Dynamics 1: First Models

April 9, 2020

Course Roadmap

1. First Models
2. SIR models with demography
3. Reproductive Number, Thresholds, Equilibria
4. Lab: Dynamic Models in R
5. Heterogeneous mixing and temporal modeling
6. Emerging infections: takeoff, growth, extinction
7. Lab: Emerging infections
8. Vectors, zoonoses, & environmental transmission
9. Stochastic dynamics
10. Spatial models, networks
11. Interventions and sensitivity analyses
12. Lab: Interventions and sensitivity analyses
13. Competition and evolutionary models
14. Within host evolution
15. Lab on Parameterization, calibration, and uncertainty
16. Health policy and economic evaluation models
17. Uses and abuses of models

Practical Questions

What determines whether a disease will spread in a population and how many people will become infected?

What stops infectious diseases from infecting everyone?

Learning Objectives

- Distinguish static from dynamic models of infectious diseases
- Become familiar with the components and properties of a SIR model
- Become comfortable with common terminology in models: effective contact rate, force of infection, incidence, recovery rate
- Understand the basic reproductive number and its importance in infectious disease epidemics
- Identify conditions under which an outbreak may occur and the role of herd immunity in preventing spread

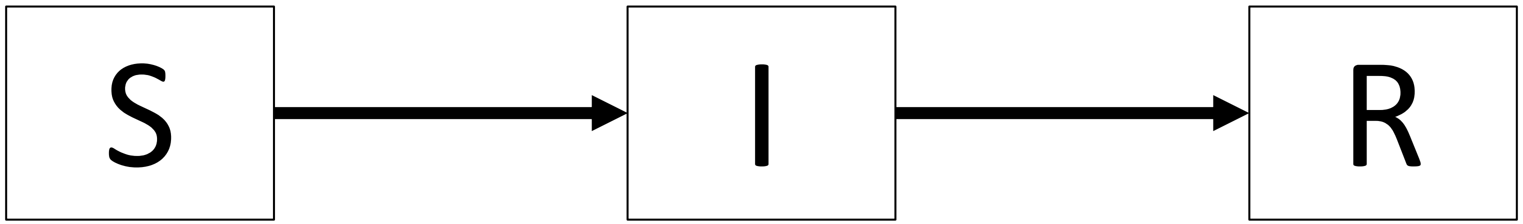
About the math

- Goal is to understand the connections between concepts
- Show basic properties of models without rigorous derivations
- Course is focused on more practical skills; problem sets and exams will not require mathematical proofs or any complex mathematical procedures

Seemingly complex observed patterns of infectious disease epidemics can be explained by simple models

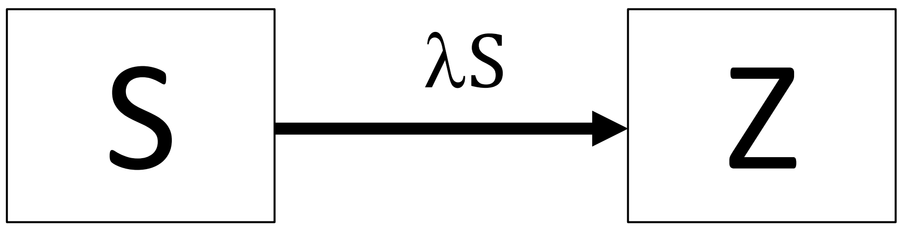
Compartmental Models

- Represent individuals according to health states
  - Here S, I, R = fractions of population in each state (S+I+R = N = 1)
  - S, I, R can be numbers of people (Keeling and Rohani use X, Y, Z for this)
- Model changes in those states over time
- Often analyzed by ordinary differential equations



The Catalytic Model

- Susceptible (S)
- Ever Infected (Z)
- Assume infection risk (λ) is static, not driven by changes in population burden
- Useful in sero-epidemiology



The Catalytic Model

- Assume that 100% of individuals are born susceptible to disease
- If the probability of infection is constant at 5% per year, what % of the population will have been infected by age 10?

λ= annual risk of infection

$$\boxed{S} \xrightarrow{\lambda S} \boxed{Z}$$

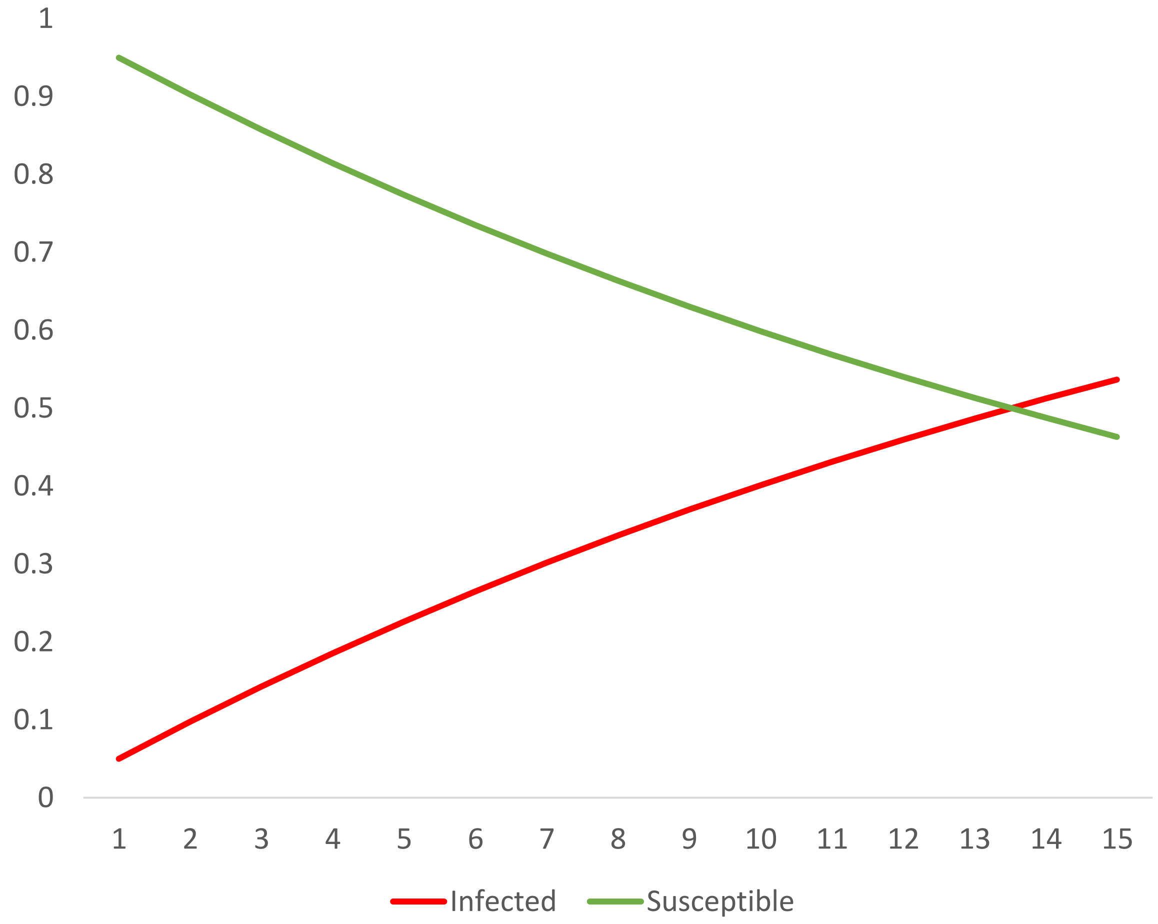
The Catalytic Model

S(0) = 1.00
S(1) = 1.00*(1-0.05) = 0.95
S(2) = 0.95*(1-0.05) = 0.9025
S(3) = 0.9025*(1-0.05)= 0.857

$S(t) = S(0)*(1-p)^t = \mathbf{(1\text{-}p)^t}$
p=0.05

Z(t) = 1 – S(t)
$Z(t) = 1 - S(0)*(1-p)^t = \mathbf{1\text{-}(1\text{-}p)^t}$

Z(10) = 0.40



Uses for the Catalytic Model

- A cross-sectional survey found that 2/3 of children were infected with TB by the age of 15 in one community in Western Cape, South Africa
- What is the annual risk of infection?

$$Z(t) = 1 - (1-p)^t$$

$$1 - Z(t) = (1-p)^t$$

$$\left(1 - Z(t)\right)^{\frac{1}{t}} = (1-p)$$

$$p = 1 - \left(1 - Z(t)\right)^{\frac{1}{t}}$$

$$t \;\; = 15$$

$$Z(15) = 0.67$$

$$p = 1 - (1 - 0.67)^{\frac{1}{15}}$$

$$p = 0.07$$

Continuous time catalytic models

$$\boxed{S} \xrightarrow{\lambda S} \boxed{Z}$$

$$\frac{dS(t)}{dt} = -\lambda S(t)$$

$$\frac{dS(t)}{S(t)} = -\lambda dt$$

$$\ln\big(S(t)\big) = -\lambda t + C$$

$$S(t) = e^{C} e^{-\lambda t} = S(0)\, e^{-\lambda t}$$

Rates versus Probabilities

$$S(t) = S(0) \times (1 - p)^t$$

p = probability event occurs during a time interval

$$S(t) = S(0) \ \times \ e^{-\lambda t}$$

λ = rate = events / time

$$p = 1 - e^{-\lambda t}$$

$$\lambda = -\frac{1}{t}\ln(1 - p)$$

Rates versus Probabilities

Suppose on average, individuals have 2 upper respiratory infections per year. What is the probability that an individual will have at least 1 respiratory infection in a given year?

$$p = 1 - e^{-\lambda t}$$

$$\lambda = 2,\ t=1$$

$$p = 0.86$$

Summary: Catalytic Models

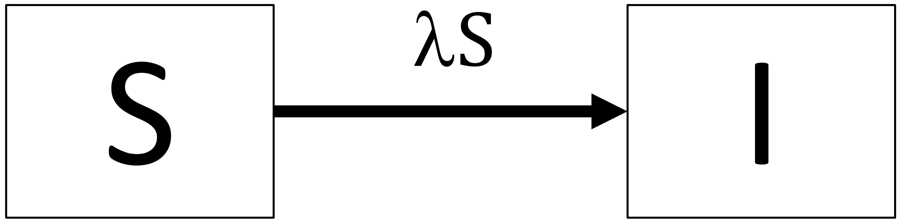
- Can be useful for relating cumulative disease risk over time with infection rates
- Can be adapted to time- or age-varying rates
- Don’t account for dynamic changes in infection rates that occur as the proportion of infected individuals changes
- Static models

Dynamic Compartmental Models

Brief Intro to Differential Equations

$$\frac{dS(t)}{dt} = -\lambda S(t)$$

$$\frac{dI(t)}{dt} = \lambda S(t)$$



Have to specify initial conditions (S(0) and I(0))

If rate is negative, compartment is declining, if positive, increasing

The rates on the right side must add up to 0.

These are a series of ordinary differential equations (ODE)

Dynamic Compartmental Models

- Now assume that the rate of infection depends on infection, it is changing (dynamic)
- $\lambda(t) = \beta I(t)$

$$\boxed{S} \xrightarrow{\lambda S} \boxed{I}$$

Catalytic (Static) Model

$$\boxed{S} \xrightarrow{\beta SI} \boxed{I}$$

Dynamic Model

Force of Infection

- The **force of infection** (λ) is the rate at which susceptible individuals are infected.
- It is a function of the proportion (or number) of infected individuals and the rate at which they infect others
- We call this the **effective contact rate** (β)

$$\lambda(t) = \beta I(t)$$

Effective Contact Rate (ECR)

- The ECR is the number of infections generated by an infectious person, over a defined period of time (i.e. daily, monthly, yearly) to a susceptible population
- ECR is sometimes broken down into multiple components, for example:

$$\beta = k * p$$

Where:

k = number of contacts per unit time

p= probability of infection for each contact

Effective contact rate example

- Suppose I have measles and contact 10 people per day, and 90% of those exposed to me are infected
- What is my effective contact rate?
- Per week?

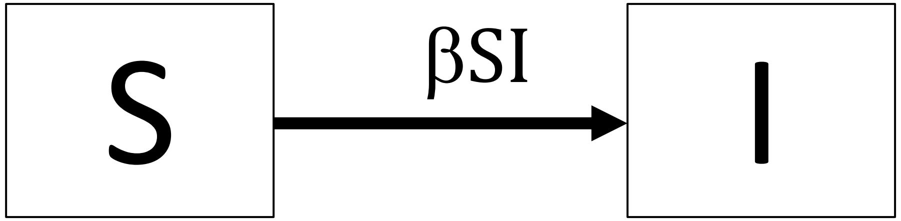
Force of Infection vs Incidence

- What is the difference between the force of infection and incidence?
- Force of infection = $\lambda(t) = \beta I(t)$

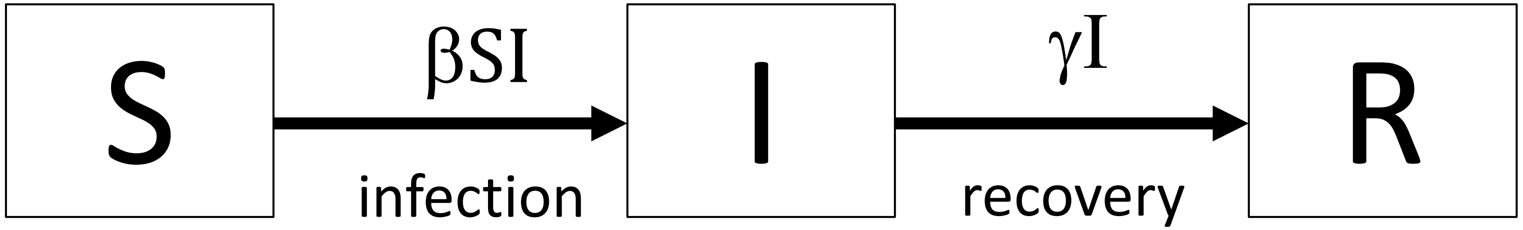
$$\boxed{S} \xrightarrow{\beta SI} \boxed{I}$$

Force of Infection, Incidence, Prevalence

- Force of infection = $\beta I(t)$
- Incidence = $\beta S(t) I(t)$
- Prevalence = $I(t)$



The SIR Model



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

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

$$\frac{dR(t)}{dt} = \gamma I(t)$$

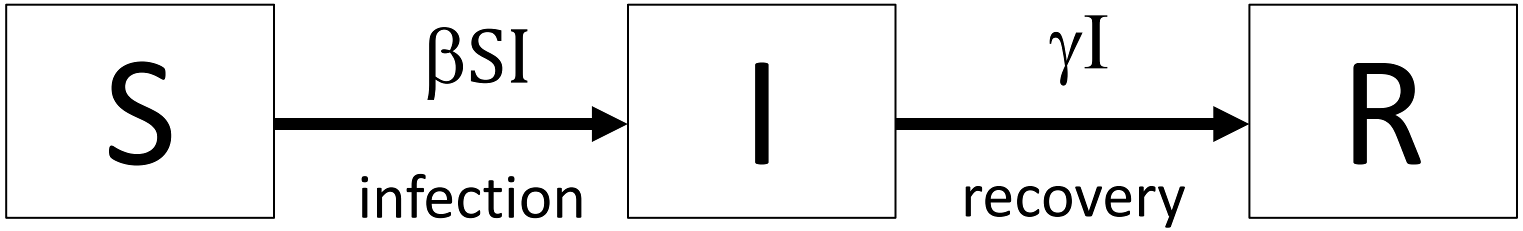
From here on out, I'll drop the "(t)"

On Rates

- The inverse of a rate is the average time until the event occurs
- For example, suppose a train stops 4 times per hour
- What is the average time between stops?

- In epidemiologic models, we often measure the average time between events, and then convert to rates.
- Suppose the average duration of influenza infection is 1 week, what is the daily rate of recovery?
- What is the yearly rate of recovery?

Model Behaviors



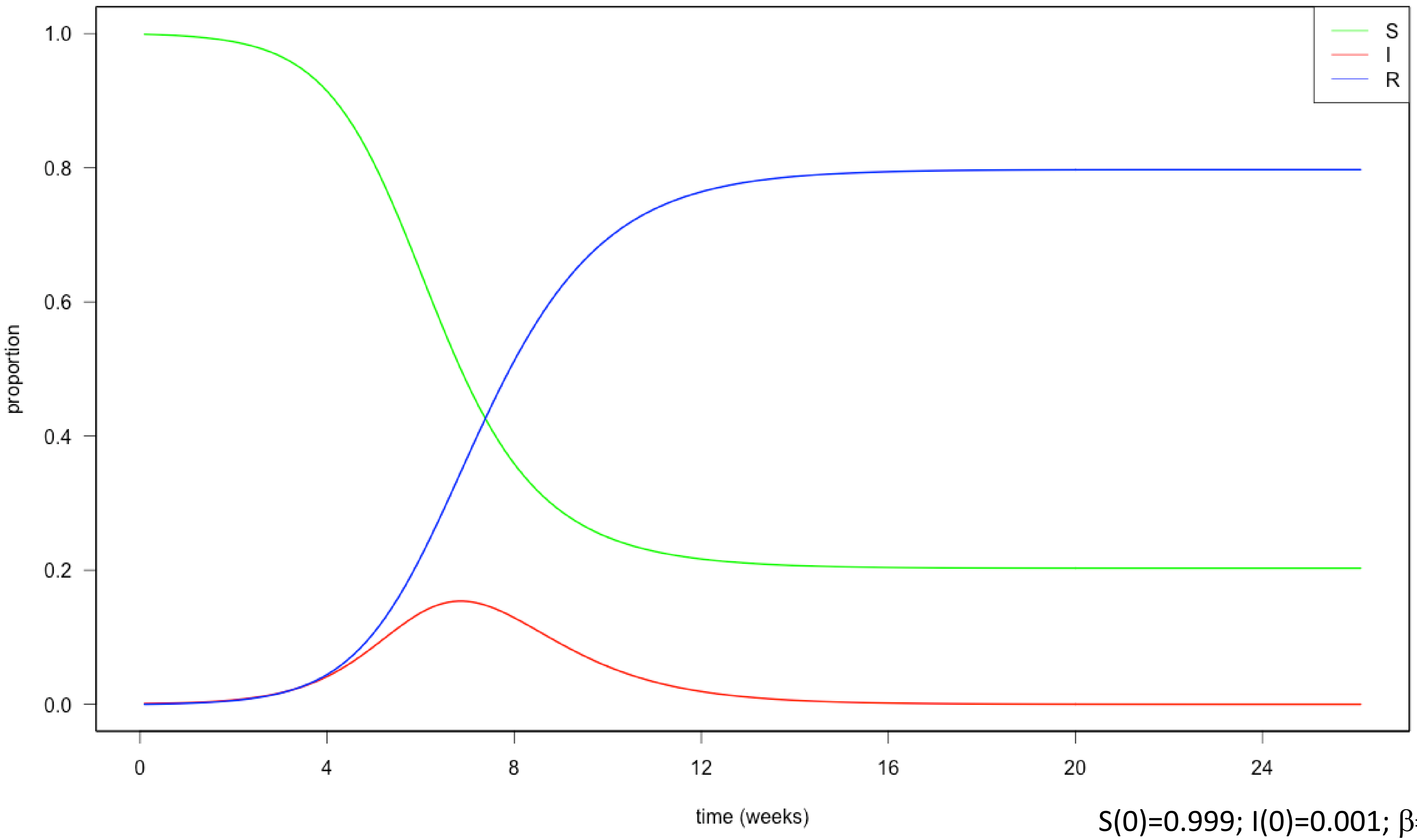
$$\frac{dS}{dt} = -\beta SI$$

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

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

“Solving” SIR Models

- We want to solve for S, I and R over time
- Because of the S x I term, there is no exact analytical solution
- Numerical methods using discrete time algorithms



S(0)=0.999; I(0)=0.001; β=2; γ=1

Questions we can ask of this model

- Under what conditions can an epidemic occur?
- Under what conditions can an epidemic be prevented?
- What will be the total size of the epidemic?

Under what conditions can an epidemic occur?

Scenario 1: $S(0) = 1$, $I(0) = 0$

Scenario 2: $S(0) = 0.99$, $I(0)=0.01$

Scenario 3: $S(0) = 0.01$, $I(0) =0.01$, $R(0)=0.98$

Under what conditions can an epidemic occur?

Scenario 1: S(0) = 1, I(0) = 0

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

$$\beta SI - \gamma I > 0$$

$$I(\beta S - \gamma) > 0$$

No epidemic if I = 0

Under what conditions can an epidemic occur?

Scenario 2: S(0) = 0.99, I(0)=0.01

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

$$\beta SI - \gamma I > 0$$

$$I(\beta S - \gamma) > 0$$

$$(\beta S - \gamma) > 0$$

$$S > \frac{\gamma}{\beta}$$

For epidemic to start, S(0) > γ/β and I(0) > 0

Under what conditions can an epidemic occur?

Scenario 3: S(0) = 0.01, I(0)=0.01, R(0)=0.98

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

$$\beta SI - \gamma I > 0$$

$$I(\beta S - \gamma) > 0$$

$$(\beta S - \gamma) > 0$$

$$S > \frac{\gamma}{\beta}$$

For epidemic to start, S(0) > γ/β and I(0) > 0

Under what conditions can an epidemic occur?

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

$$\beta SI - \gamma I > 0$$

$$I(\beta S - \gamma) > 0$$

$$(\beta S - \gamma) > 0$$

If S(0) = 1 $$(\beta - \gamma) > 0$$

$$\beta > \gamma$$

$$\frac{\beta}{\gamma} > 1$$

β = effective contact rate

γ = rate of recovery

$\mathrm{D} = 1/\gamma$ = duration of infectiousness

$\beta\mathrm{D} =$ (infections generated / time)(time)

$=$ total infections generated

Epidemic can occur if $\beta\mathrm{D} > 1$

Basic Reproductive Number

- The basic reproductive number (R_0) is the average number of infectious individuals generated by a single infectious individual in a fully susceptible population

- In the SIR model, $R_0 = \beta/\gamma$ or βD, where D= duration of infectiousness

- If >1, an epidemic can occur

- For an epidemic to begin, the susceptible population has to be greater than $1/R_0$

Under what conditions can an epidemic occur?

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

$$\beta SI - \gamma I > 0$$

$$I(\beta S - \gamma) > 0$$

$$(\beta S - \gamma) > 0$$

$$S > \frac{\gamma}{\beta}$$

For epidemic to start, $S(0) > \gamma/\beta$ and $I(0) > 0$

R_0 for various diseases

Disease	Estimated R0
Tuberculosis	1-3
Influenza	1.5-4
Rubella	6-7
Chickenpox	10-12
Measles	16-25

Basic Reproductive Number and Vaccine Critical Proportion

P_I: proportion immunized

$S = 1 - P_I$

$S(0) > 1/R_0$

$1-P_I > 1/R_0$

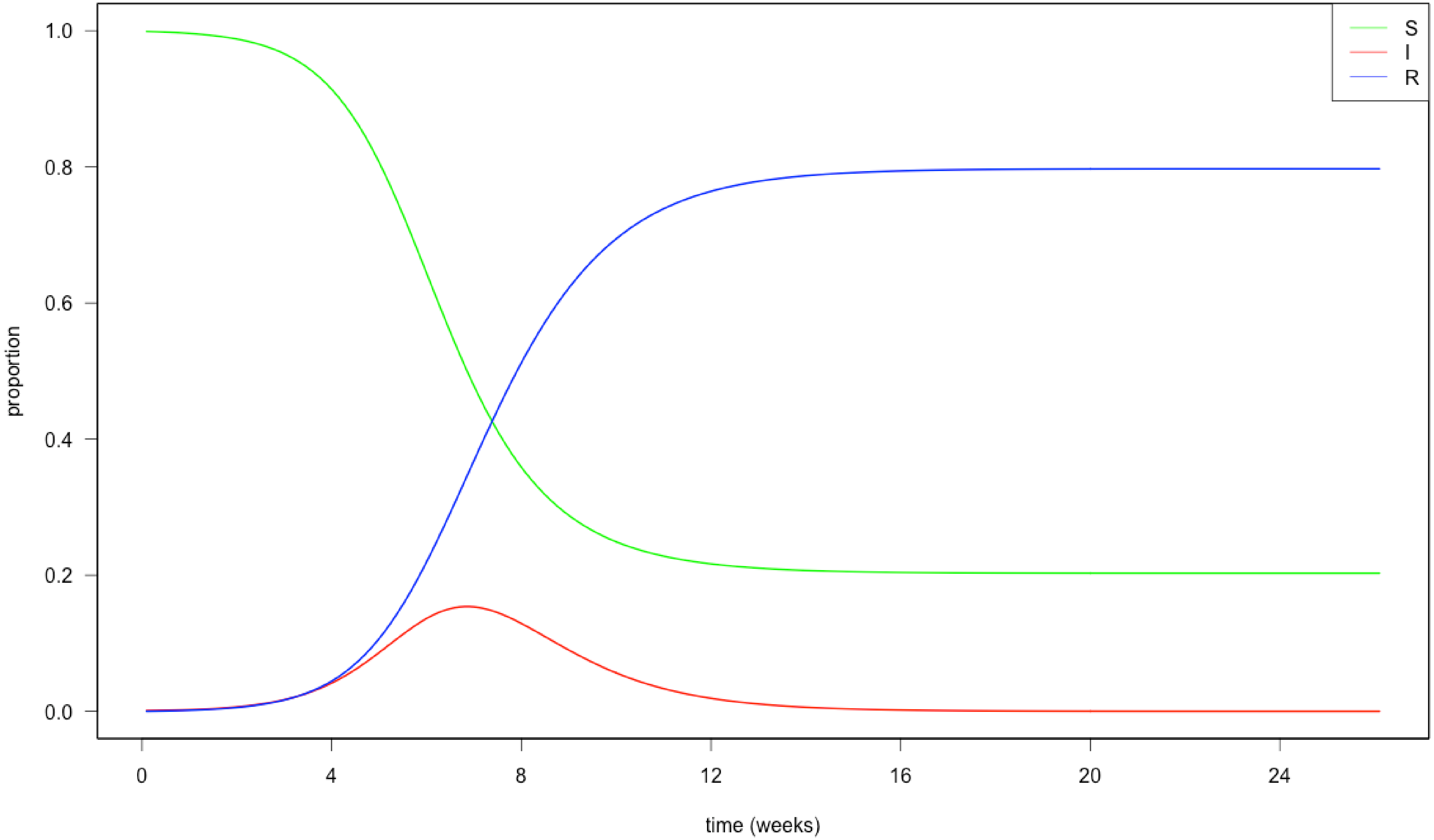
$P_I < 1-1/R_0$

P_c: critical proportion to immunize to avert epidemic

$P_c > 1-1/R_0$

What is the critical proportion to immunize for Measles? (R_0=20)

Why does an epidemic decline?



Basic vs Effective Reproductive Number

- Effective Reproductive Number (R_e): number of infections generated by average infectious person during epidemic
- R_t : Effective reproductive number at time t
- $R_t = R_0 * S_t$

$$(\beta S - \gamma) > 0$$

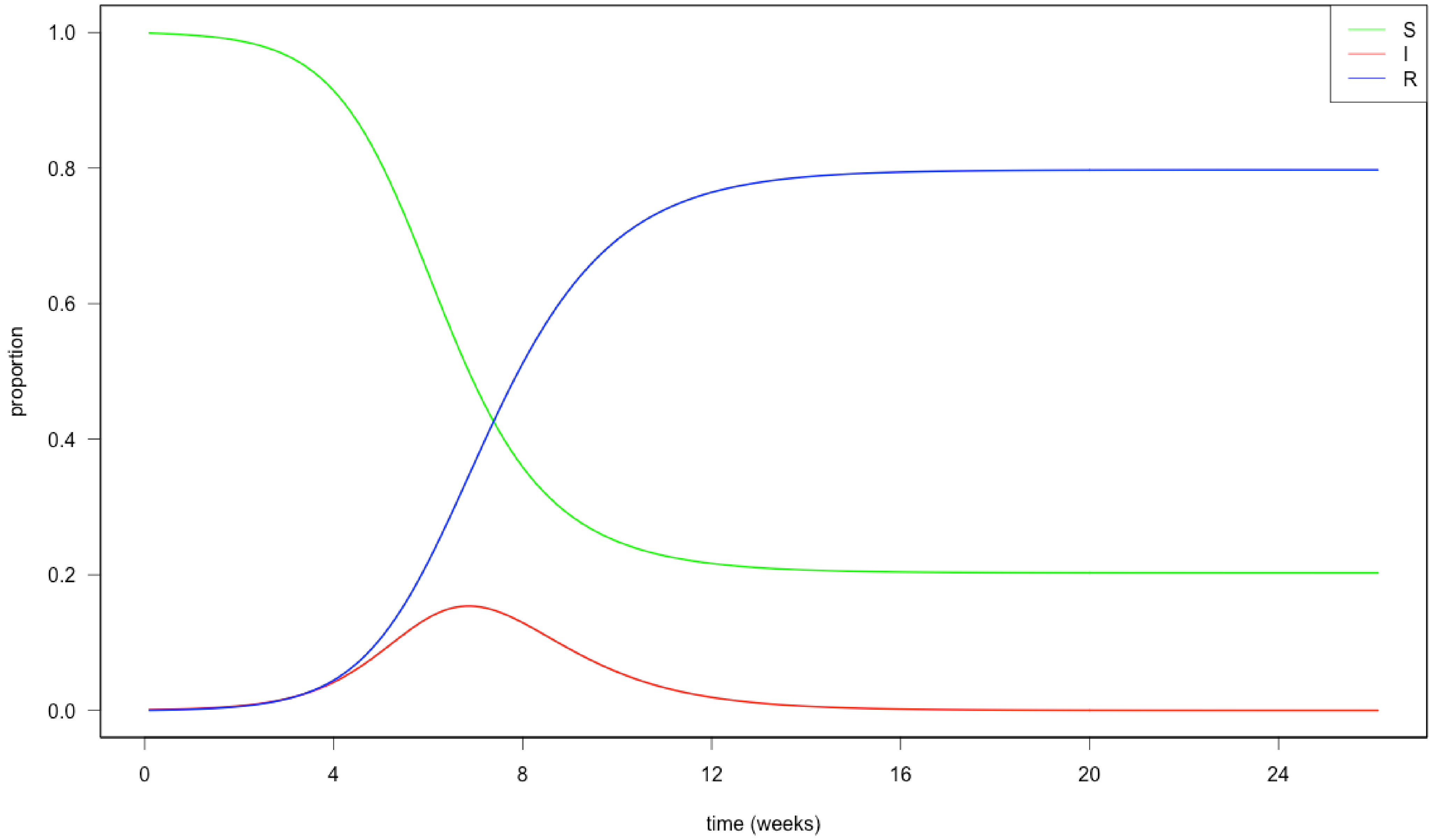
$$(\frac{\beta}{\gamma}\gamma S - \gamma) > 0$$

$$(R_0\gamma S - \gamma) > 0$$

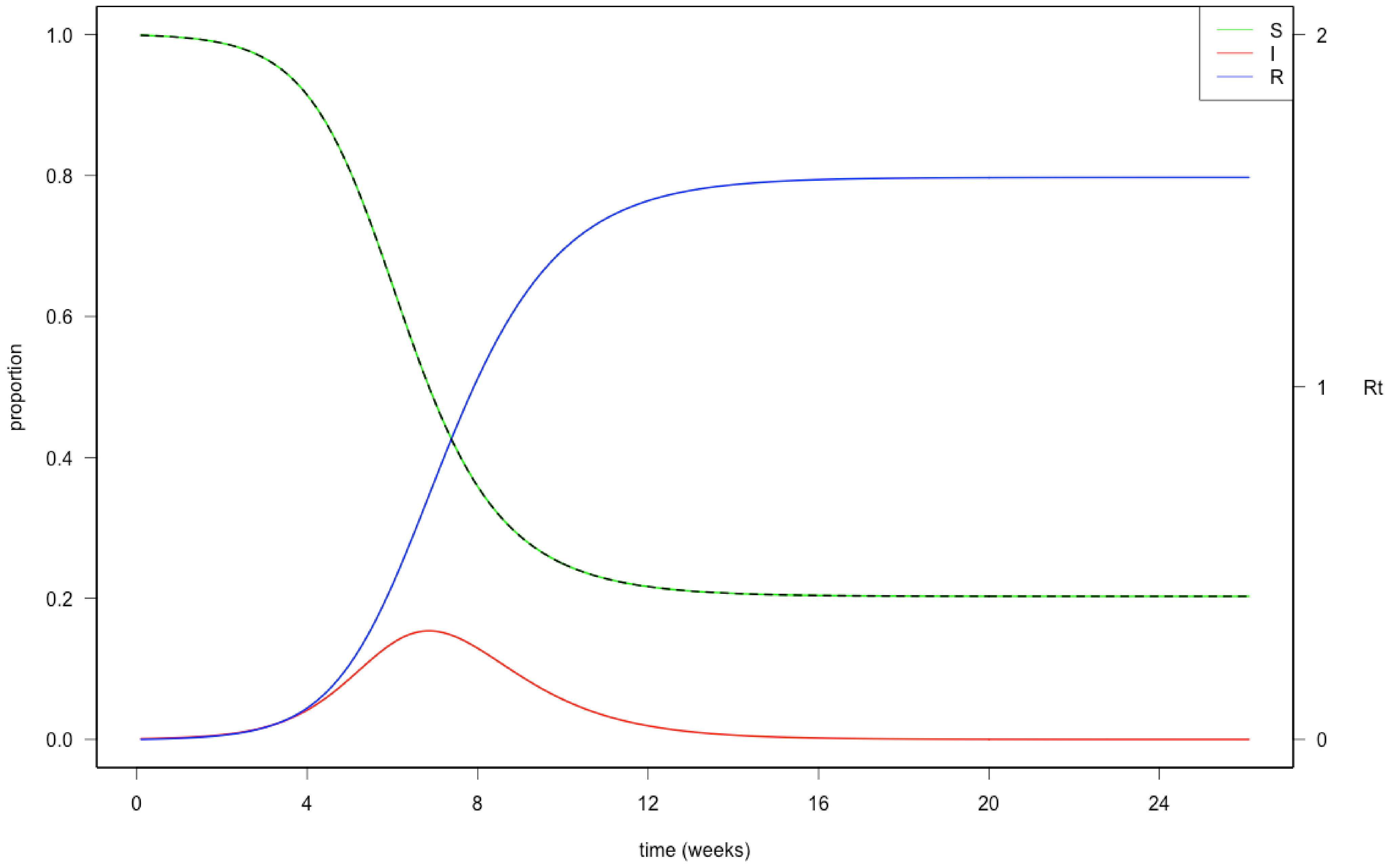
$$\gamma(R_0 S - 1) > 0$$

$$(R_t - 1) > 0$$

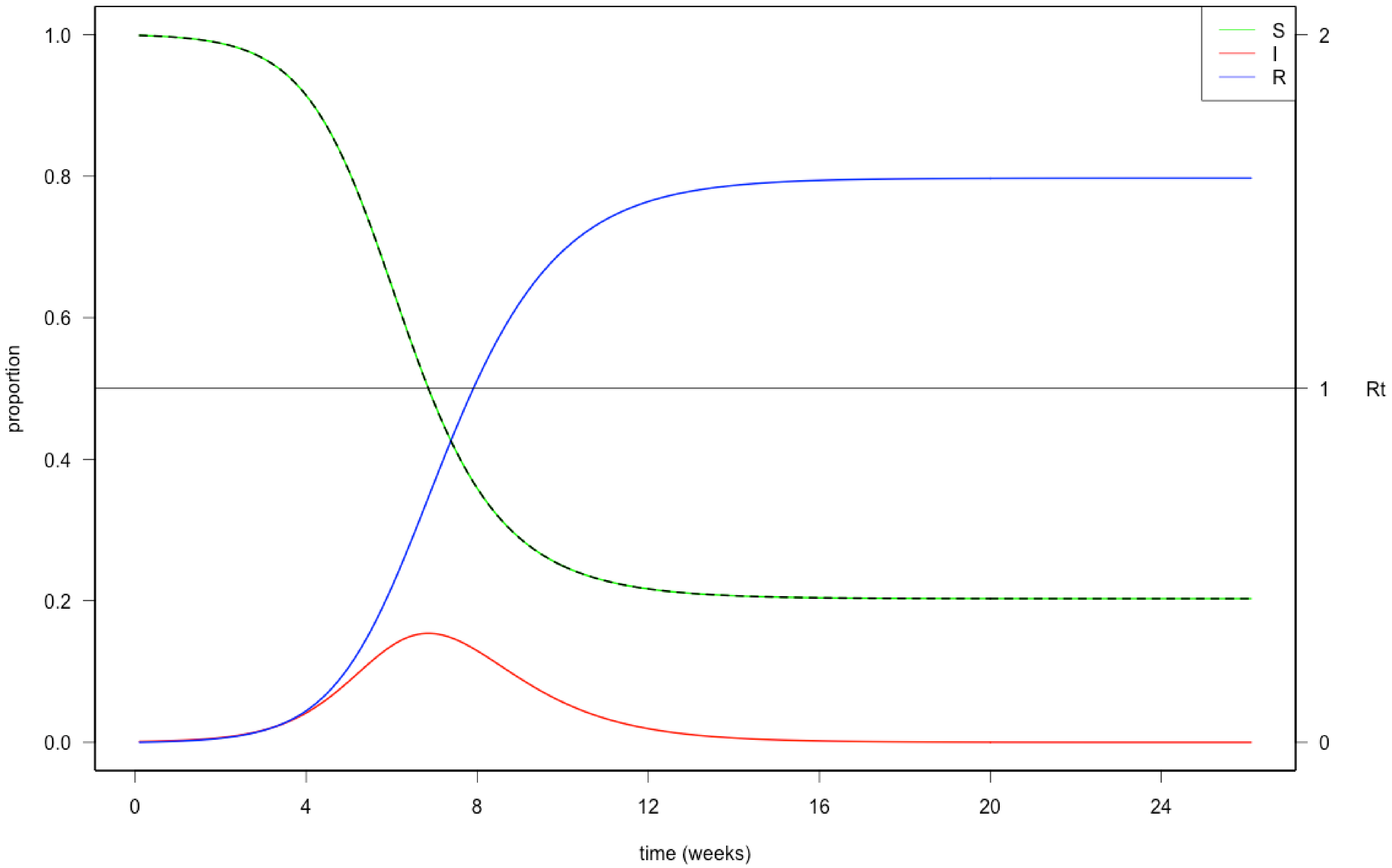
Infections grow while $R_t > 1$



S
I
R
1.0
0.8
0.6
0.4
0.2
0.0
proportion
0
4
8
12
16
20
24
time (weeks)

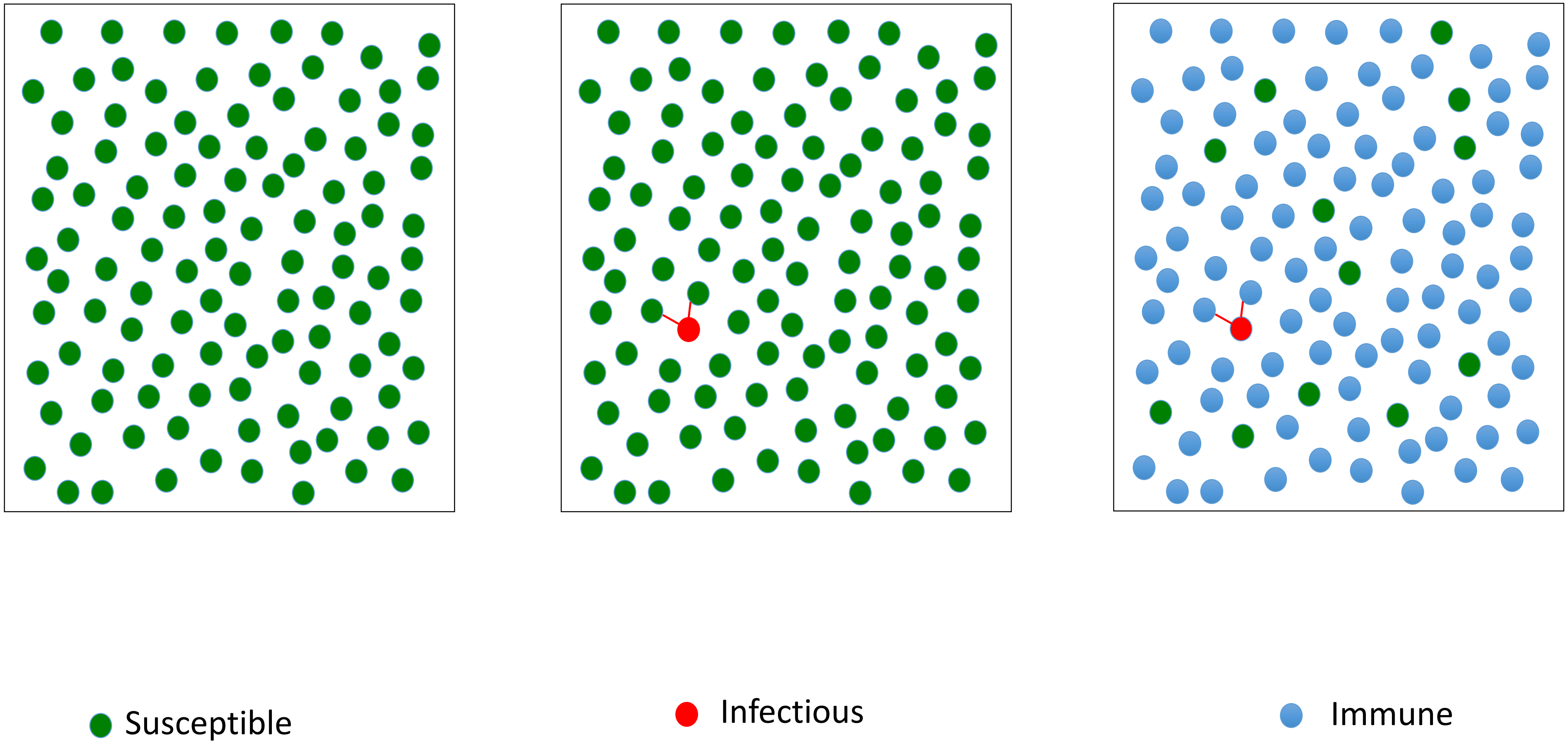


S
I
R
proportion
1.0
0.8
0.6
0.4
0.2
0.0
2
1
0
Rt
0
4
8
12
16
20
24
time (weeks)



1.0
0.8
0.6
0.4
0.2
0.0
proportion
0
4
8
12
16
20
24
time (weeks)
S
I
R
2
1
0
Rt

Herd Immunity



The susceptible fraction is the critical limiting factor to the start and decline of an epidemic

Final Epidemic Size

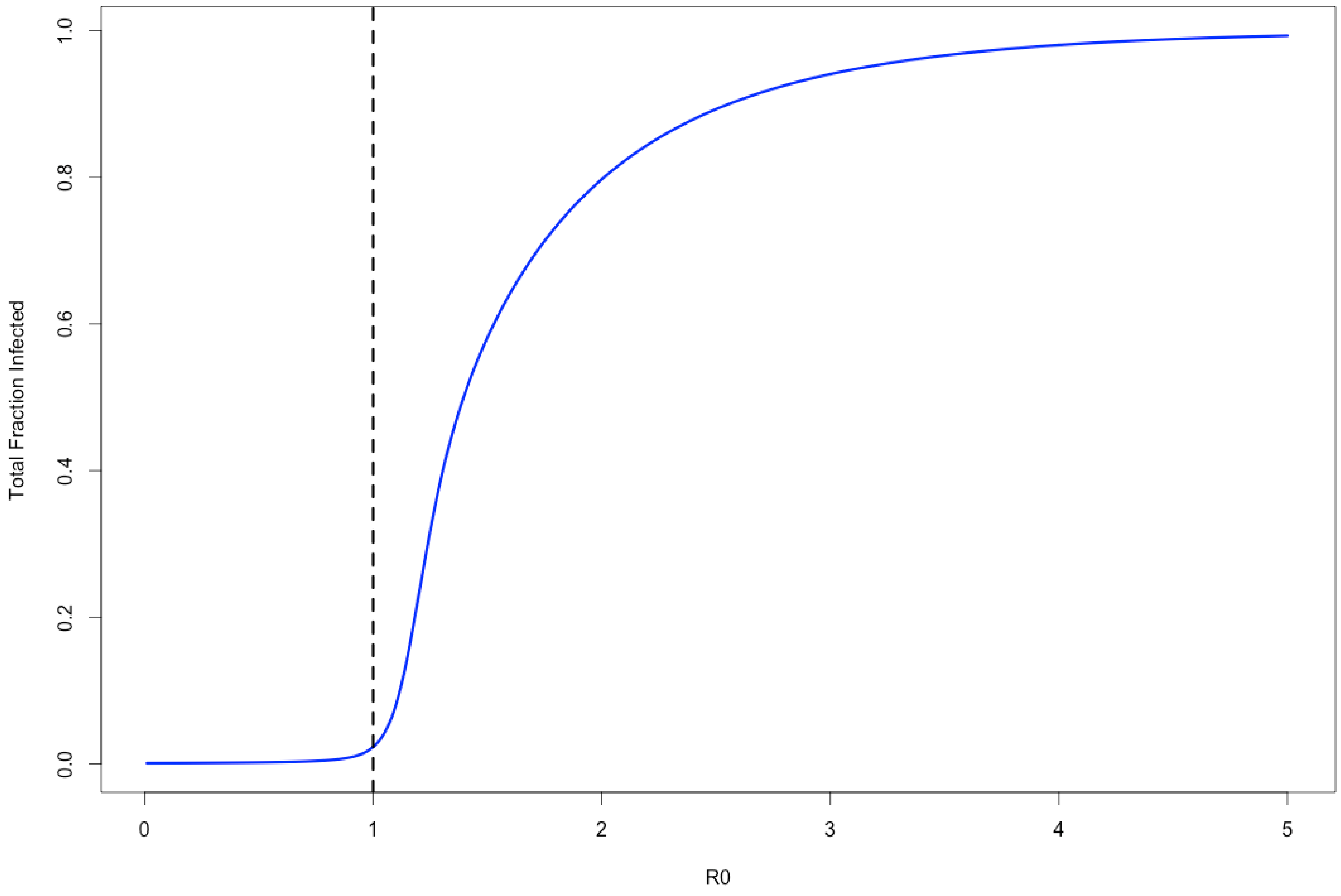
How many people will be infected by the end of the epidemic?

$$S(\infty) = 1 - R(\infty) = S(0)e^{-R(\infty)R_0}$$

$$1 - R(\infty) - S(0)e^{-R(\infty)R_0} = 0$$

$$1 - x - e^{ax} = 0$$

- No exact analytical solution
- Requires numerical solution


1.0
0.8
0.6
0.4
0.2
0.0
Total Fraction Infected
0
1
2
3
4
5
R0

SIR Model Summary

- Using a simple model with 3 equations and 2 parameters, we can:
  - characterize epidemics
  - understand conditions required to have an epidemic
  - predict when they will peak and decline
  - quantify vaccine coverage needed to prevent them
  - project how many people will be affected

Frequency vs density dependence

- Frequency dependence(“true mass action”): number of effective contacts is unchanged as population grows
- Density dependence (“pseudo mass action”): number of effective contacts scales with population density

<u>Density Dependent</u>

Plant diseases

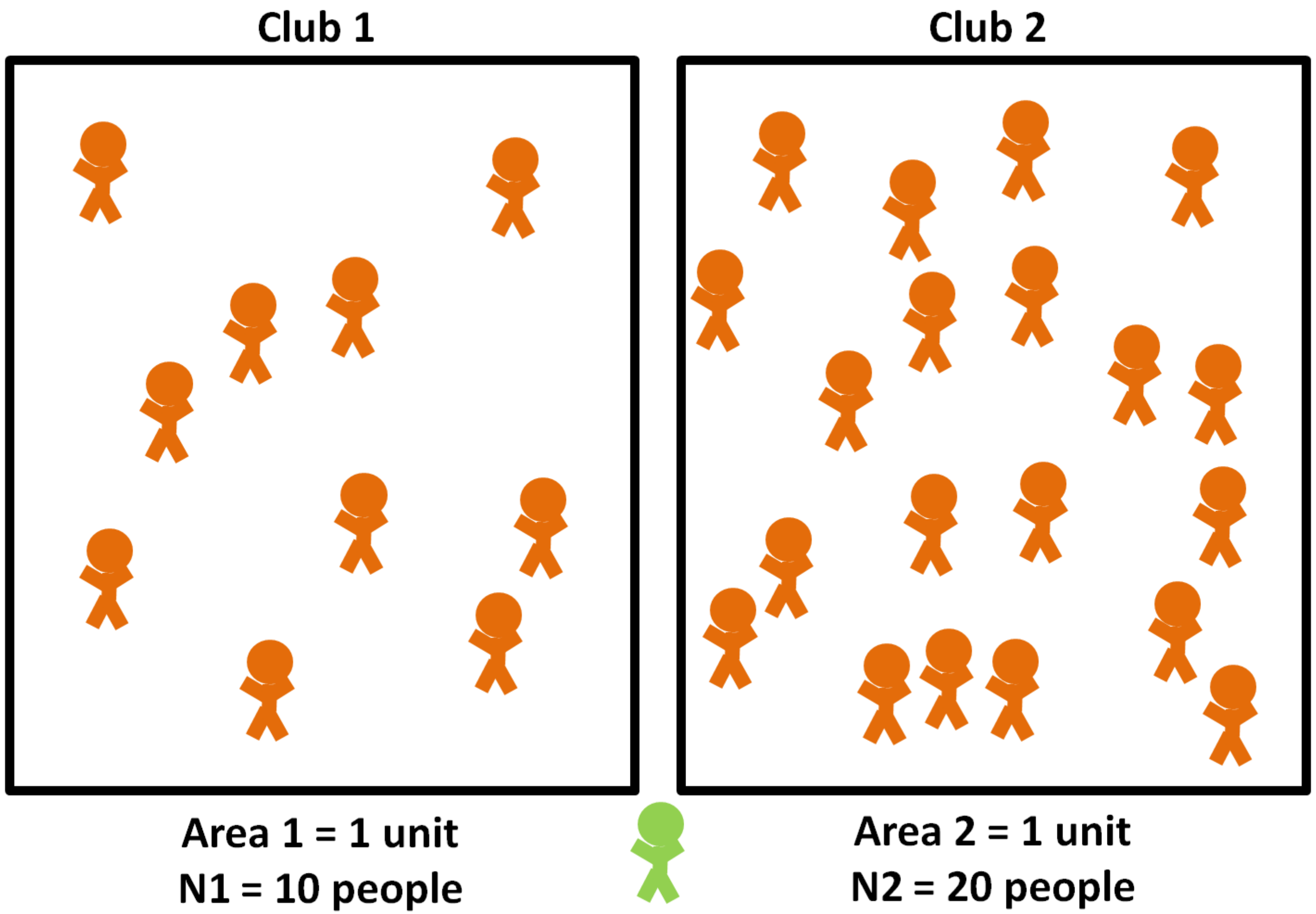
Animal diseases

<u>Frequency Dependent</u>

Respiratory Infections

Sexually Transmitted Infections

Frequency vs density dependence



Frequency vs Density Dependence

In model terms, consider **number** of individuals who are:

- Susceptible as X
- Infectious as Y
- Recovered as Z
- N= X+Y+Z = total population size

The force of infection (λ) is:

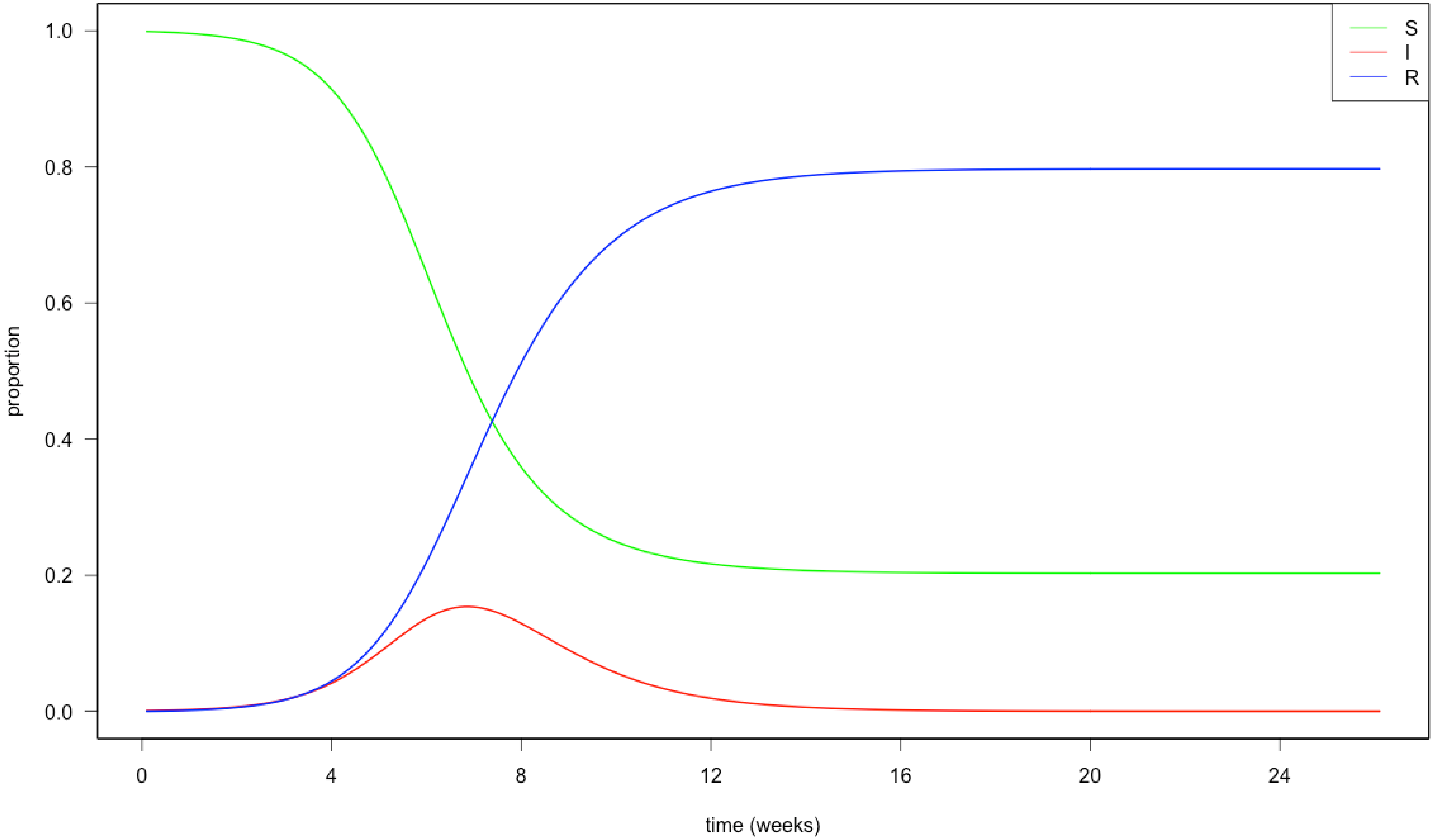
$$\beta \frac{Y}{N} = \beta I$$

Frequency dependent

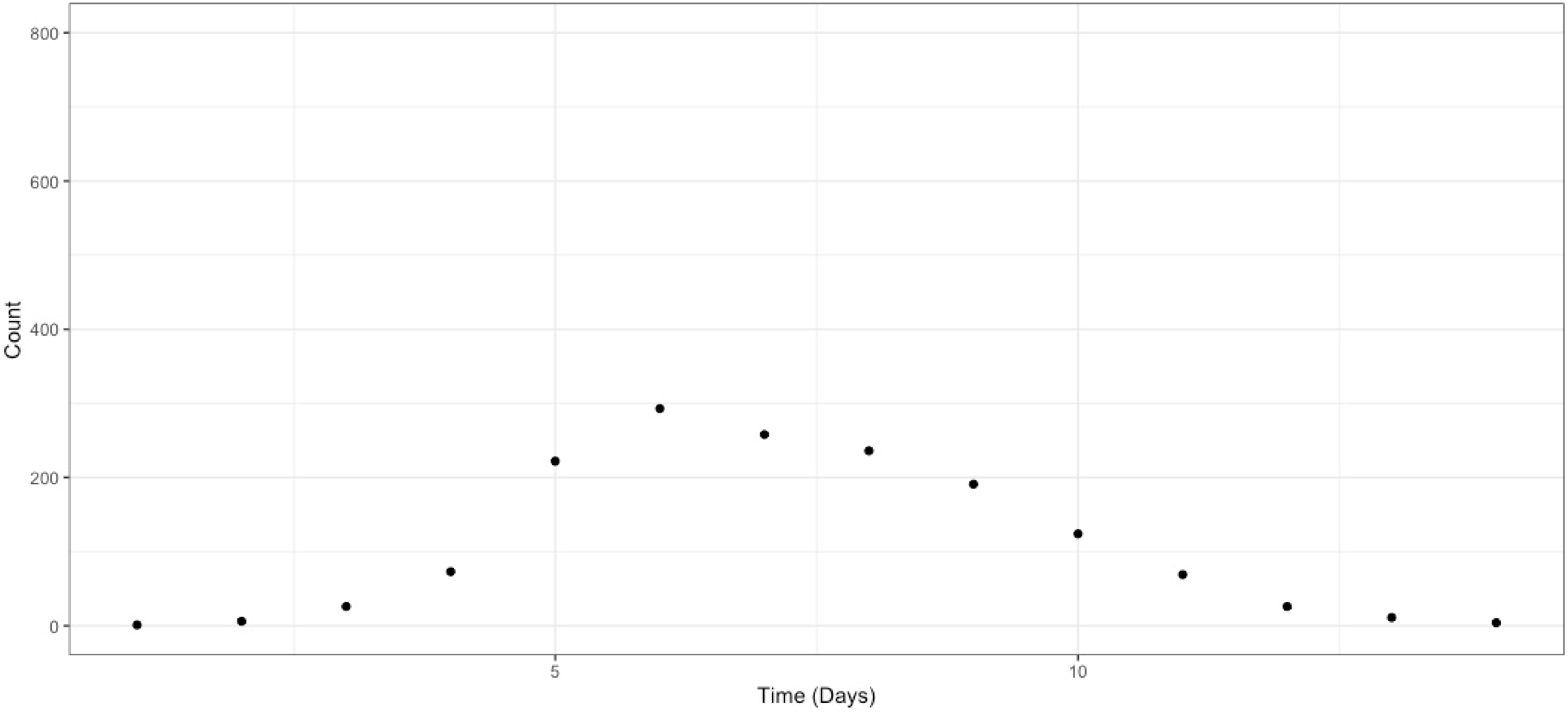
$$\beta Y = \beta \frac{Y}{N} N = (\beta N) I$$

Density dependent

Do these models realistically describe outbreaks?

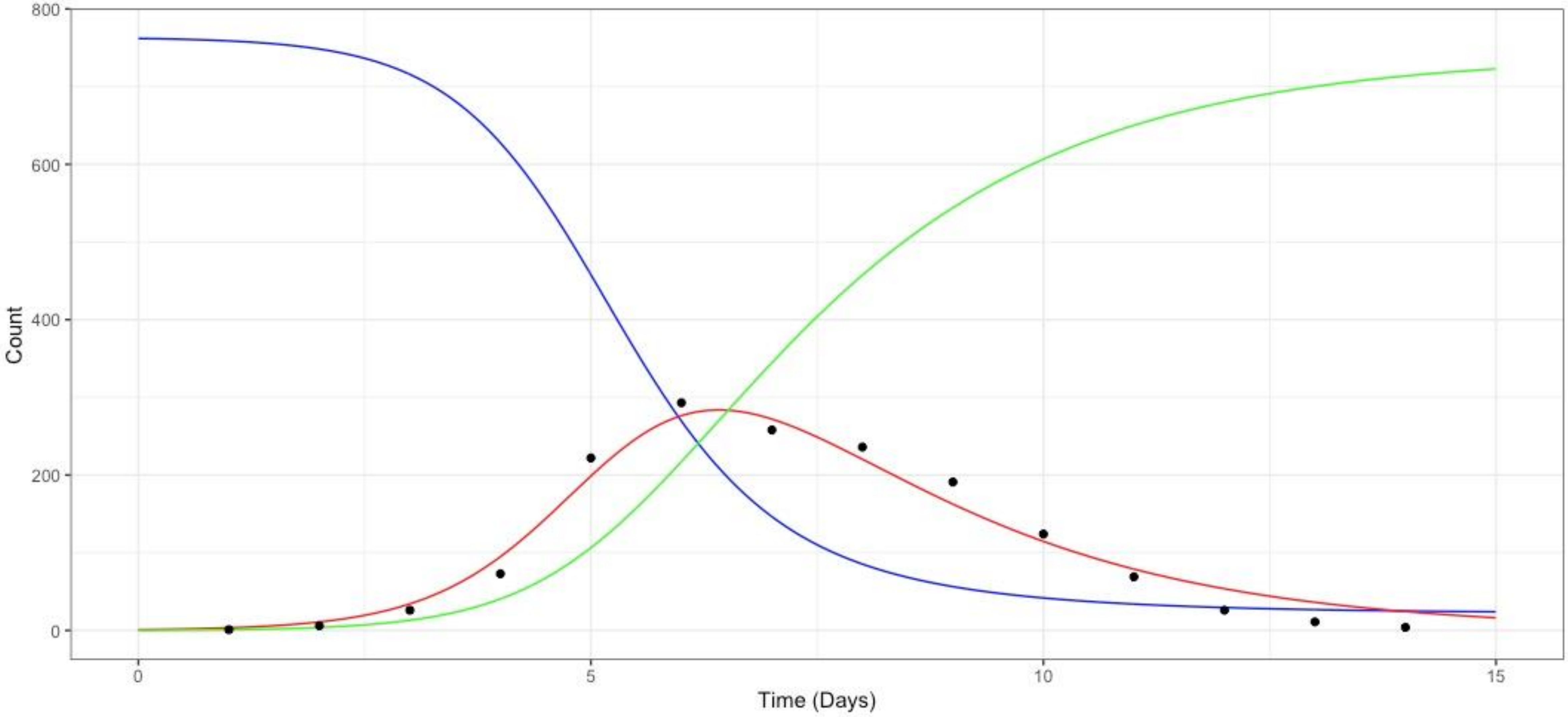


SIR Model of English Boarding School



SIR Model of English Boarding School

β=1.66/day $\qquad D = 1/\gamma = 2.2 \text{ days}$



Concepts Review

- The effective contact rate is the rate at which infectious individuals infect susceptible individuals
- R_0 is the average number of infectious individuals generated by a single infectious individual in a fully susceptible population
- If $R_0 < 1$, an epidemic cannot be sustained; when $R_t < 1$, epidemic declines
- The critical threshold for vaccination is the level above which outbreaks can’t occur ($1-1/R_0$)
- The fraction of susceptible individuals is the limiting factor in epidemics, dictates whether they start, and when they end