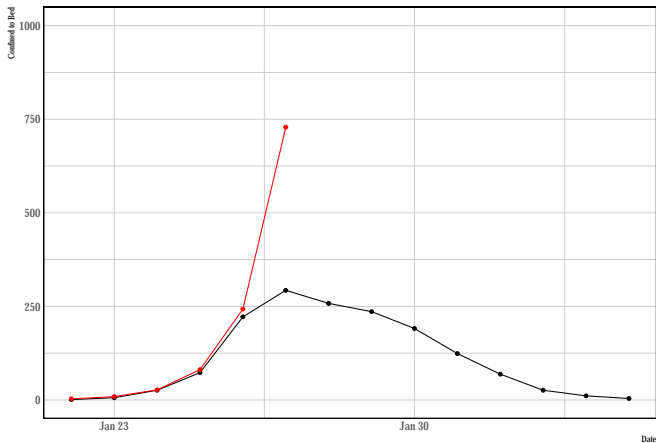
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Exponential growth *too simple*. Need to account for population effect

SIR Model

Figure 2: Classic Susceptible-Infected-Recovered (SIR) Model.

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States:

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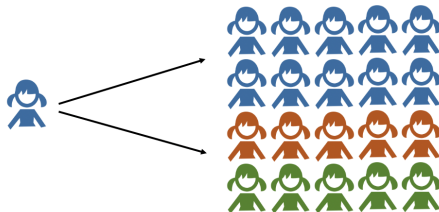Figure 2: Classic Susceptible-Infected-Recovered (SIR) Model.

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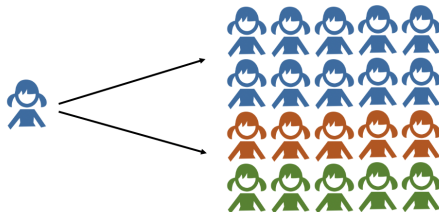
Parameters:

- α: Contact rate per individual, per unit time
- τ: Probability of transmission per infectious, susceptible contact
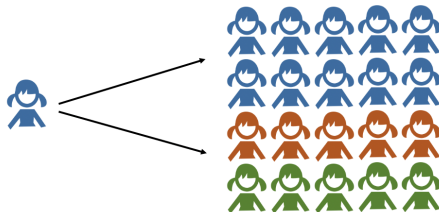- ρ: Recovery rate per unit time

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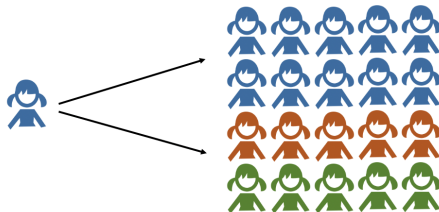
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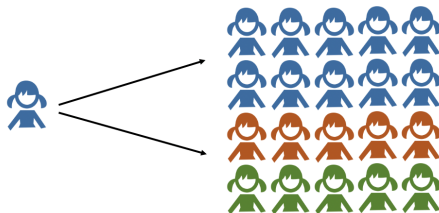
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Applying to entire susceptible population (and including recovered):

$$\frac{dS(t)}{dt} = -S(t)\left(\frac{\tau \alpha}{N}I(t)\right) = -\frac{\beta}{N}S(t)I(t), \tag{2}$$

with $\beta := \alpha \tau$.

SIR Model

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Dynamical Equations:

$$\frac{dS(t)}{dt} = -\frac{\beta}{N}S(t)I(t) \tag{3}$$

$$\frac{dI(t)}{dt} = \frac{\beta}{N}S(t)I(t) - \rho I(t) \tag{4}$$

$$\frac{dR(t)}{dt} = \rho I(t) \tag{5}$$

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Notable assumptions: homogeneous within compartments, complete mixing

SIR Model: Fit to Data

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Simulate dynamics using $i_0 = 1$, $\beta = 1.7$ and $\rho = 0.5$.

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Statistical Methods

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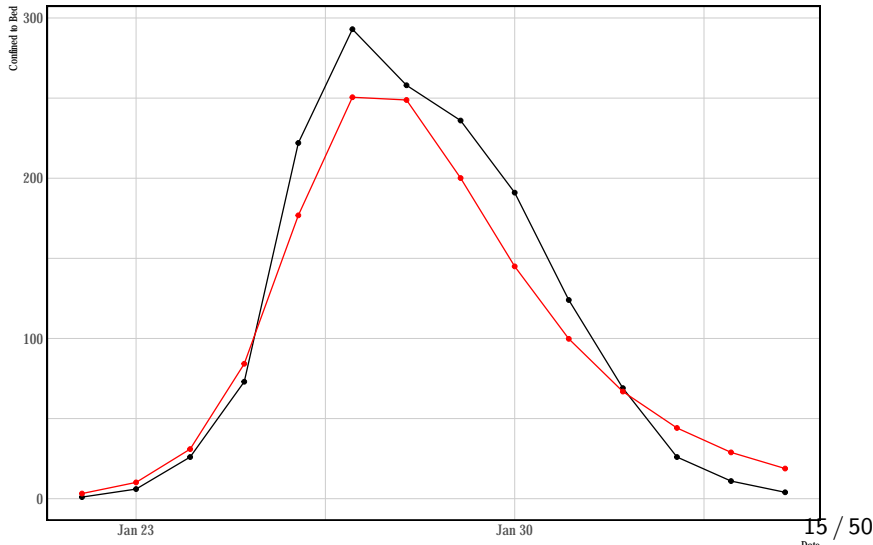
Prediction estimates the response for unseen data.

- Model $\hat{f}$ is trained on observed data $\{(x_i, y_i)\}_{i=1}^{n}$
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Forecasting is a *subset* of prediction

- Predicting *future values* of time series
- $\hat{f}(y_{t+\tau}; y_{1:t})$ with $\tau > 0$

Forecasting Infectious Diseases: Why?

Long-term forecasts

Forecasting under assumed mitigation scenarios informs policy decisions

- synthesize sparse data early in an epidemic to guide policy under uncertainty
- Quantify expected cost of allowing an epidemic to run its course
- Baseline to evaluate the impact of interventions

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Short-term forecasts

Often of interest to forecast count data: cases, hospitalizations, deaths

- resource allocation, i.e. PPE, respirators, increase bed capacity, cancel non-urgent procedures etc
- flatten the curve and prevent overwhelming healthcare systems

Forecasting Infectious Diseases: Challenges

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- Spatio-temporal data.

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- Not unique to epidemiology: for example, similar difficulties with ranking algorithms on social media sites

Forecasting Methodologies

Typically divide into *mechanistic* and *statistical* models. (These are really two ends of a spectrum)

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Covid-19 Forecast Hub

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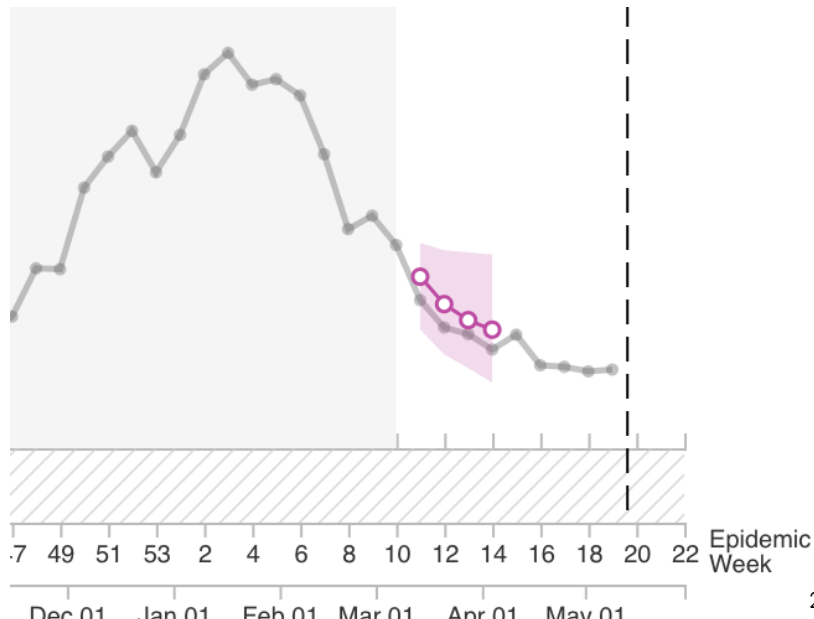Individual forecasts combined into an *ensemble forecast*

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Ensembles can outperform individual forecasts[3]
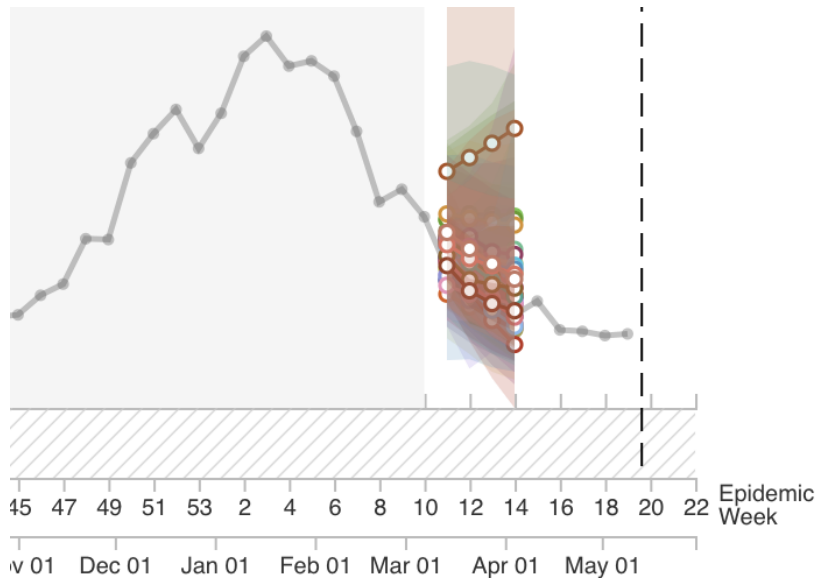
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Statistical Methods: Berkeley-Yu Model

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Observe that some counties experience exponential growth, some sub-exponential growth

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Separate exponential predictor:

$$\mu_{t+\tau} := \mathbb{E}\left[Y_{t+\tau}^c \mid \mathcal{F}_t\right] = \exp\left(\beta_0^c + \beta_1^c(t+\tau)\right) \tag{6}$$

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Distributional Model:

$$Y_{t+\tau}^c \sim \mathsf{Poisson}(\mu_{t+\tau}^c) \tag{8}$$

M linear and exponential predictors $\hat{y}_{t+\tau}^{(1)}, \dots, \hat{y}_{t+\tau}^{(M)}$

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Combine into an ensemble predictor based on recent performance of each predictor

- i.e.

$$\hat{y}_{t+\tau} = \sum_{m=1}^{M} w_m \hat{y}_{t+\tau}^{(m)}, \tag{9}$$

where w_m chosen based on recent performance

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Letting $\mu_t := \mathbb{E}(Y_t \mid \mathcal{F}_t)$. Model

$$g(\mu_t) = \beta_0 + \sum_{k=1}^{p} \beta_k \tilde{g}(Y_{t-i_k}) + \sum_{l=1}^{q} \alpha_l g(\mu_{t-j_l}) + \eta^T X, \qquad (10)$$

where

- $g : \mathbb{R}^+ \to \mathbb{R}$ is the *link function*
- $\tilde{g} : \mathbb{N}_0 \to \mathbb{R}$ is a transformation function
- $0 < i_1, ... < i_p < \infty$ and $0 < j_1, < ... <, j_q < \infty$
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Distribution: $Y_t \mid \mathcal{F}_t \sim \text{Poisson}(\mu_t)$ or $Y_t \mid \mathcal{F}_t \sim \text{NegBinom}(\mu_t, \phi)$

Aggregate a bunch of different prediction methods:

Statistical Methods: Caltech Model

Aggregate a bunch of different prediction methods:

- Feed-forward Neural Network
- LSTM (Long Short-Term Memory)
- Autoregressive Model
- Seasonal Autoregressive Model
- Gradient Boosted Decision Trees
- k-Nearest Neighbors
- Bayesian epidemiological Model
- *... and many others...*

Semi-Mechanistic Models

Task: Quantify the effects of non-pharmaceutical interventions (NPIs) on the dynamics of Covid-19.

Effects of NPIs

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Follow the the method of Flaxman et al. 2020[4]

- uses death data from 11 European countries
- partial pooling to estimate effect sizes

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This is a **semi-mechanistic model**; statistical model with constraints motivated by epidemiological considerations
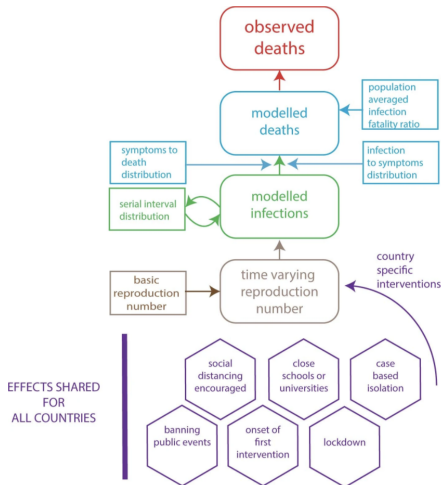
Figure 5: **Top**: Overview of the model schematic

Daily deaths Y_{tm} a function of past infections $\{i_{sm} : s < t\}$

Observational Model (Survival Process)

Daily deaths Y_{tm} a function of past infections $\{i_{sm} : s < t\}$

Distributional Assumption:

- $Y_{tm} \sim \text{NegBinom}(y_{tm}, \phi)$ where $y_{tm} := \mathbb{E}(Y_{tm} \mid \mathcal{F}_t)$
- ϕ is dispersion parameter

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Model the expected value:

$$y_{tm} = \alpha_m \sum_{s<t} i_{sm} \pi_{t-s}, \tag{11}$$

where α_m is an *unknown* country specific IFR and $\{\pi_k\}$ is an *assumed* density for time from an infection to death

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- ϕ is dispersion parameter

Model the expected value:

$$y_{tm} = \alpha_m \sum_{s<t} i_{sm} \pi_{t-s}, \tag{11}$$

where α_m is an *unknown* country specific IFR and $\{\pi_k\}$ is an *assumed* density for time from an infection to death

Example prior on IFR: $\alpha_m = \tilde{\alpha}_m N(1, 0.3)$ where $\tilde{\alpha}_m = 0.01$

Observational Model (Survival Process)
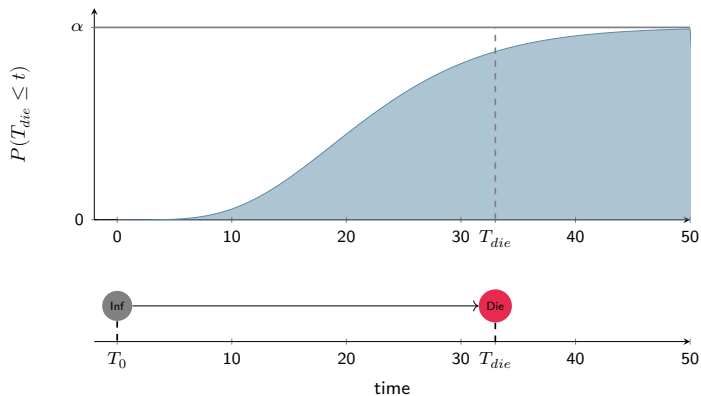
Figure 6: **Top**: Assumed cumulative probability of death t days after infection. **Bottom**: Illustration of random time to death.

Infection Model (Renewal Process)

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Infections are driven by a *discrete-time point process*

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Convolution:

$$i_{tm} = R_{tm} \sum_{s<t} i_{sm} g_{t-s}, \tag{12}$$

where $\{g_k\}$ is density function for the *generation time*

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Convolution:

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where $\{g_k\}$ is density function for the *generation time*

R_{tm}: are instantaneous reproduction numbers.

- i.e. average secondary infections of infections at time t if conditions at time t were to persist
- tempers infections for time and country specific factors. -i.e. R_{tm} lower if more restrictions (i.e. social distancing in place).

Infection Model
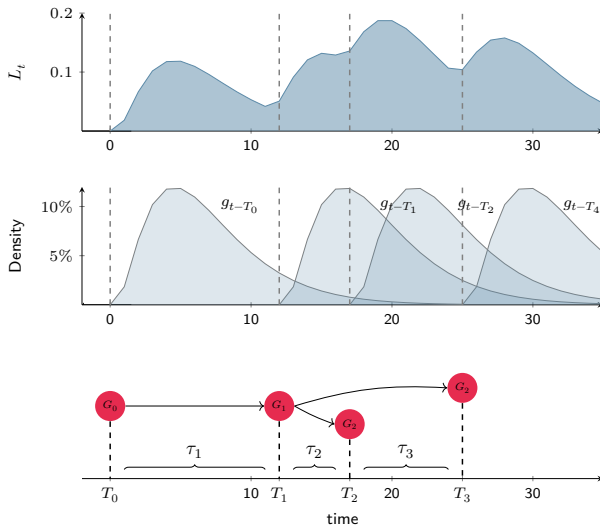
Paramaterize R_{tm} in terms of binary policy indicators

Transmission Model

Paramaterize R_{tm} in terms of binary policy indicators

No pooling:

$$R_t^{(m)} = R' g^{-1} \left(b_0^{(m)} + \sum_{i=1}^{5} \beta_i^{(m)} I_{i,t}^{(m)} \right) \qquad (13)$$

Transmission Model

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$$R_t^{(m)} = R' g^{-1}\left(b_0^{(m)} + \sum_{i=1}^{5} \beta_i^{(m)} I_{i,t}^{(m)}\right) \tag{13}$$

Complete Pooling:

$$R_t^{(m)} = R' g^{-1}\left(b_0^{(m)} + \sum_{i=1}^{5} \beta_i I_{i,t}^{(m)}\right) \tag{14}$$

Transmission Model

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$$R_t^{(m)} = R' g^{-1} \left(b_0^{(m)} + \sum_{i=1}^{5} \beta_i^{(m)} I_{i,t}^{(m)} \right) \qquad (13)$$

Complete Pooling:

$$R_t^{(m)} = R' g^{-1} \left(b_0^{(m)} + \sum_{i=1}^{5} \beta_i I_{i,t}^{(m)} \right) \qquad (14)$$

Partial Pooling:

$$R_t^{(m)} = R' g^{-1} \left(b_0^{(m)} + \sum_{i=1}^{5} \left(\beta_i + b_i^{(m)} \right) I_{i,t}^{(m)} \right) \qquad (15)$$
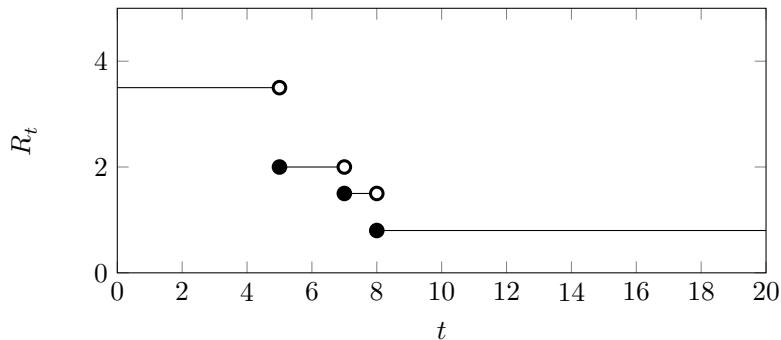
Figure 7: An example path of R_t given its parameterization in terms of binary NPI indicators. Piecewise constant.
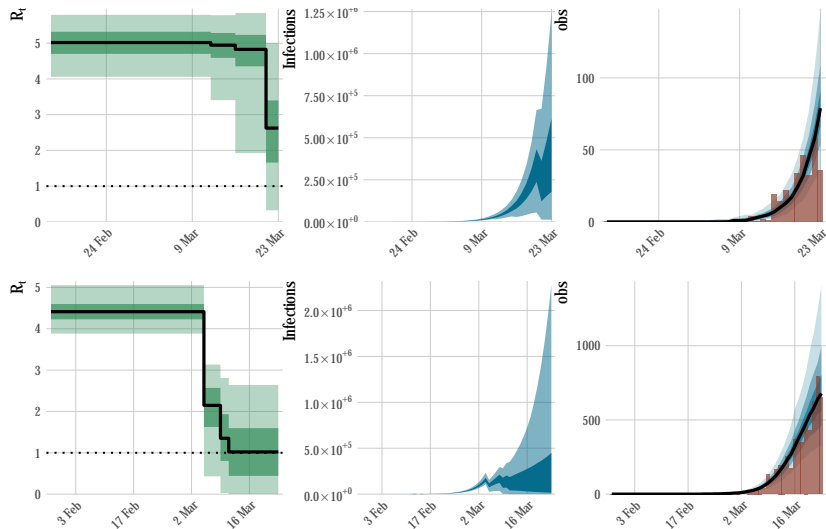
Figure 8: Fit to 24/03/2020
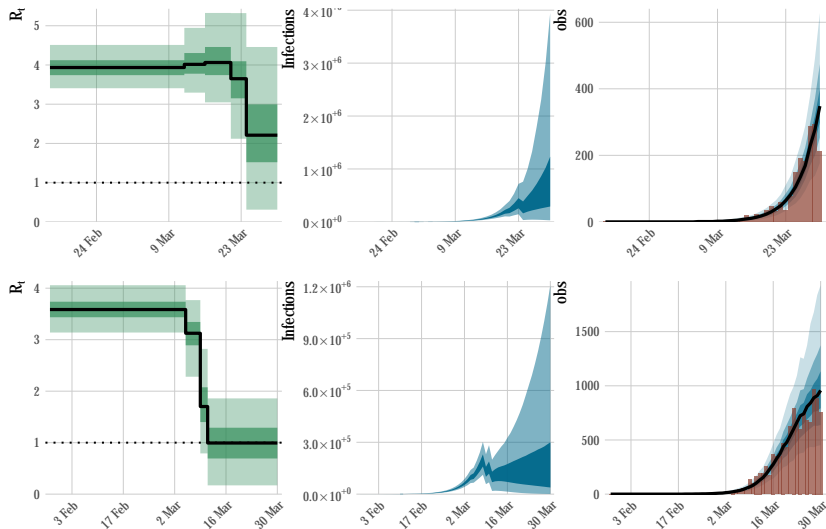
Figure 9: Fit to 31/03/2020
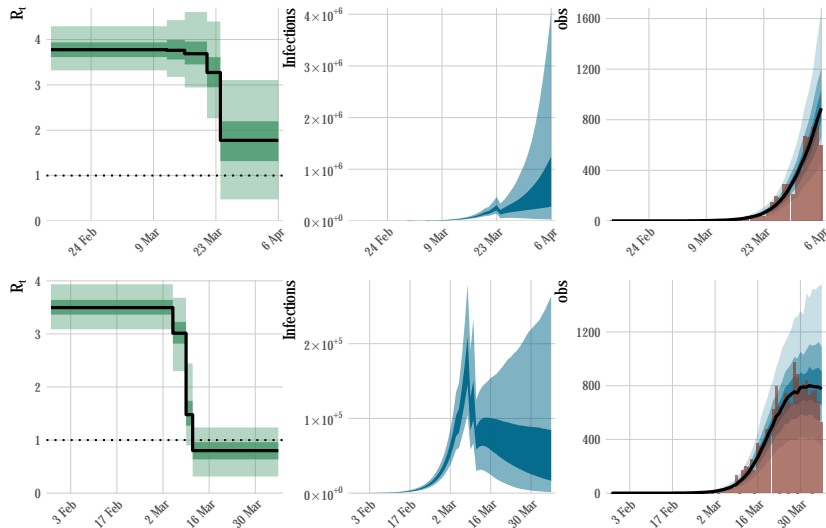
Figure 10: Fit to 07/04/2020
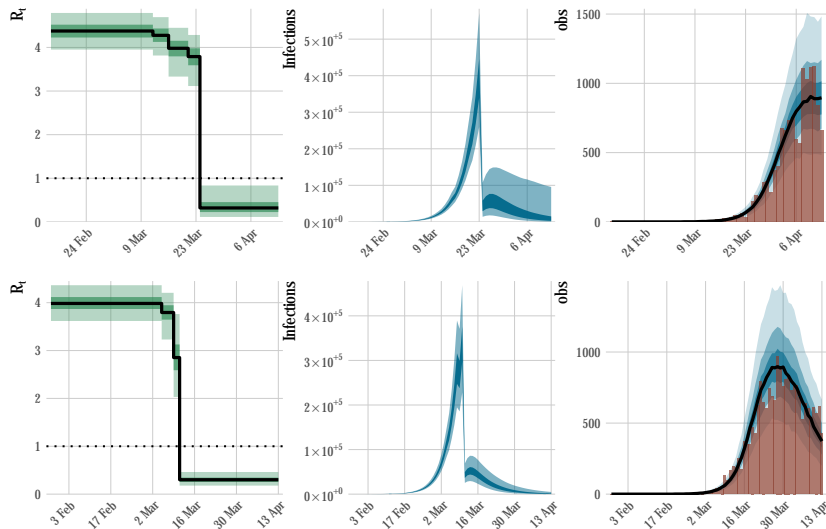
Figure 11: Fit to 14/04/2020
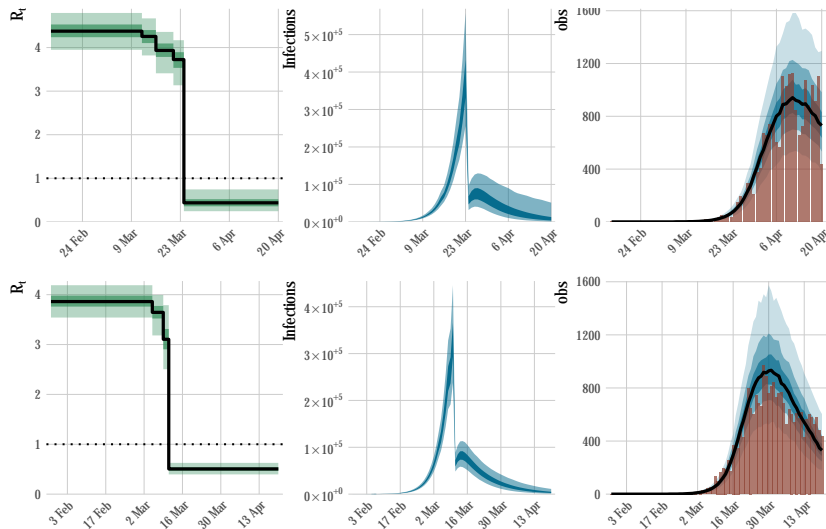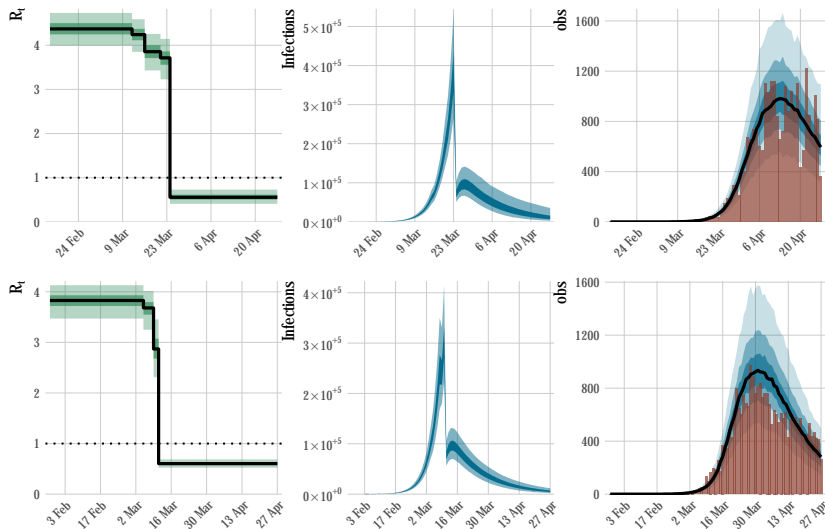
Figure 12: Fit to 21/04/2020
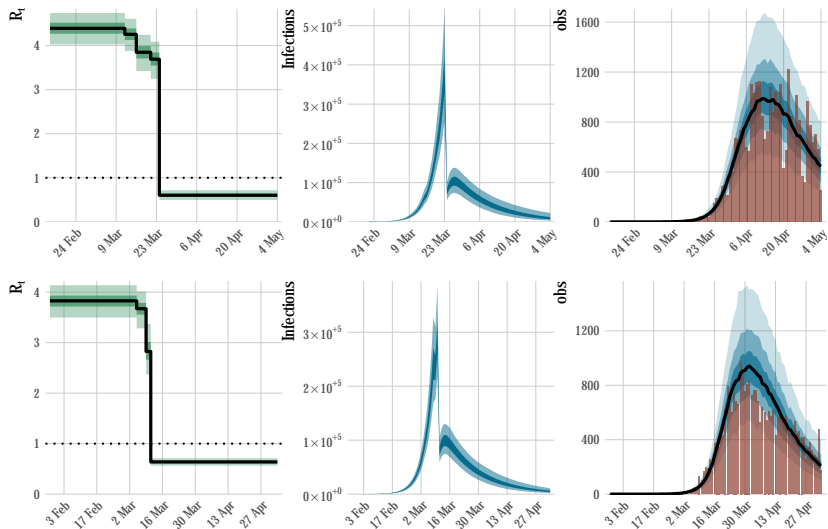
Figure 13: Fit to 28/04/2020
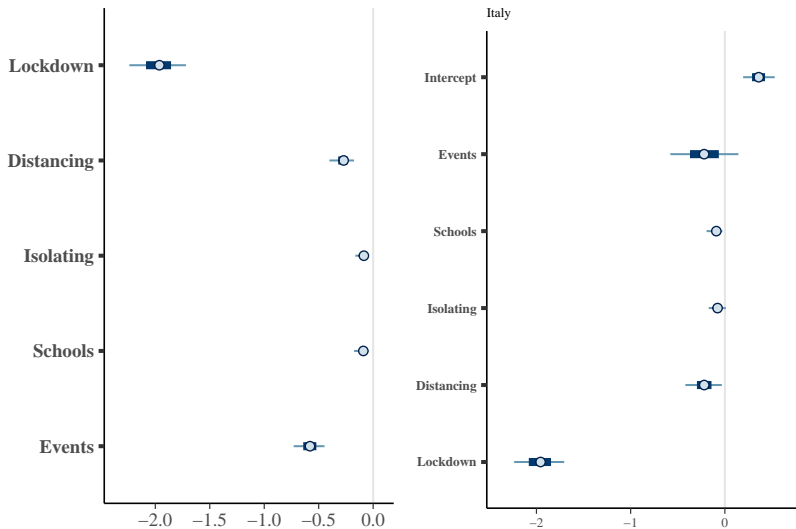
Figure 14: Fit to 05/05/2020

Effect Sizes

Figure 15: Effect Sizes for Policy Indicators

Paper Discussion Questions

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2 What are some important assumptions underlying the model?

3 Why is identifying the effects of non-pharmaceutical interventions difficult in this context?

Paper Discussion Questions

4 The initial reproduction number in each country is an important baseline for estimating the total effect of NPIs. i.e. higher R0 implies greater effects of mitigation within the model. What are some potential challenges in estimating R0 in this context?

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- What is the purpose of this effect?

- Suppose full pooling is used, i.e. the effect of NPIs is assumed to be exactly the same in all countries, and nothing else can explain changes in transmission rates within the model. What problems could occur? (Think Sweden)

- What difficulties might be faced if this analysis was done with each country individually? I.e. effects are not shared between countries (no pooling)

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