

Lecture + Laboratory 2: Emerging Infections

April 28, 2020

Announcements

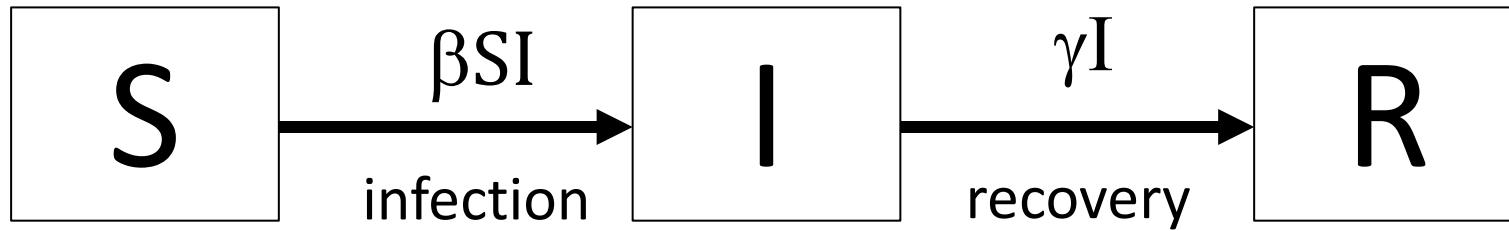
- Problem Set 2
- Office Hours
- Reviewing Problem Set 1 Solutions
- Midterm

Covid-19

- What is the growth rate of Covid-19?
- Is it changing?
- How does it vary across communities?
- What is the R_0 ?
- Is R_t changing?

Learning Objectives

- Learn about the relationship between transmission intervals, the epidemic growth rate, and R_0
- Become familiar common methods for estimating the R_0 and R_t from case counts
- Understand how variation in secondary case generation can affect outbreak size and extinction



$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

In the early period of the epidemic $S \approx N \approx 1$

$$\frac{dI}{dt} = (\beta S - \gamma)I$$

$$\frac{dI}{dt} = (\beta - \gamma)I$$

$$\frac{dI}{dt} = \Lambda I$$

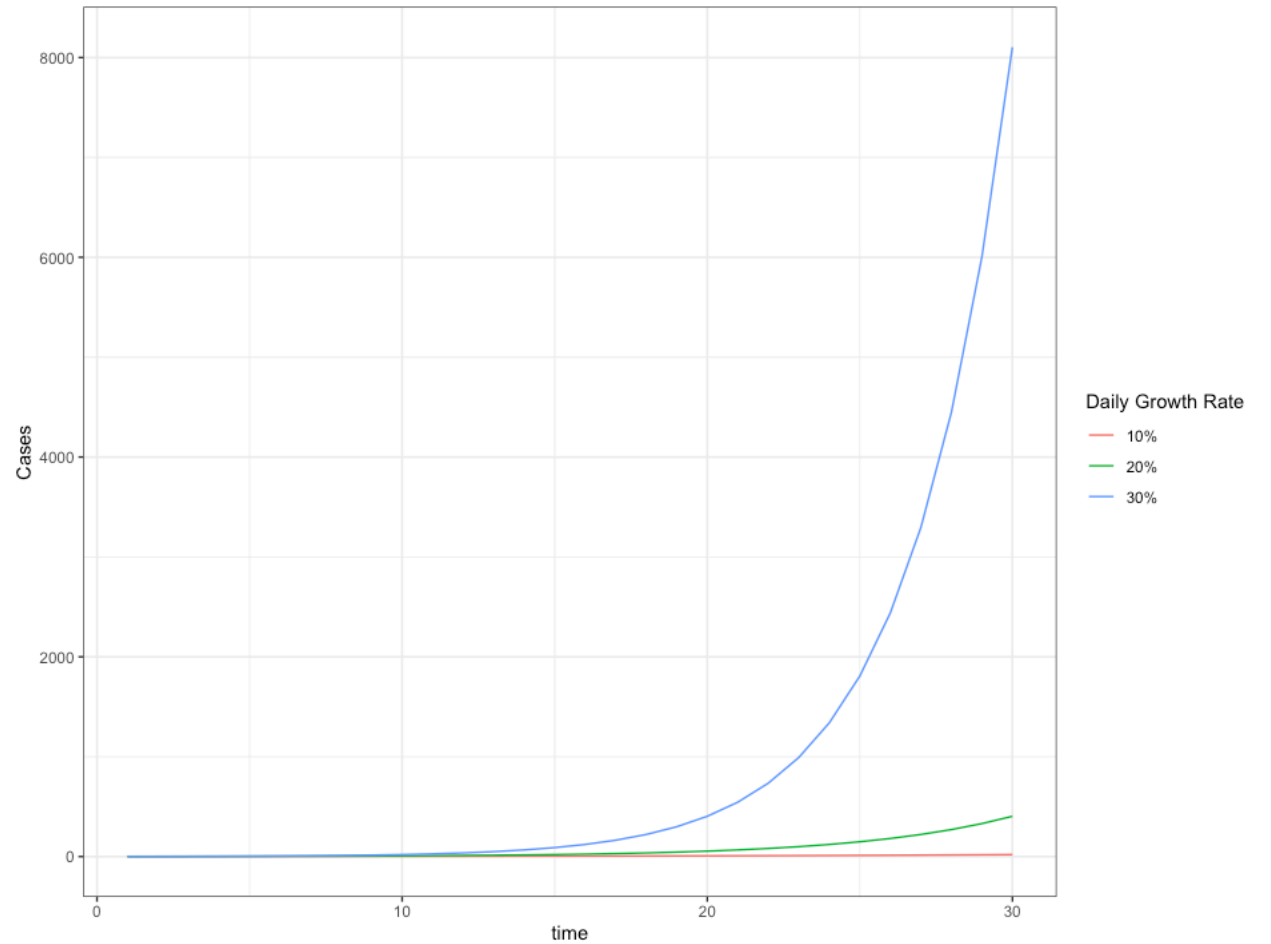
$$\Lambda = (\beta - \gamma) = \text{growth rate}$$

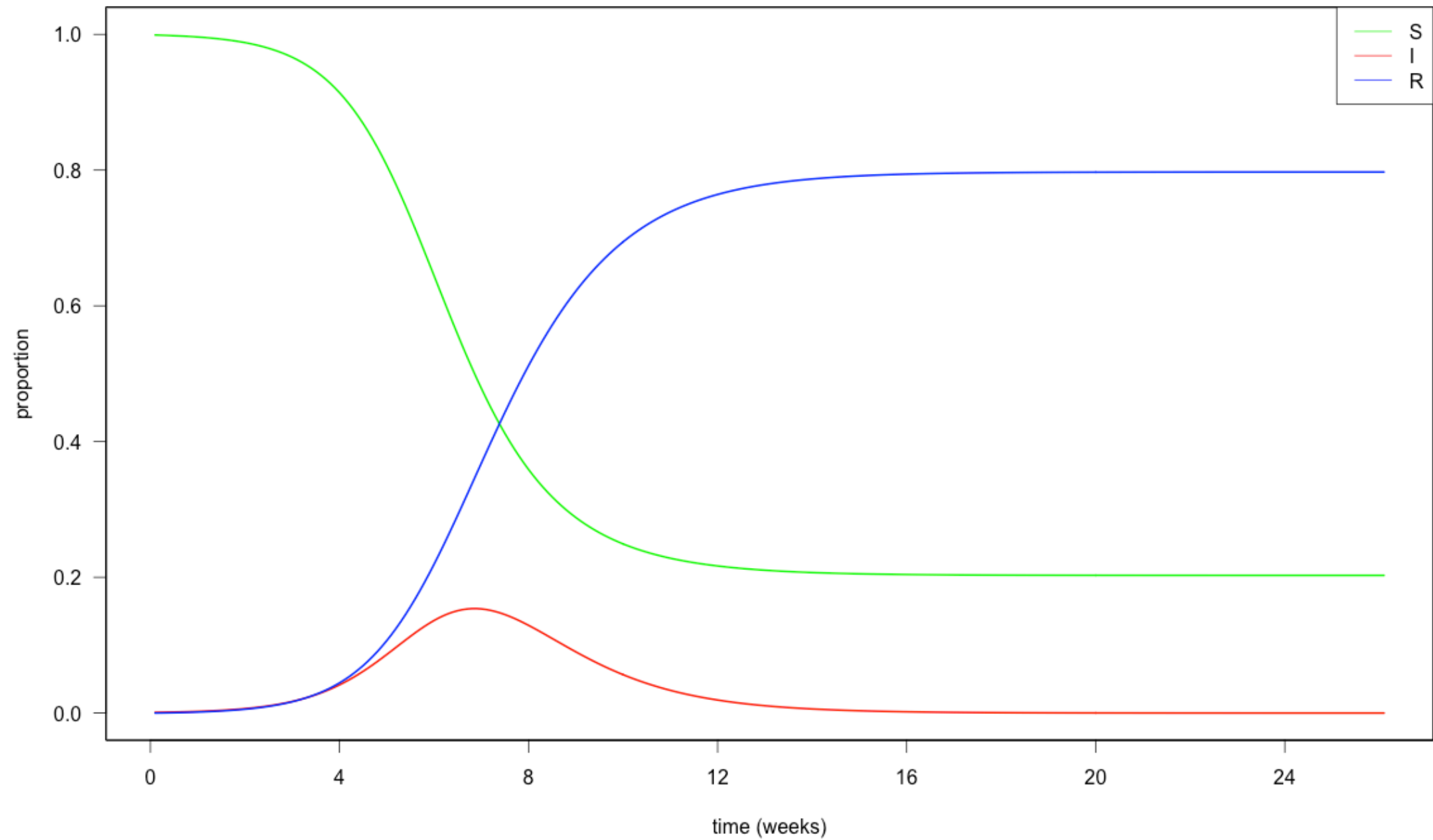
A constant growth rate means exponential growth in cases

$$\frac{dI}{dt} = \Lambda I$$

$$\Lambda = (\beta - \gamma) = \text{growth rate}$$

$$I(t) = I(0)e^{\Lambda t}$$





Exponential growth is not forever

$$\frac{dI}{dt} = (\beta S - \gamma)I$$

In the early period of the epidemic $S \approx N \approx 1$

$$\frac{dI}{dt} = (\beta - \gamma)I$$

$$\frac{dI}{dt} = \Lambda I$$

$$\Lambda = (\beta - \gamma) = \text{growth rate}$$

Epidemic Growth Rates

$$I(t) = I(0)e^{\Lambda t}$$

$$\ln(I(t)) = \ln(I(0)e^{\Lambda t})$$

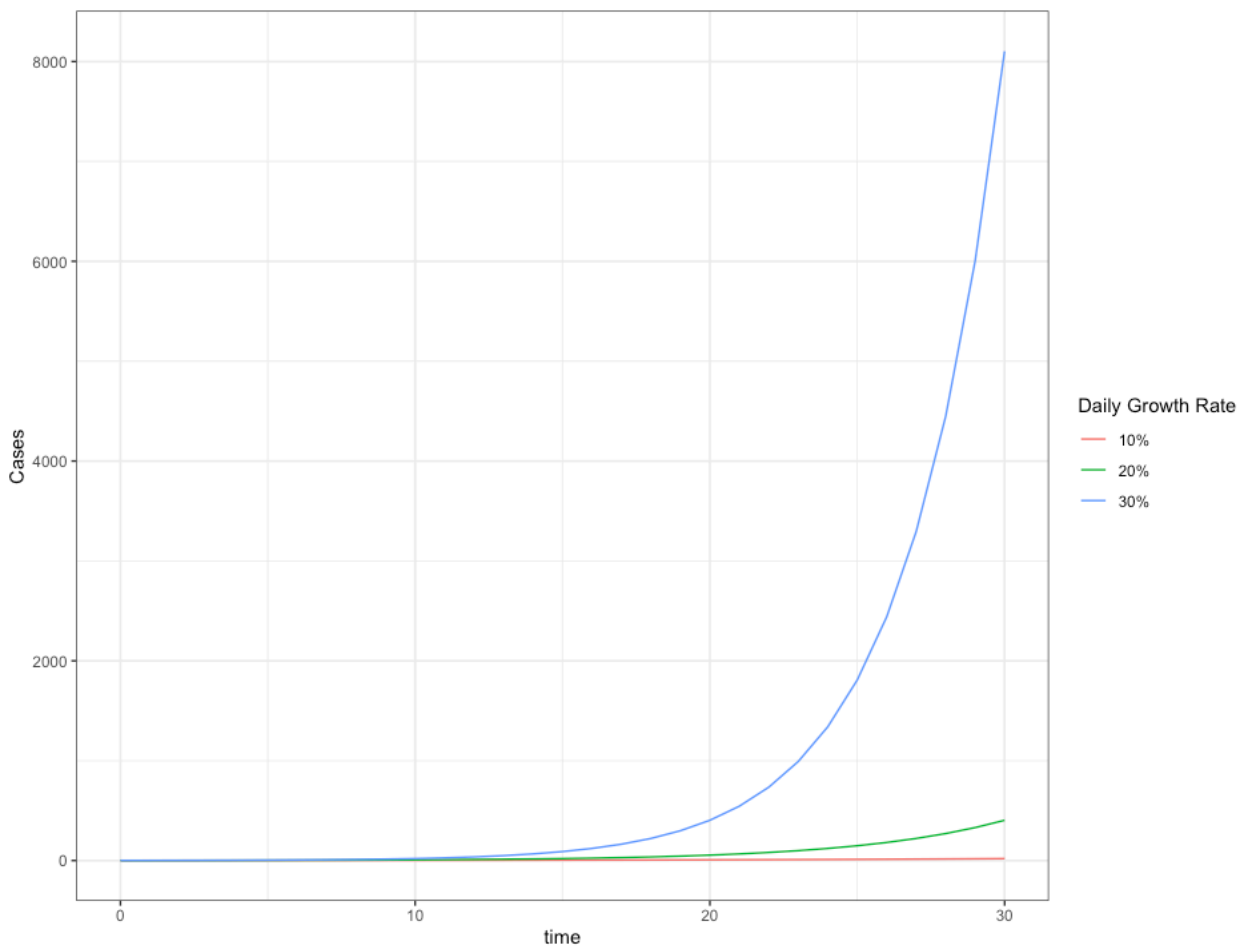
$$\ln(I(t)) = \ln(e^{\Lambda t}) + \ln(I(0))$$

$$\ln(I(t)) = \Lambda t + \ln(I(0))$$

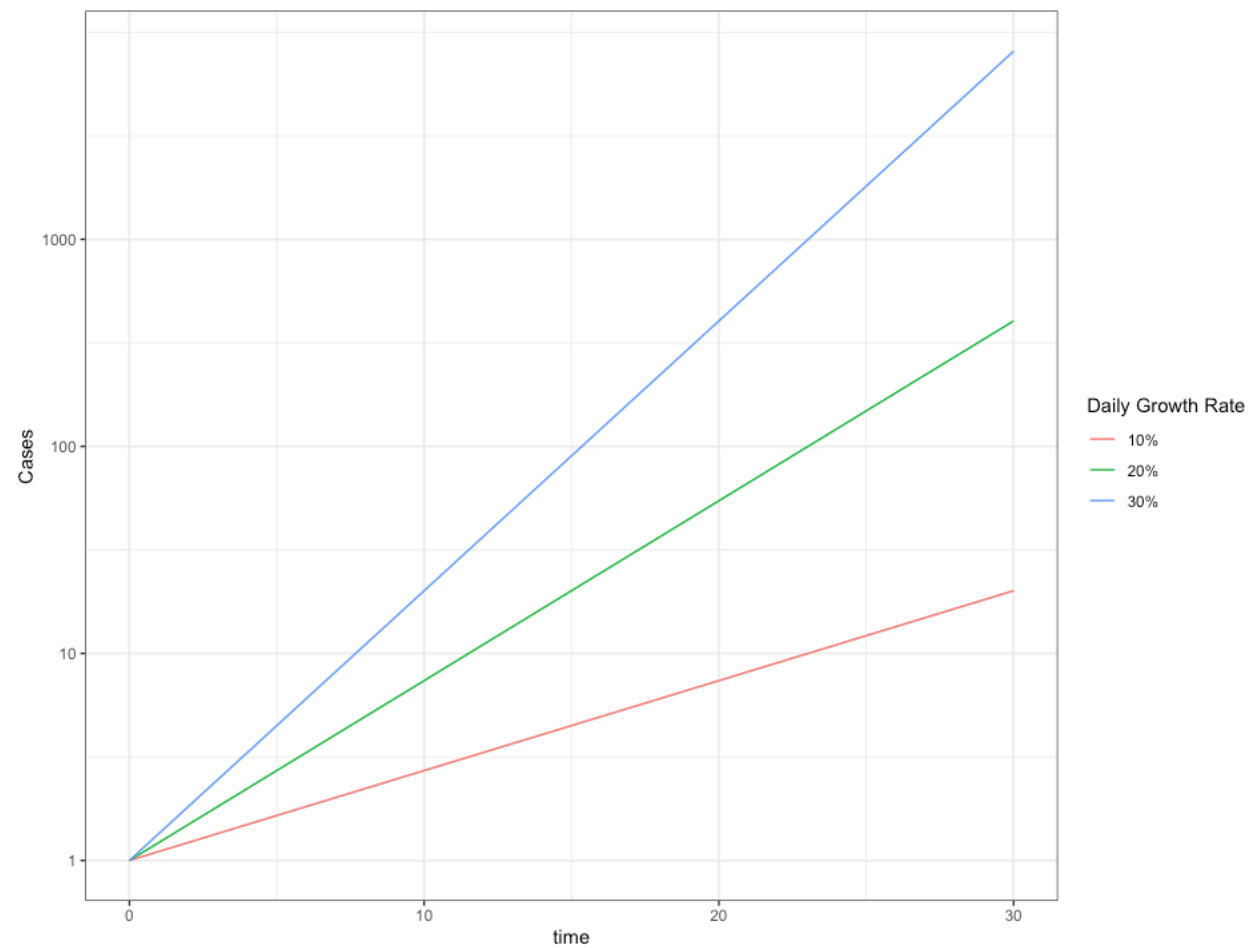
$\underbrace{\hspace{1.5cm}}$
slope intercept

$$y = mx + b$$

Regular Scale



Log Scale



Slope of log cases = daily growth rate

$$\ln(I(t)) = \Lambda t + \ln(I(0))$$

Did San Mateo County Experience Exponential Growth of Covid-19?

How can we test this?

Estimating R_0 from Epidemic Growth (for SIR model)

$$\frac{dI}{dt} = \beta SI - \gamma I$$

$$\frac{dI}{dt} = (\beta - \gamma)I$$

$$\Lambda = (\beta - \gamma)$$

$$\Lambda = (R_0\gamma - \gamma)$$

$$\Lambda = \gamma(R_0 - 1)$$

$$R_0 = 1 + \frac{\Lambda}{\gamma} = 1 + \Lambda D$$

$$R_0 = \frac{\beta}{\gamma}$$



$$R_0 = 1 + \Lambda D$$

$$D = \frac{1}{\gamma} = \text{duration of infectiousness}$$

Estimating R_0 from Epidemic Growth (for SEIR model)

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SOCIETY 

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$$R_0 = (1 + \Lambda D)(1 + \Lambda L)$$

Where:

D = duration of infectiousness

L = duration of latent period

How generation intervals shape the relationship between growth rates and reproductive numbers

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Mathematical models of transmission have become invaluable management tools in planning for the control of emerging infectious diseases. A key variable in such models is the reproductive number R . For new emerging infectious diseases, the value of the reproductive number can only be inferred indirectly from the observed exponential epidemic growth rate r . Such inference is ambiguous as several different equations exist that relate the reproductive number to the growth rate, and it is unclear which of these equations might apply to a new infection. Here, we show that these different equations differ only with respect to their assumed shape of the generation interval distribution. Therefore, the shape of the generation interval distribution determines which equation is appropriate for inferring the reproductive number from the observed growth rate. We show that by assuming all generation intervals to be equal to the mean, we obtain an upper bound to the range of possible values that the reproductive number may attain for a given growth rate. Furthermore, we show that by taking the generation interval distribution equal to the observed distribution, it is possible to obtain an empirical estimate of the reproductive number.

Keywords: basic reproduction ratio; epidemiology; influenza; Lotka–Euler equation; serial interval

What was the reproductive number in the first four weeks of our data?

$$R_0 = (1 + \Lambda D)(1 + \Lambda L)$$

Assume that the average duration of latency is 3 days, average duration of infectiousness is 4 days, and growth rate in Santa Clara was 0.16

$$R_0 = (1 + 0.16 * 3) * (1 + 0.16 * 4) = 2.43$$

Intuition behind R_0 , growth rate and serial interval relationship

$$R_0 = (1 + \Lambda D)(1 + \Lambda L)$$

Imagine you have two diseases with the same R_0 , one with a faster growth rate and one with a slower growth rate. Which one would have the longer serial interval?

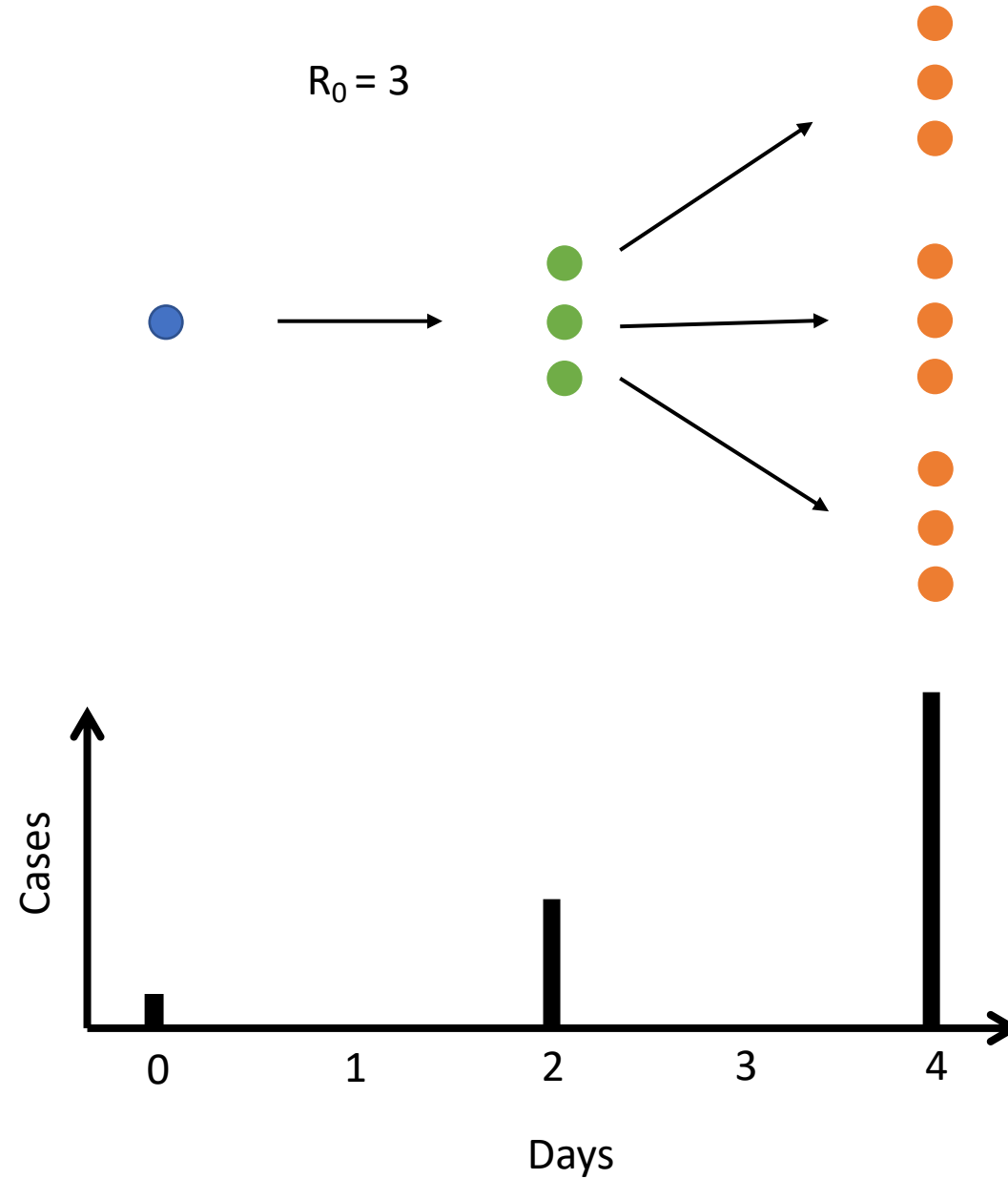
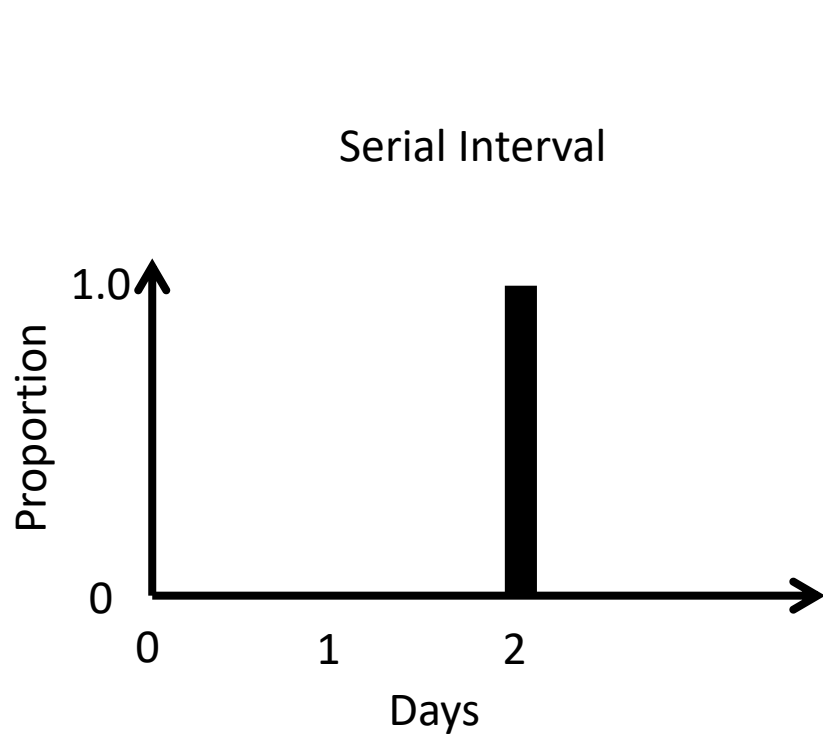
Longer serial intervals slow down epidemic growth. If we compare two pathogens with same R_0 , the pathogen with shorter serial interval will spread faster (i.e. it will have a higher growth rate).

By same logic, to achieve an equivalent growth rate, a pathogen with longer serial interval requires a higher R_0 (it spreads slower so has to spread to more people to achieve same growth rate).

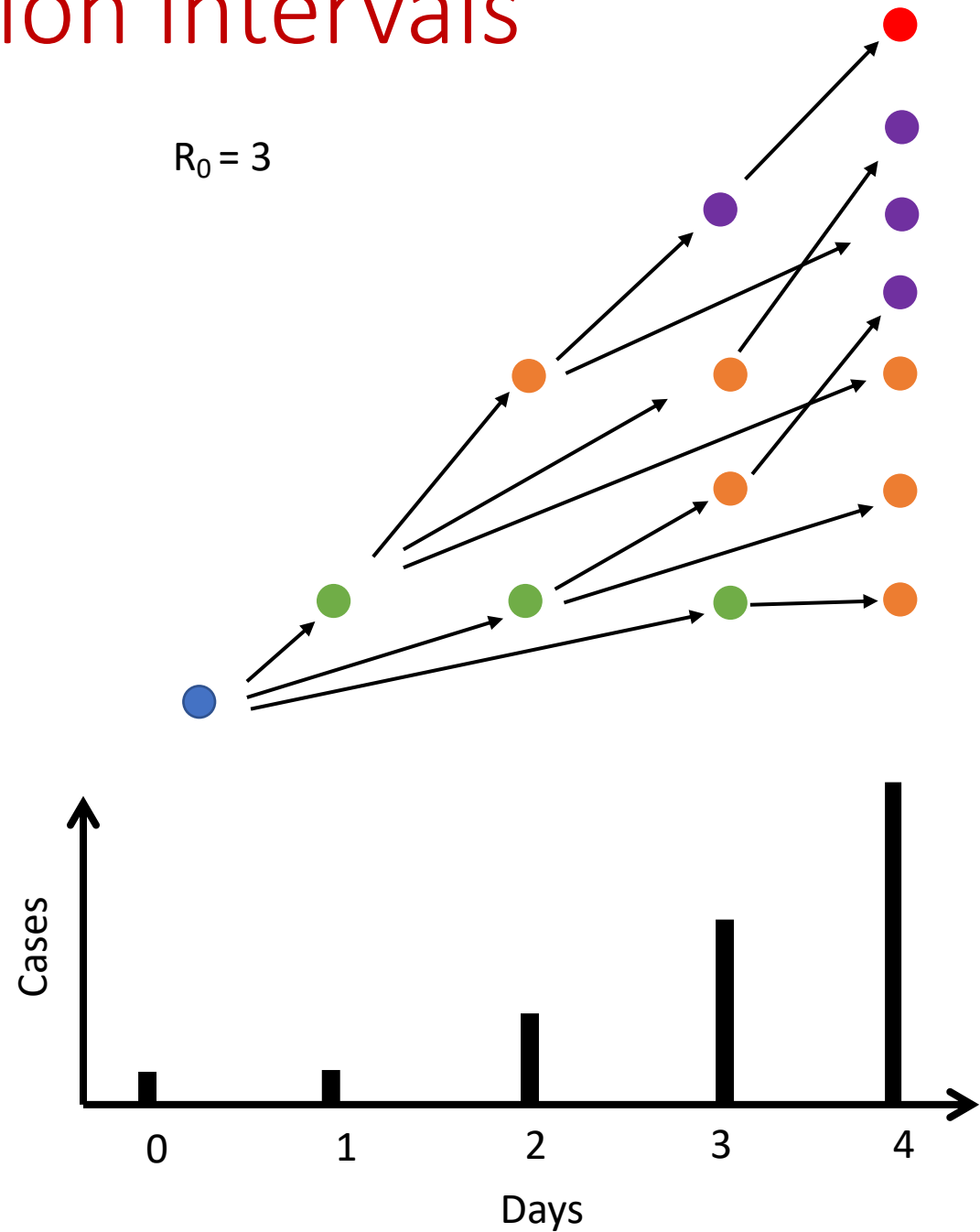
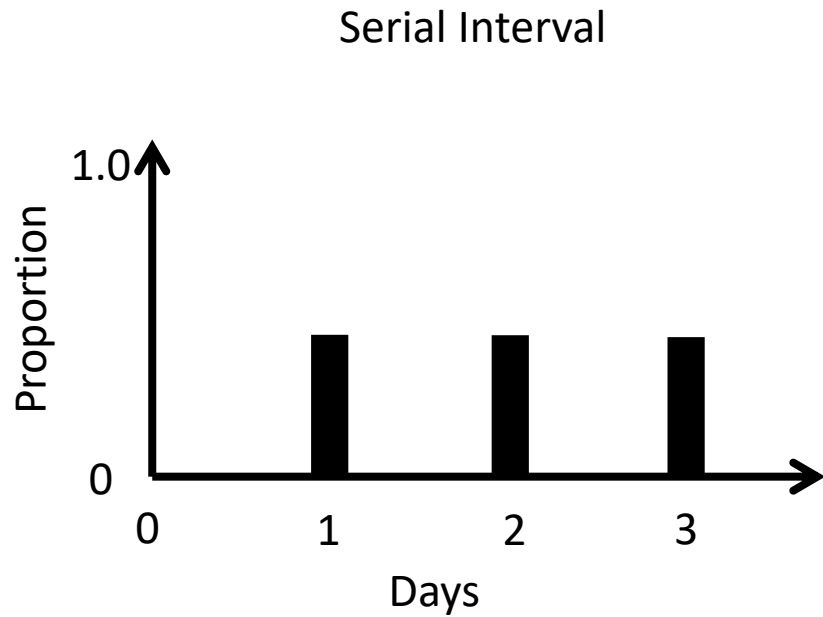
Did R_t change during the epidemic?

- What would have happened in Santa Clara if the reproductive number remained at 2.43?
- What did happen?

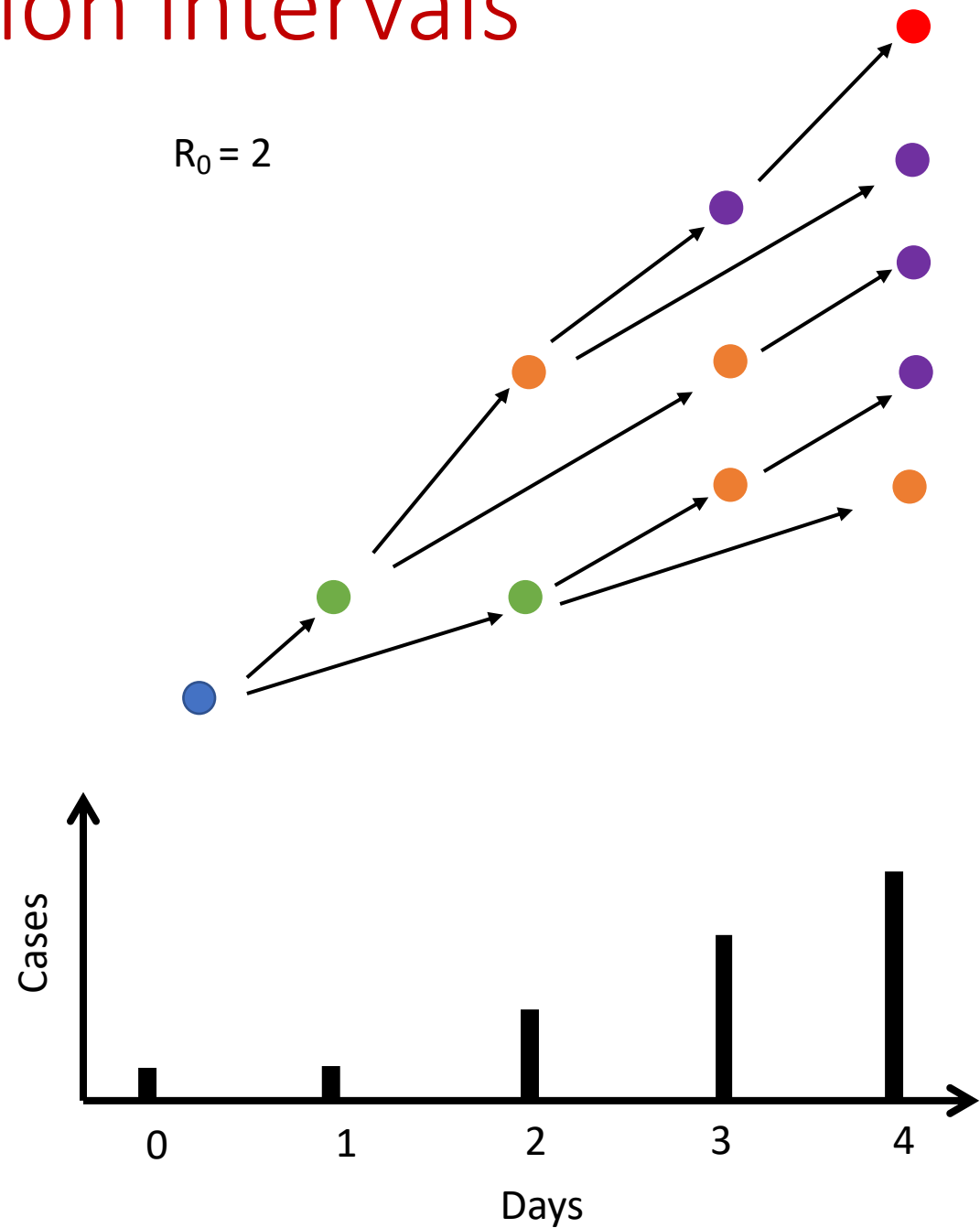
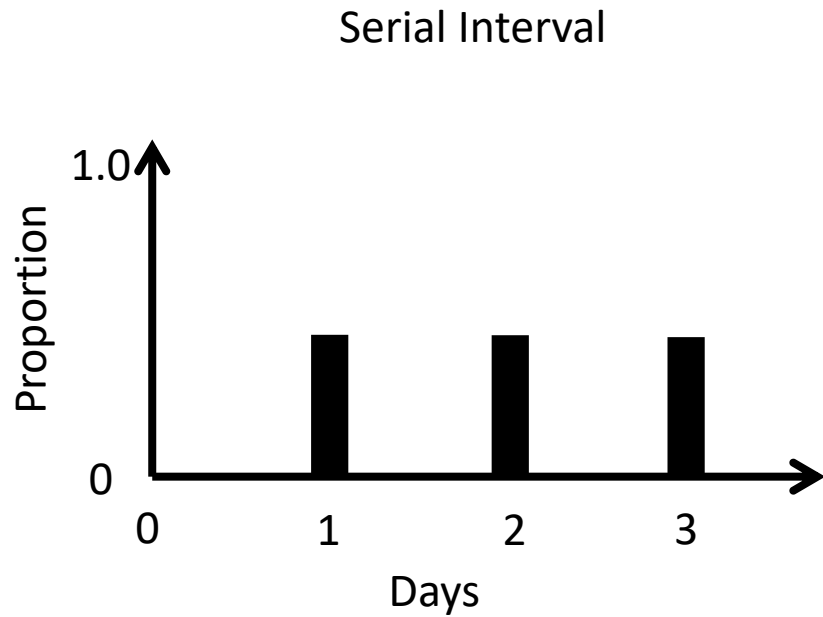
R_0 , growth and generation intervals



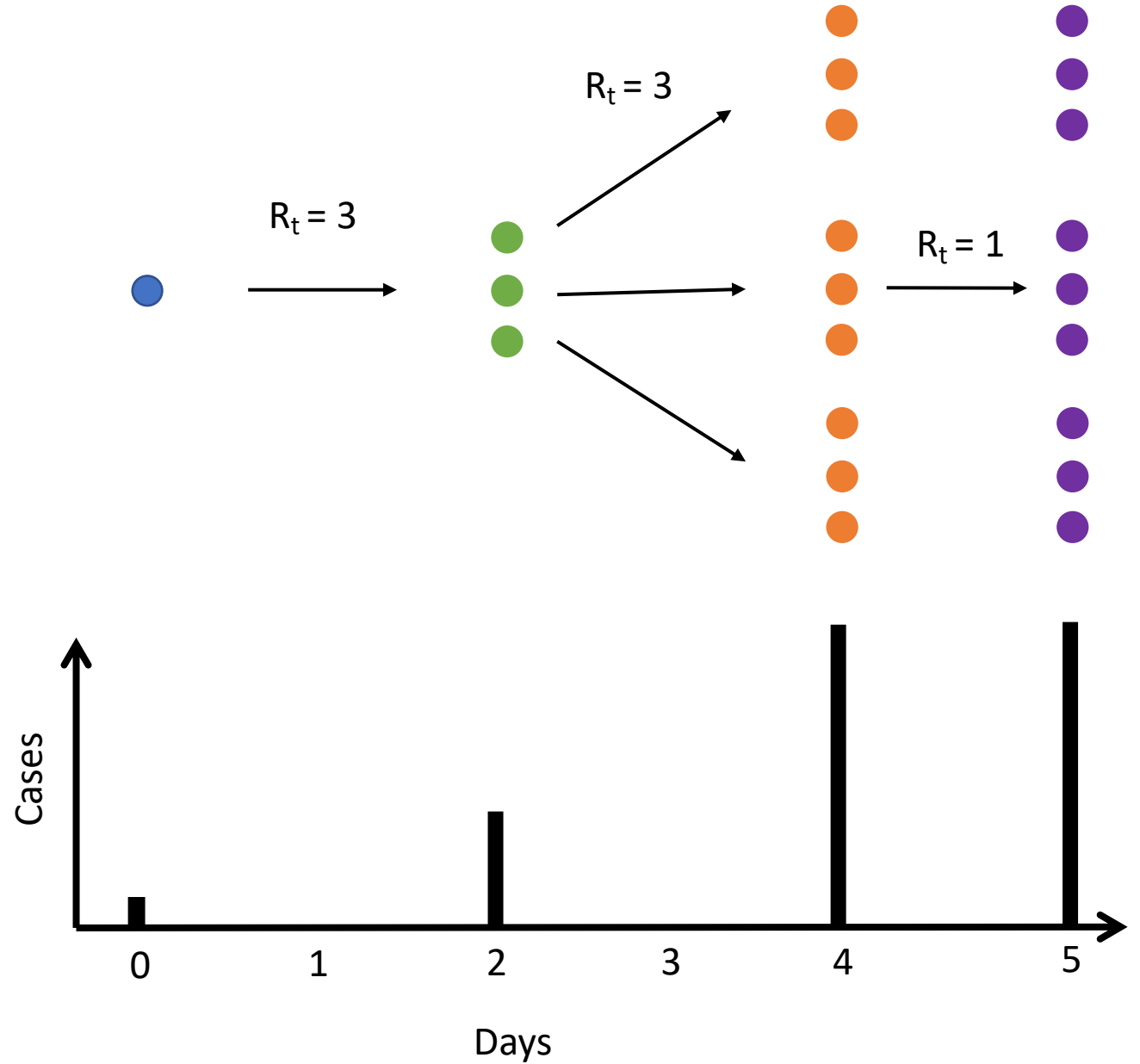
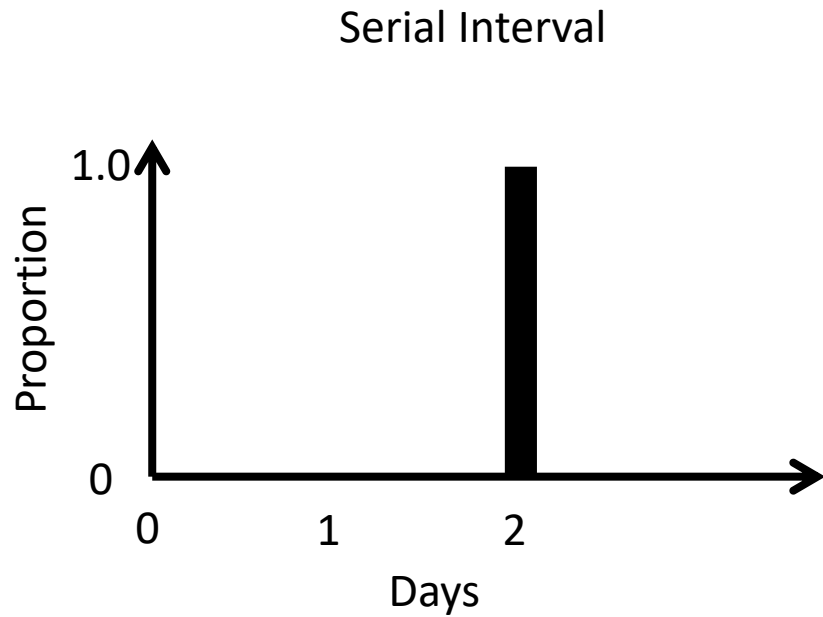
R_0 , growth and generation intervals



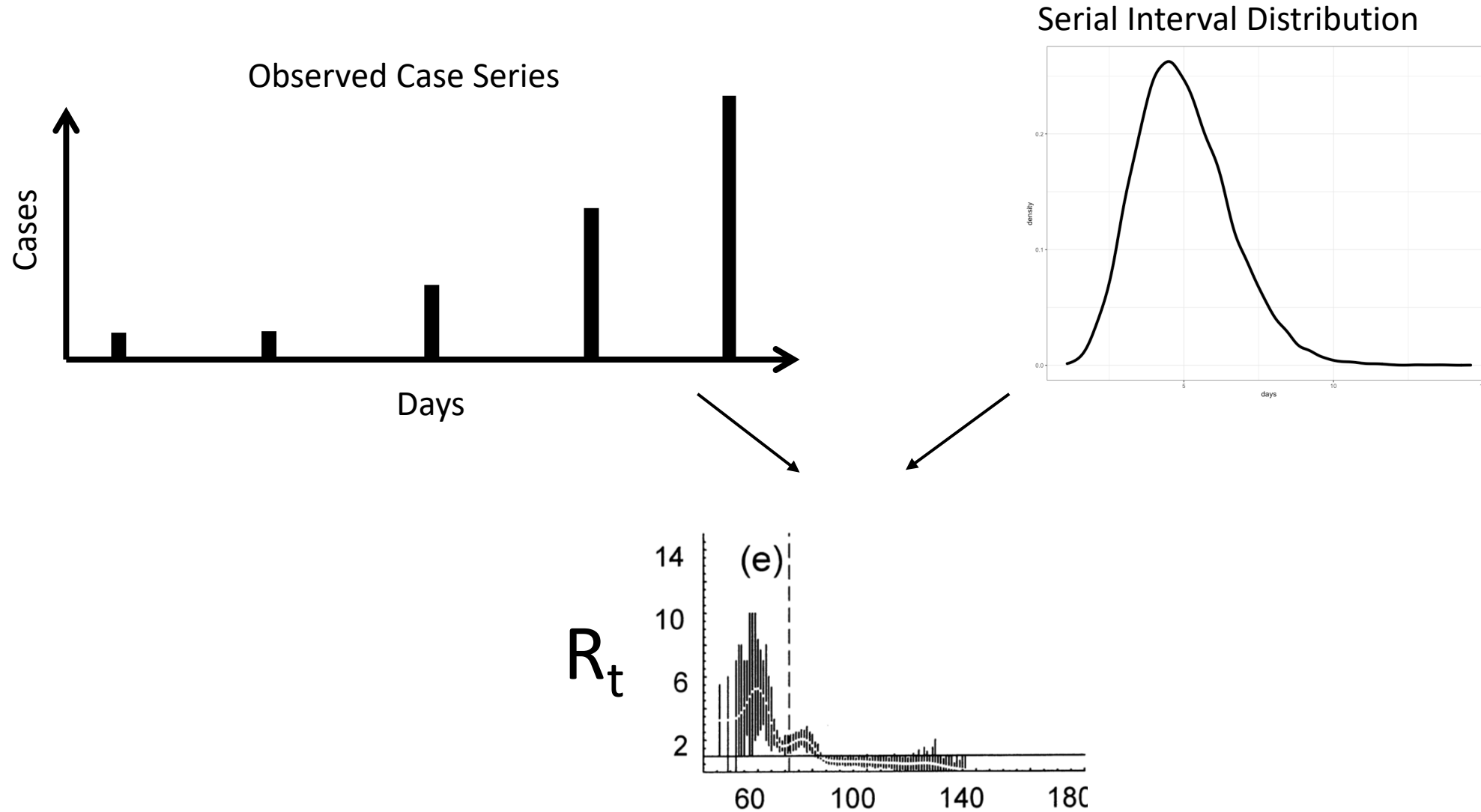
R_0 , growth and generation intervals



R_0 , growth and generation intervals



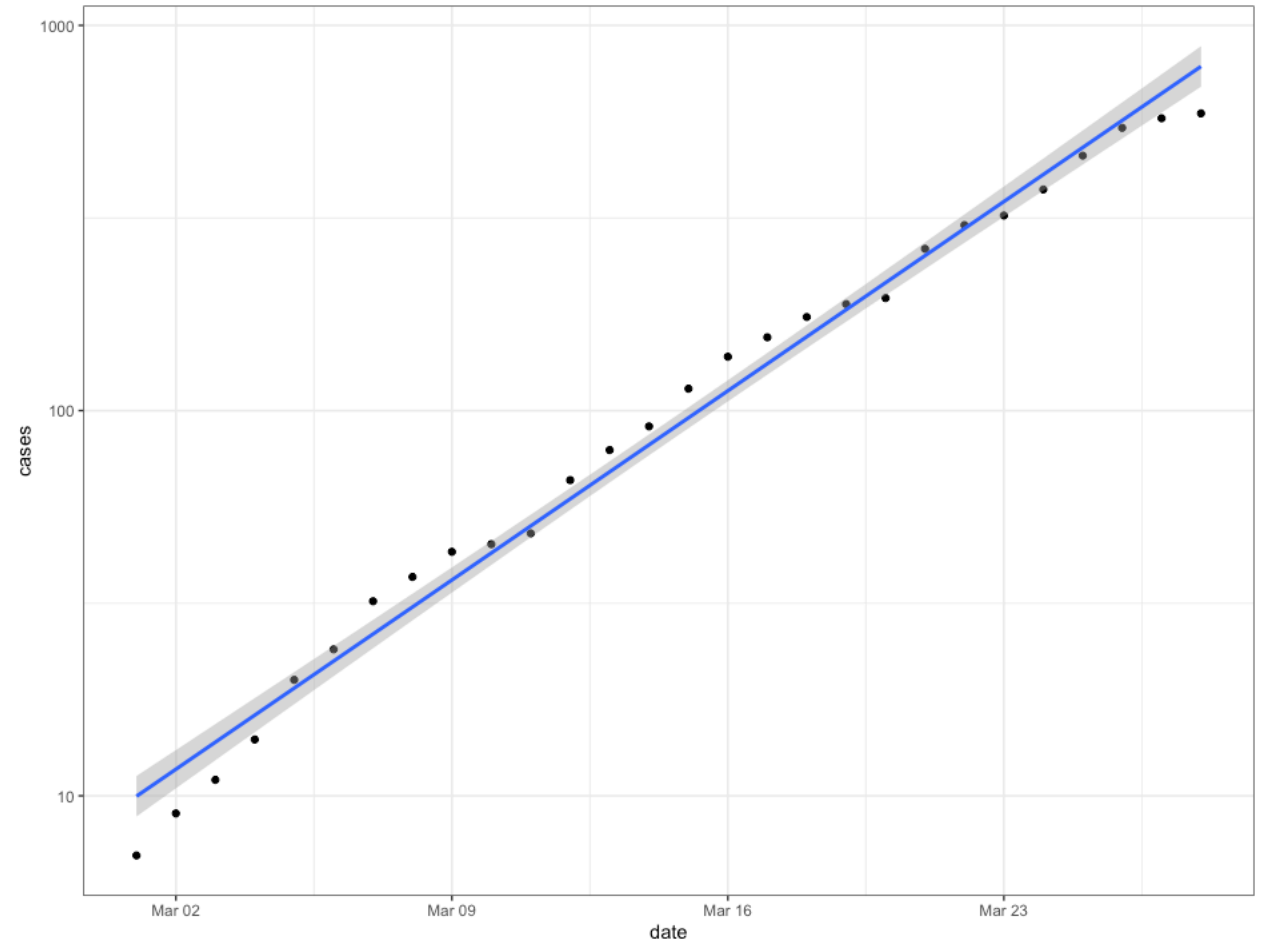
Wallinga—Teunis Method for R_t estimation



R_t for Santa Clara County

Estimating the reproductive number from “real-world” data

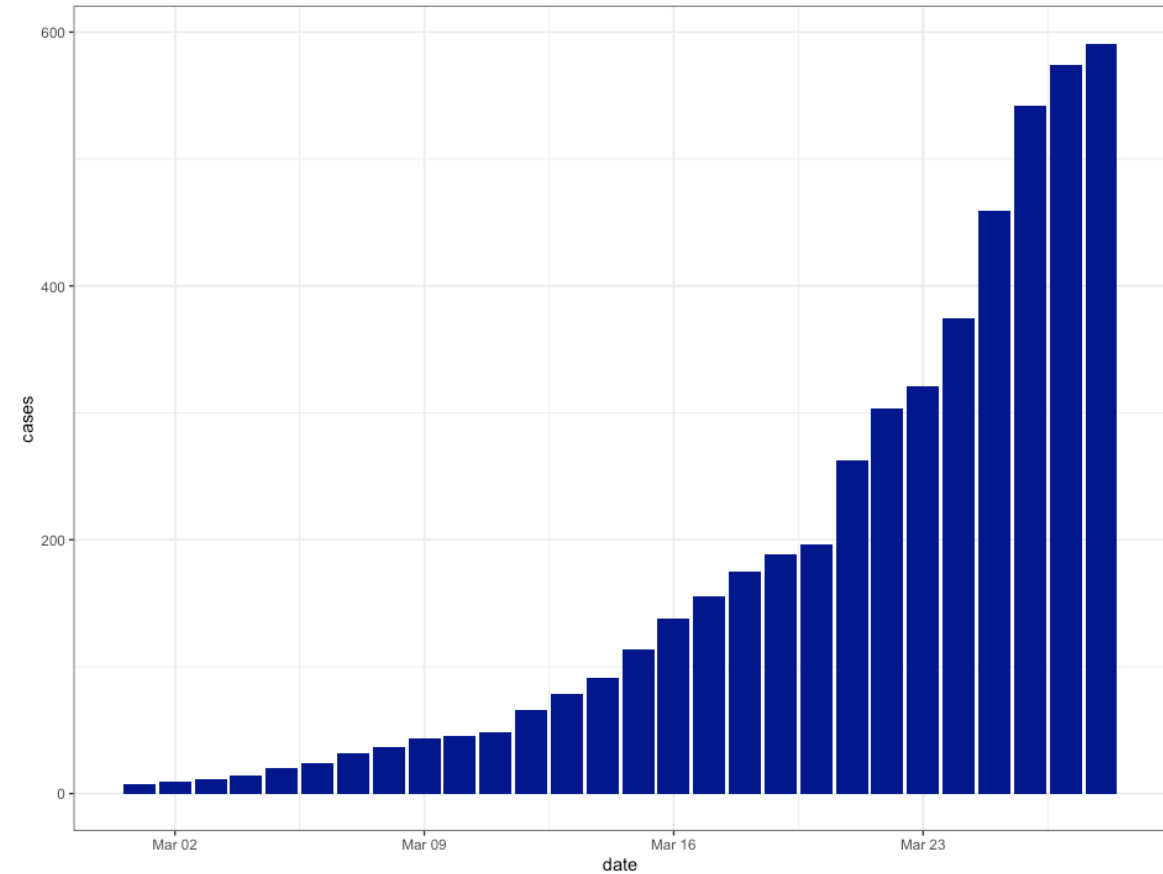
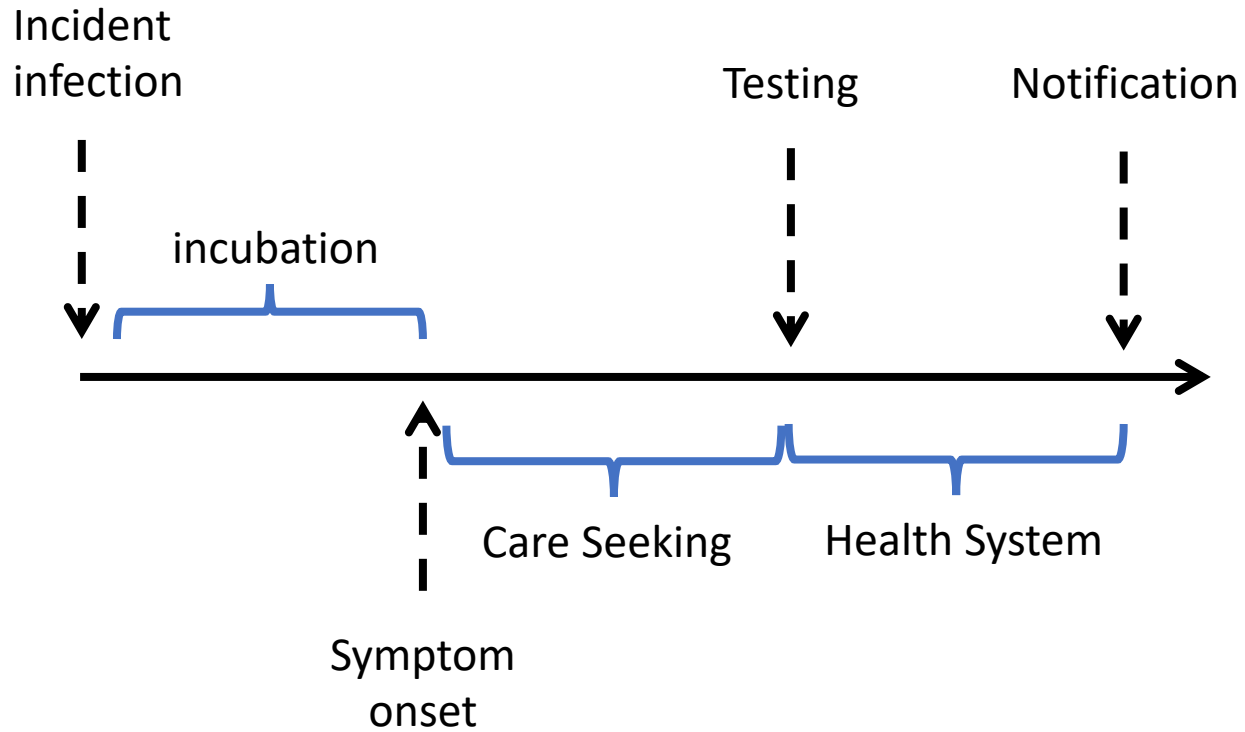
For both the “growth rate” approach and the Wallinga-Teunis approach, the estimate of R_0 is not substantially affected by the proportion of cases that are detected and reported, as long as that proportion doesn’t change across the time period



What if testing changes?

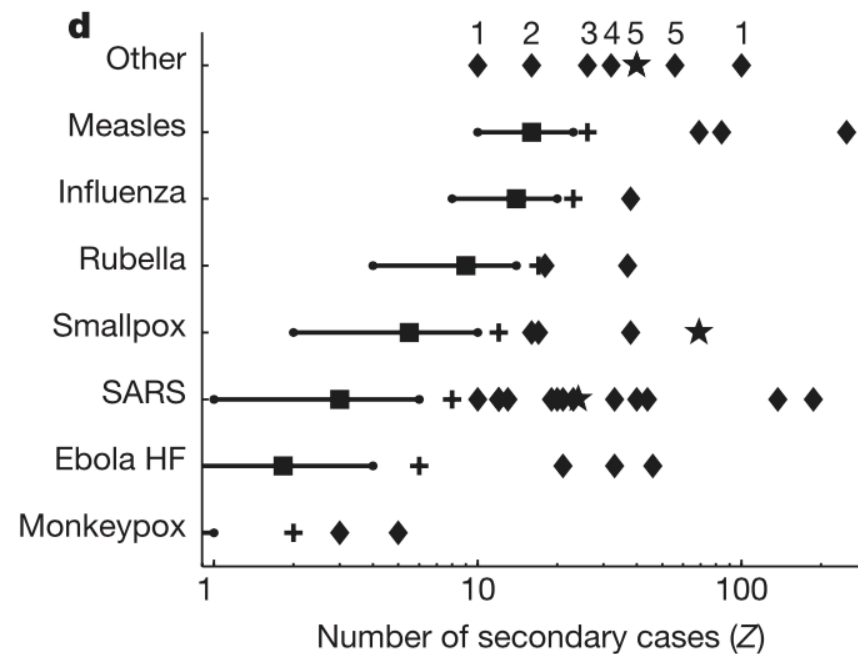
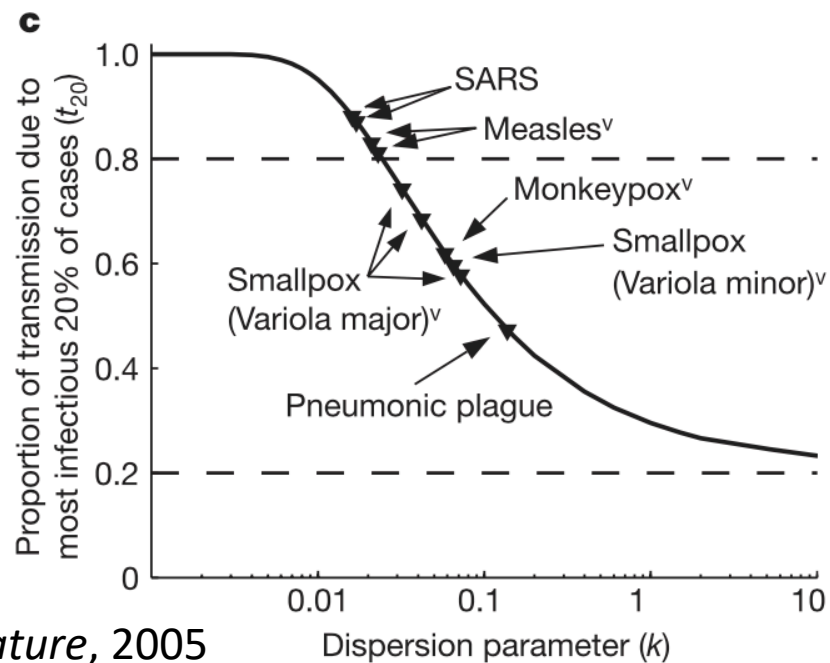
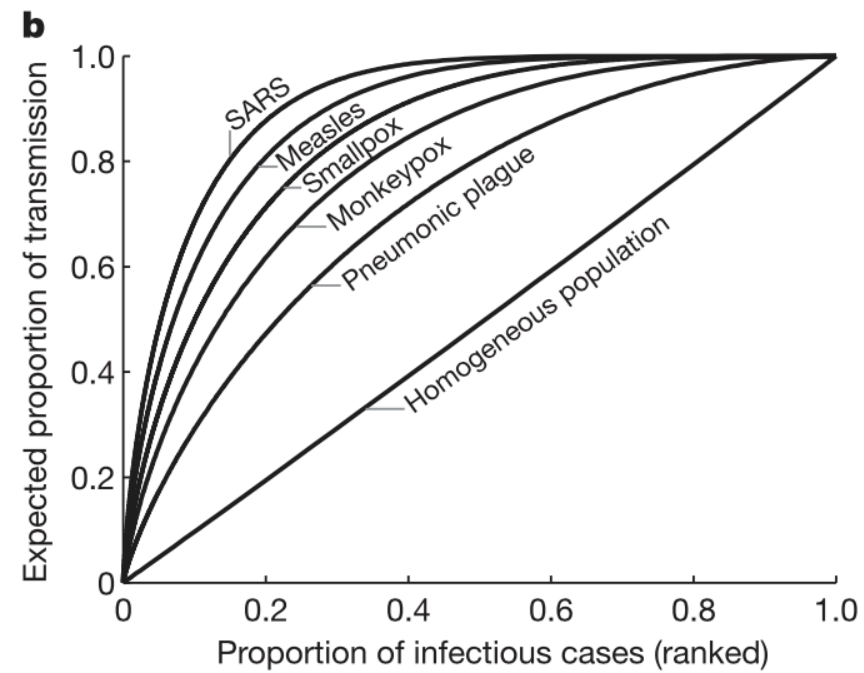
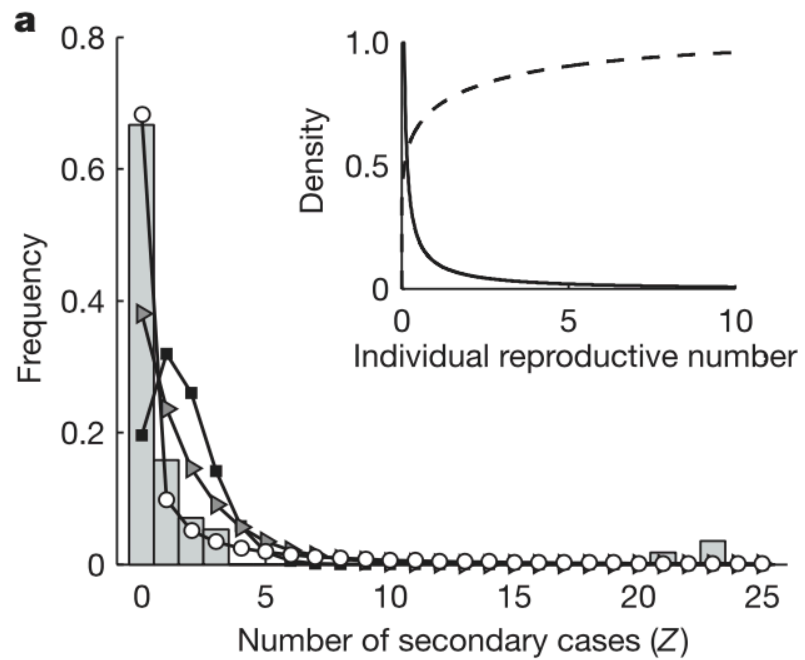
- If testing capacity grows faster than epidemic growth, what would the impact on R_0 estimate be?
- If testing capacity is saturated, forcing testing policies to become more restrictive (e.g. focused on severe cases), what would be the impact on R_0 estimate?

Incidence versus notifications

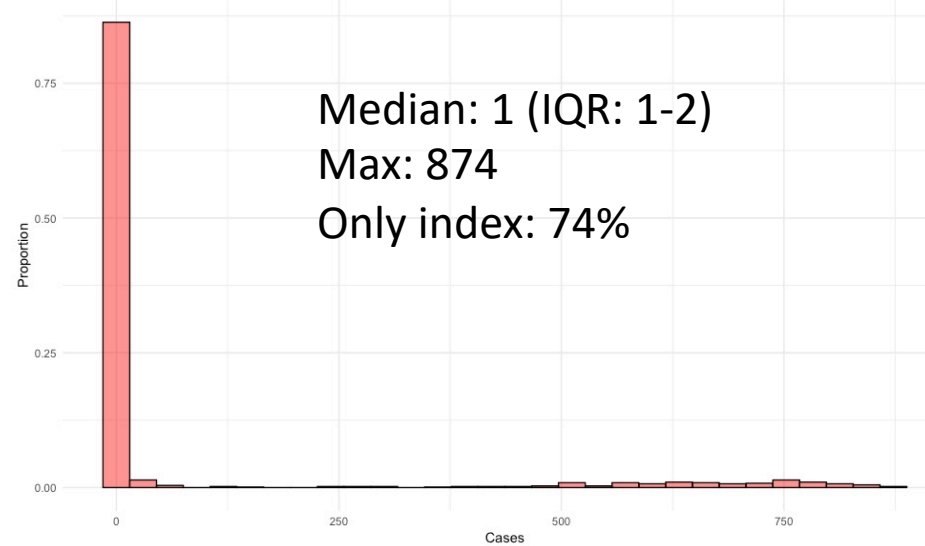
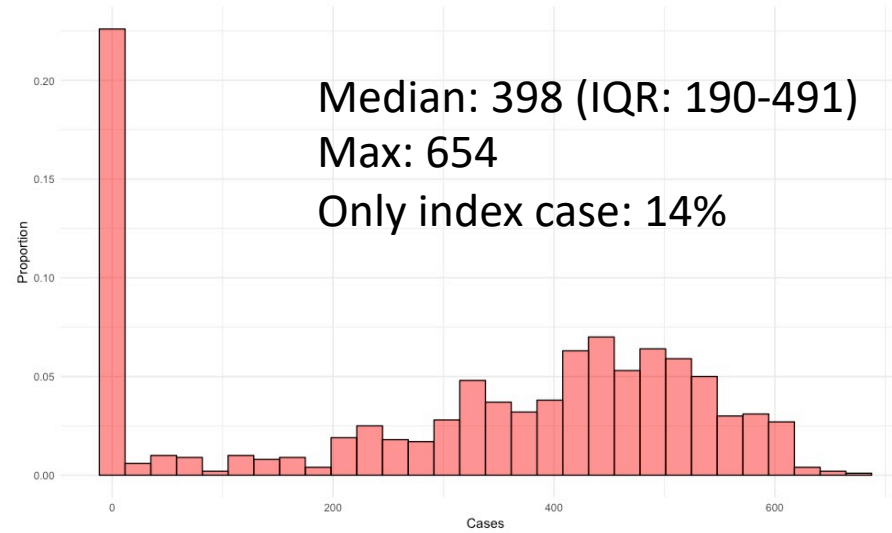
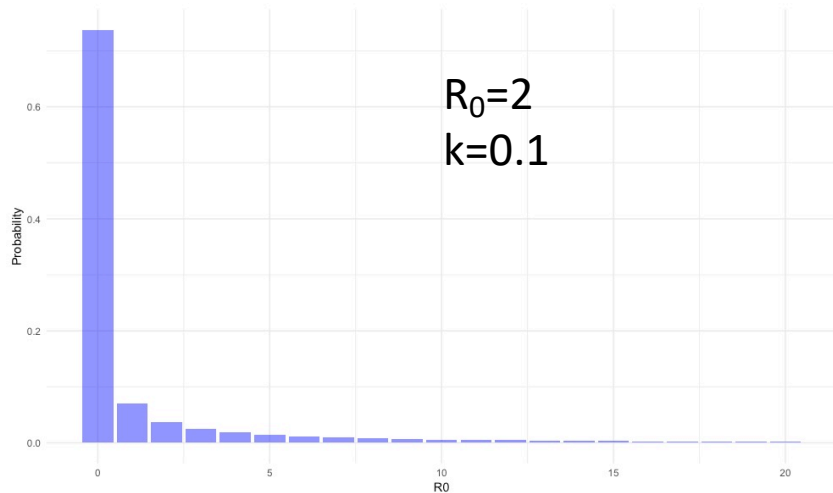
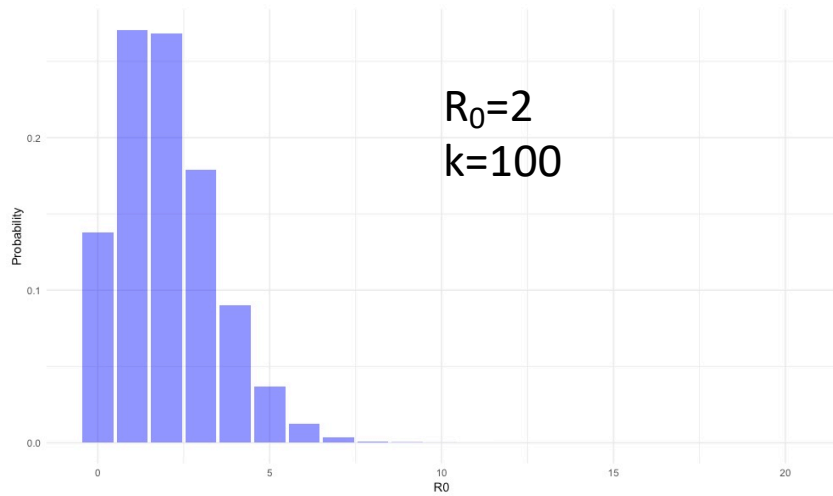


Variation in secondary cases

- R_0 is the **average** number of secondary cases generated by one infectious person in an entirely susceptible population
- What if there is substantial variation in infectiousness between individuals?
- Will outbreaks and epidemics be more or less likely to occur?



More variability = More chances for extinction



Community Transmission of SARS-CoV-2 at Two Family Gatherings — Chicago, Illinois, February–March 2020

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FIGURE 2. Likely incubation periods for confirmed and probable cases of COVID-19 following transmission of SARS-CoV-2 at two family gatherings (N = 15)* — Chicago, Illinois, February–March 2020

