# Mathematical Modelling of Infectious Diseases
# 2016/2017


**Barry Rowlingson**

*CHICAS,*

*Lancaster Medical School,*

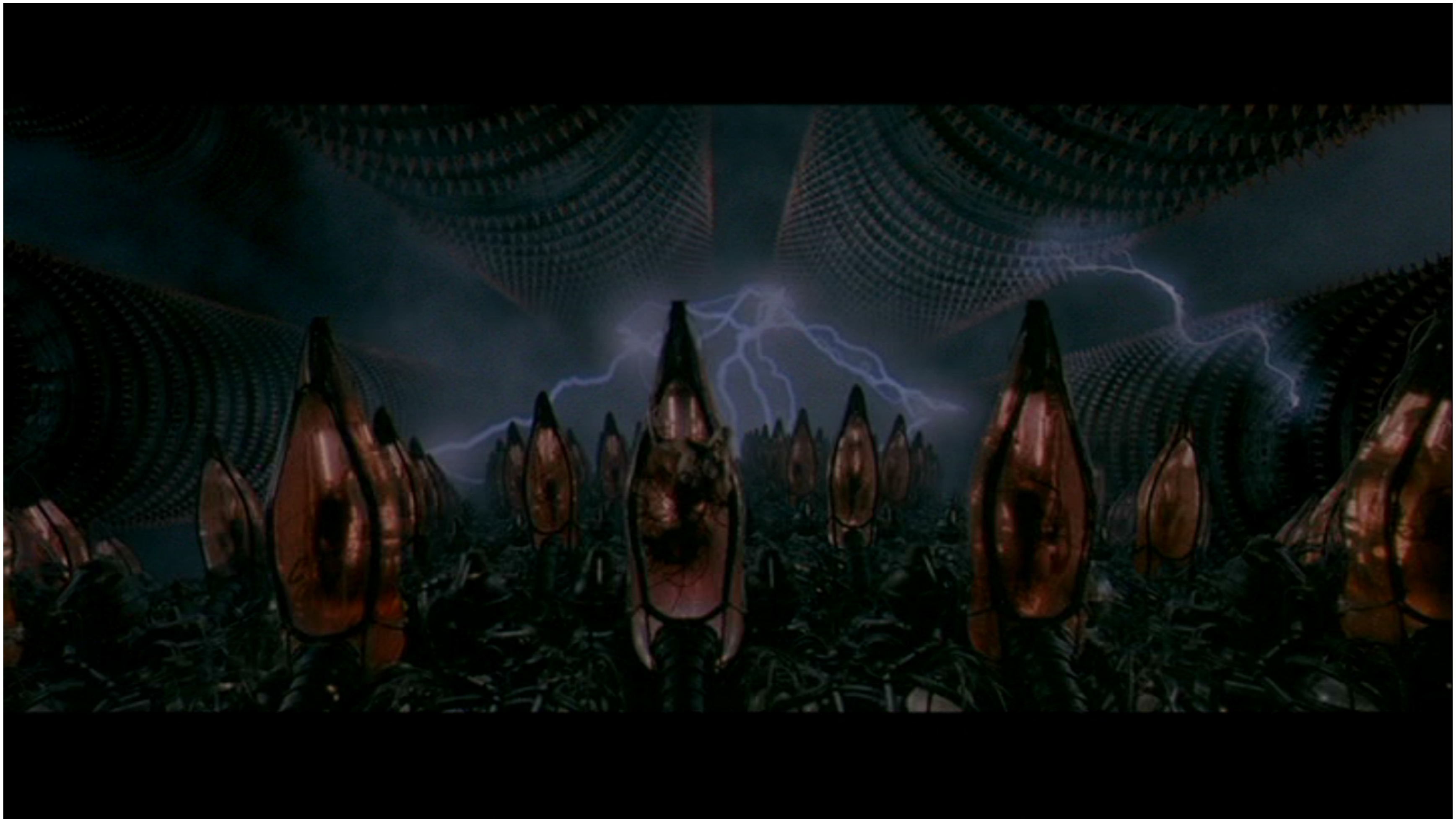
*Faculty of Health and Medicine*

*Lancaster University*

email: `b.rowlingson@lancaster.ac.uk`


KEANU REEVES LAURENCE FISHBURNE
THE MATRIX
ON APRIL 2ND THE FIGHT FOR THE FUTURE BEGINS.


Flickr: morrosv7



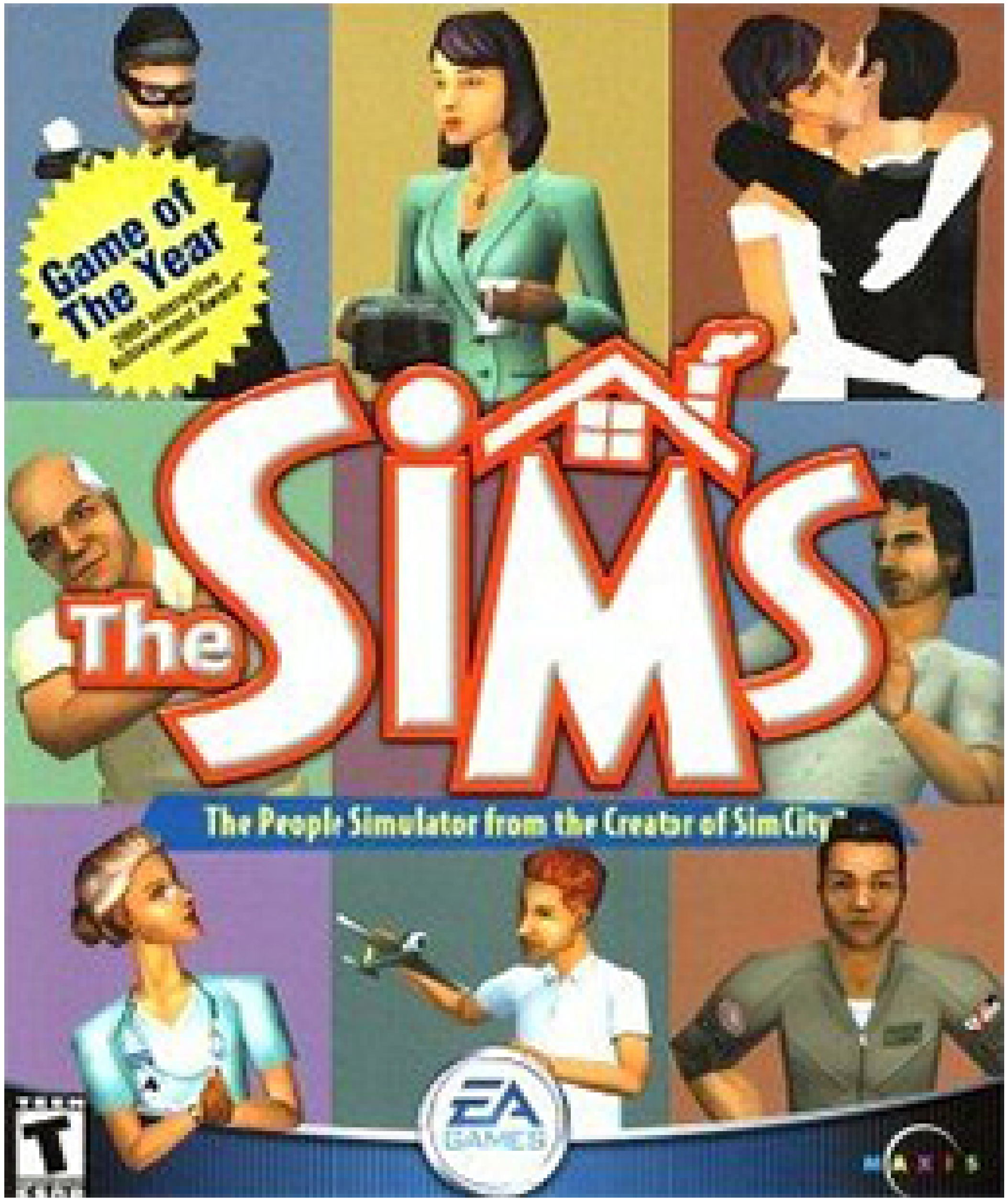
# If We Had That Much Computing Power...

- Run multiple world simulations
- Change initial conditions
  - Infect different people
  - Change behaviour
  - Change the environment
- Observe multiple outcomes

We could run experiments on something indistinguishable from reality...
But we don't have that much computing power. Yet.

# What Can We Do?

- Simulate smaller universes
- Simplify processes
- Model bulk behaviours instead of individuals


Game of The Year
The Sims
The People Simulator from the Creator of SimCity
EA GAMES
MAXIS

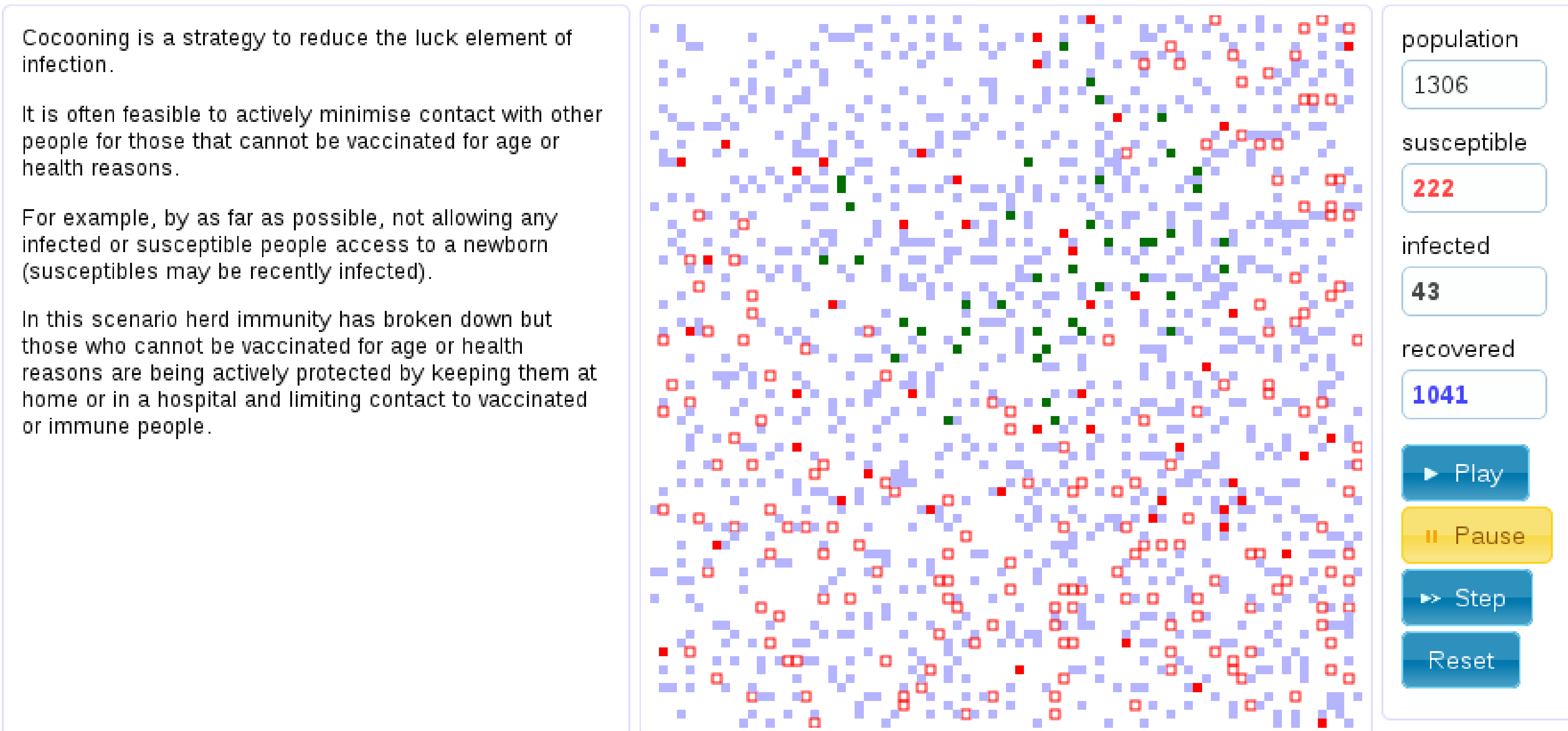
# Sims can catch “Guinea Pig Disease”

# and dysentery...

...which they can pass on to other Sims.

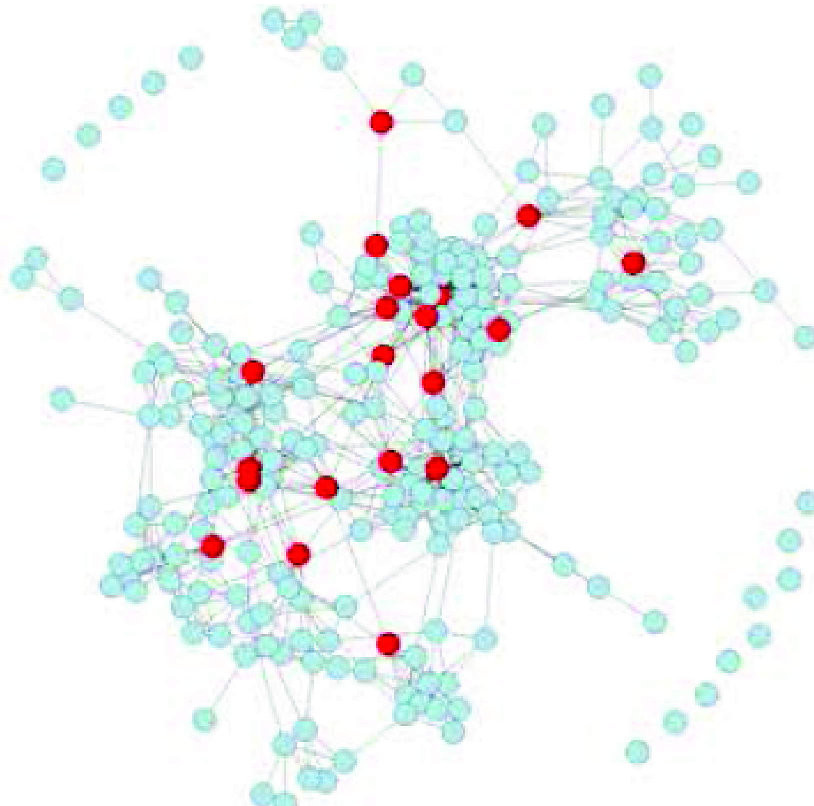
# How Simple Can We Make This?

http://op12no2.me/toys/herd/




This model has “people” as squares on a grid, running around randomly.
Can illustrate various principles of disease transmission and immunity.

# Network Model Analysis



BBC Sign in | News | Sport | Weather | iPlayer | TV | Radio | More... | Search

# NEWS HEALTH



**18 January 2015** Last updated at 00:03

Share

# Popular medical students 'should get flu jab first'

COMMENTS (168)


The government wants three-quarters of healthcare workers to be vaccinated

**Prioritising medical students with lots of friends for flu jabs could help increase the number of healthcare workers protected against the virus, say Lancaster University researchers.**

In a study in **The Lancet**, they calculated that vaccination rates would rise if people with large social networks influenced their peers.

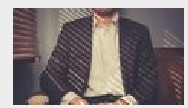
## Related Stories

- Flu cases 'highest for three years'
- 'Too few' toddlers

## Top Stories

- Rothe quits
- NZ judge to lead child abuse
- Jordan's king back for crisis t
- Taiwan plane in deadly river
- Chilcot rejects Iraq timetable

## Features

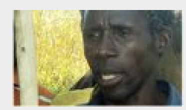


**Dark hor**

Can you st they offend

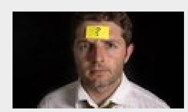
**Rail wav**

The lines r to the sea



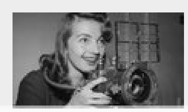
**Husband**

Man battles pregnant w



**Rodney?**

Tactics for someone's



**Been an**

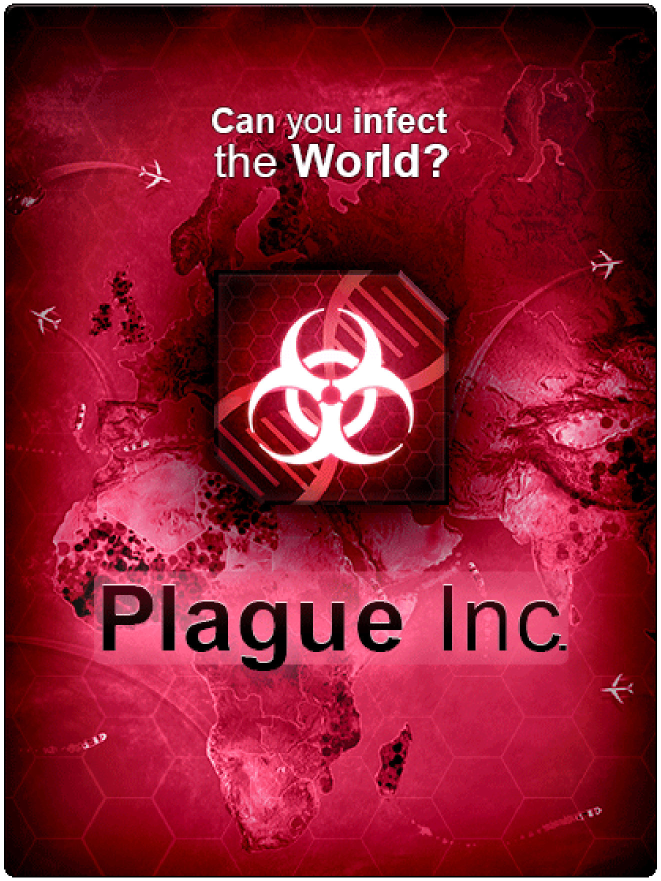
A pioneerin photograph

# Agent-based Modelling

- Smallest modelled unit is an individual
- Mathematical model of agent behaviour
- Multiple simulations to get probabilistic answers to “if” questions.
- Found in other disciplines, eg traffic modelling, finance

But what if we have too many agents to model?

# Aggregated Models




http://www.ndemiccreations.com/en/


News
UK declares national emergency
13 2 2013
DNA 37
Cure 50%
Disease
Infected
World
Dead
293 836
World
Release a Plague across the globe

# Aggregated Data

| country | alive | dead | infected |
|---|---:|---:|---:|
| China | 1367920684 | 79316 | 8536114 |
| India | 1266337077 | 2923 | 7812505 |
| USA | 320297757 | 23243 | 2157579 |
| Indonesia | 255728242 | 17758 | 1102115 |
| Brazil | 203819190 | 6810 | 1426791 |
| Pakistan | 188852320 | 14680 | 1474699 |
| Nigeria | 183509888 | 13112 | 981486 |

*What might affect how these numbers change with time?*

# Suppose...

- One initial case
- One infected person infects two new people every day
- There is a very large population
- People are infectious for one day

Then the number of infectious people on any one day doubles:

$$I_{t+1} = 2I_t$$

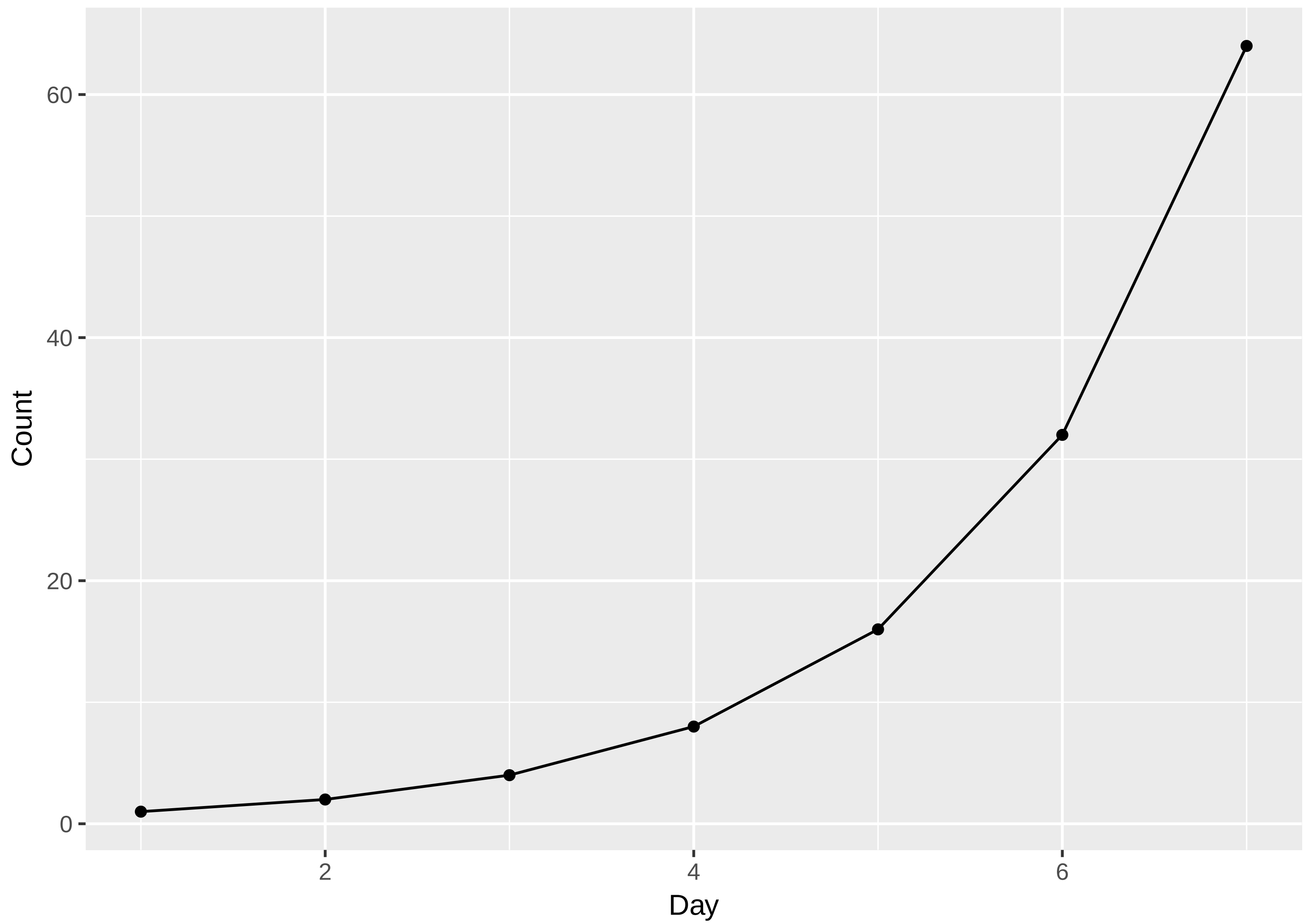
And the total number of people affected so far increases:

$$T_{t+1} = T_t + I_t$$

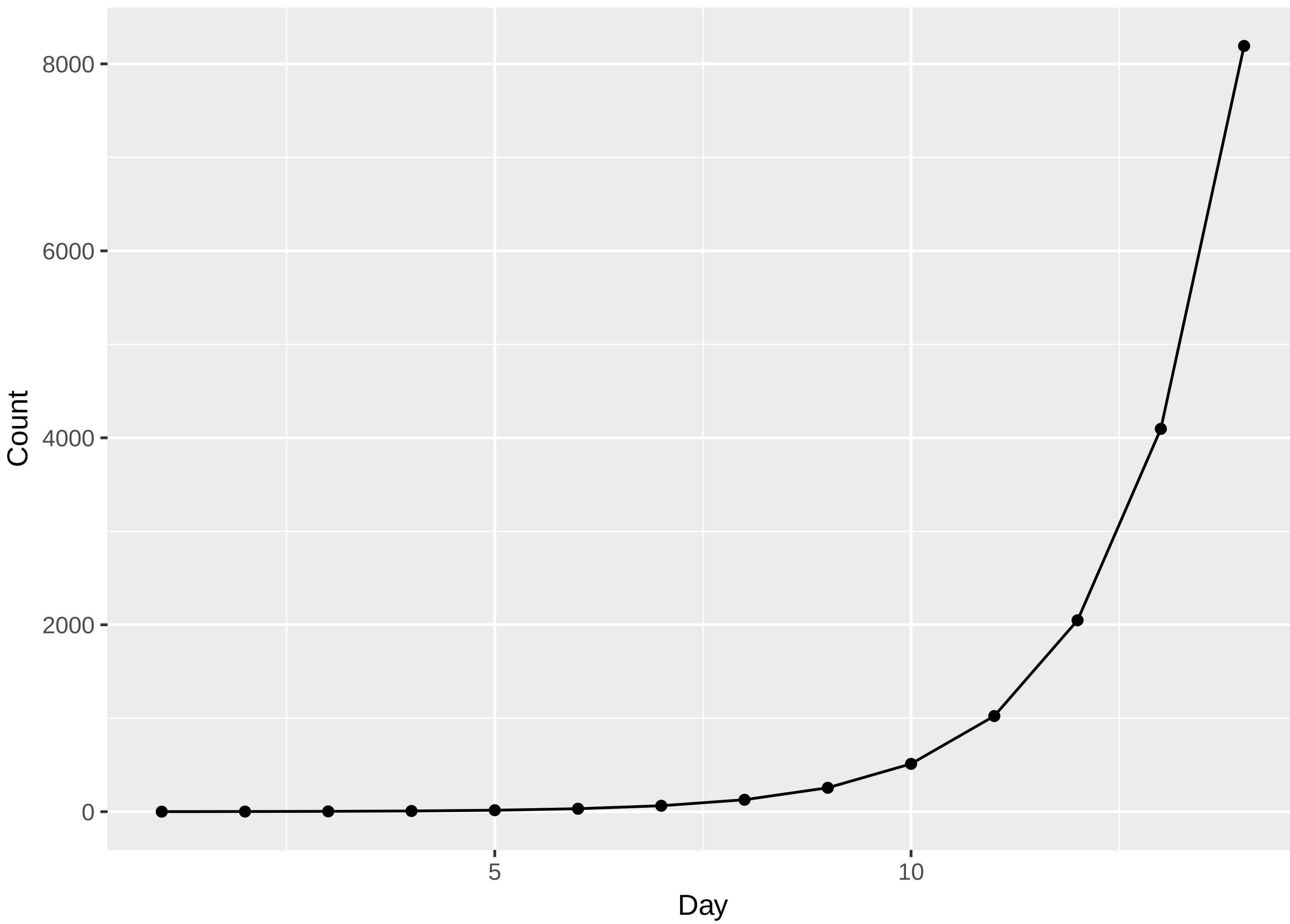
# Code

```
>>> I=1
>>> for t in 1..7:
...     I = I * 2
...     print t, I
...
1 2
2 4
3 8
4 16
5 32
6 64
7 128
```

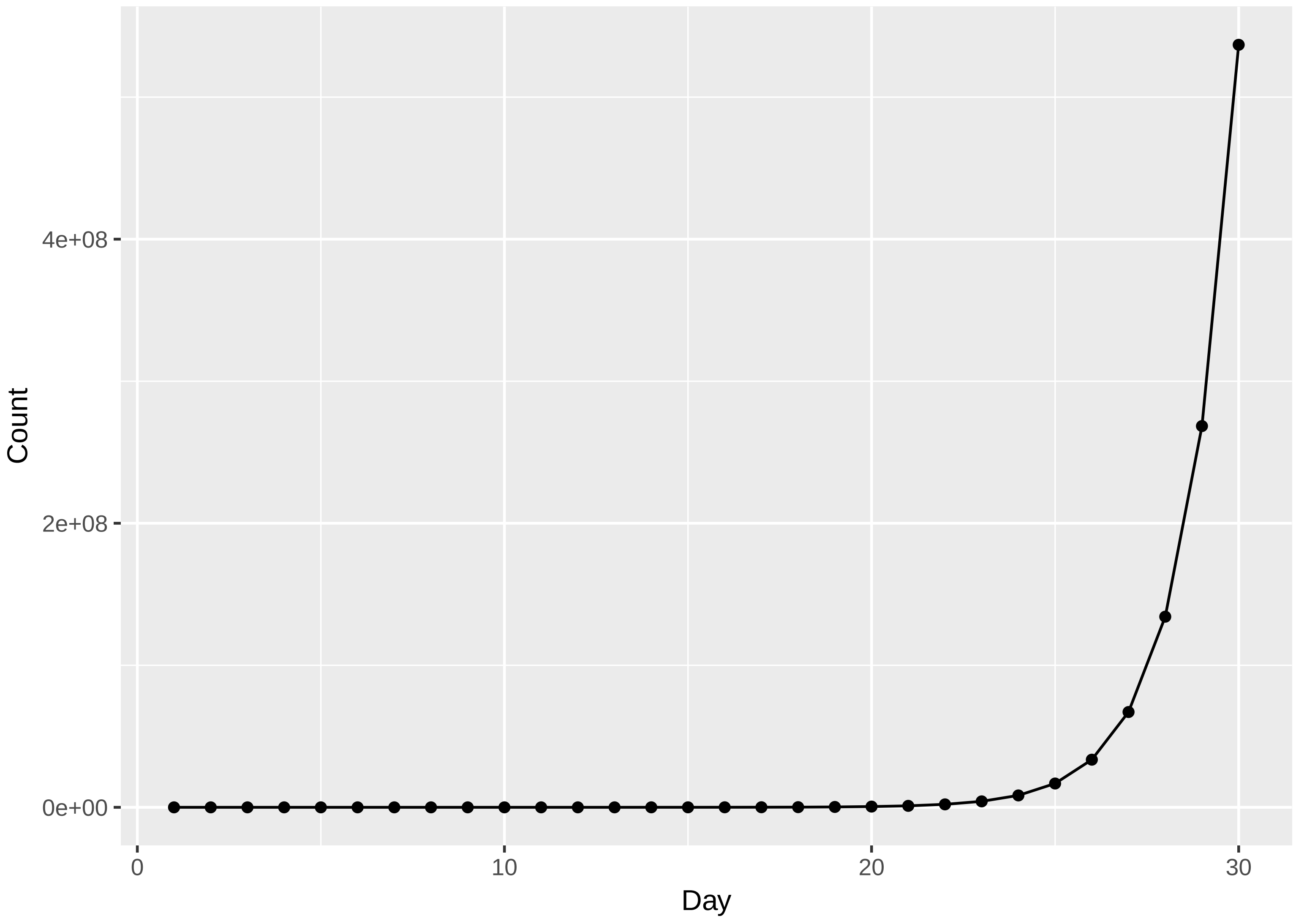
after one week...



after two weeks...



# after 30 days



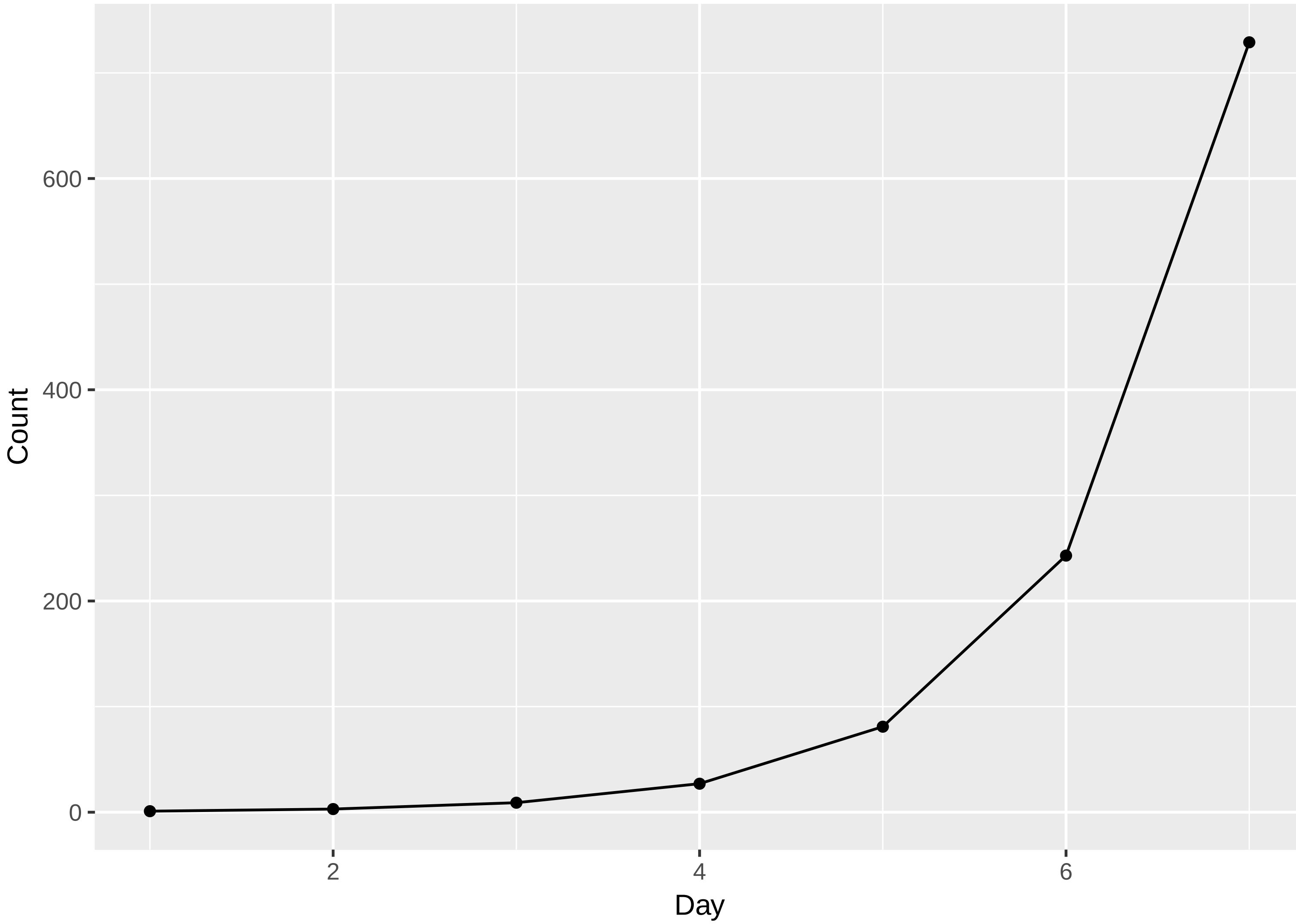
# What if people remain infectious?

Then the number of infectious people on any one day triples:

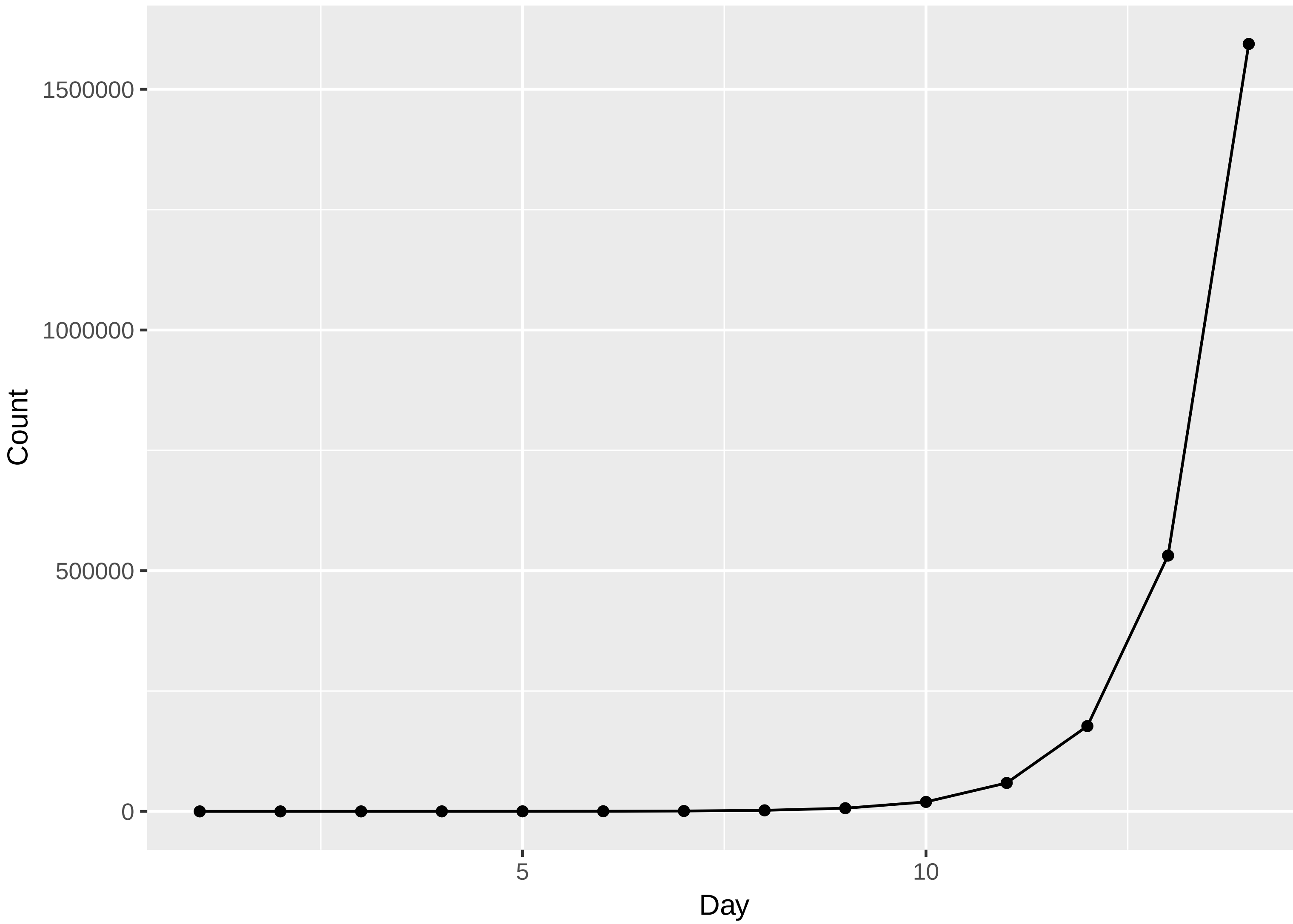
$$I_{t+1} = I_t + 2I_t$$

because its the infectious people from the previous day plus two for each of those.

after one week...



after two weeks



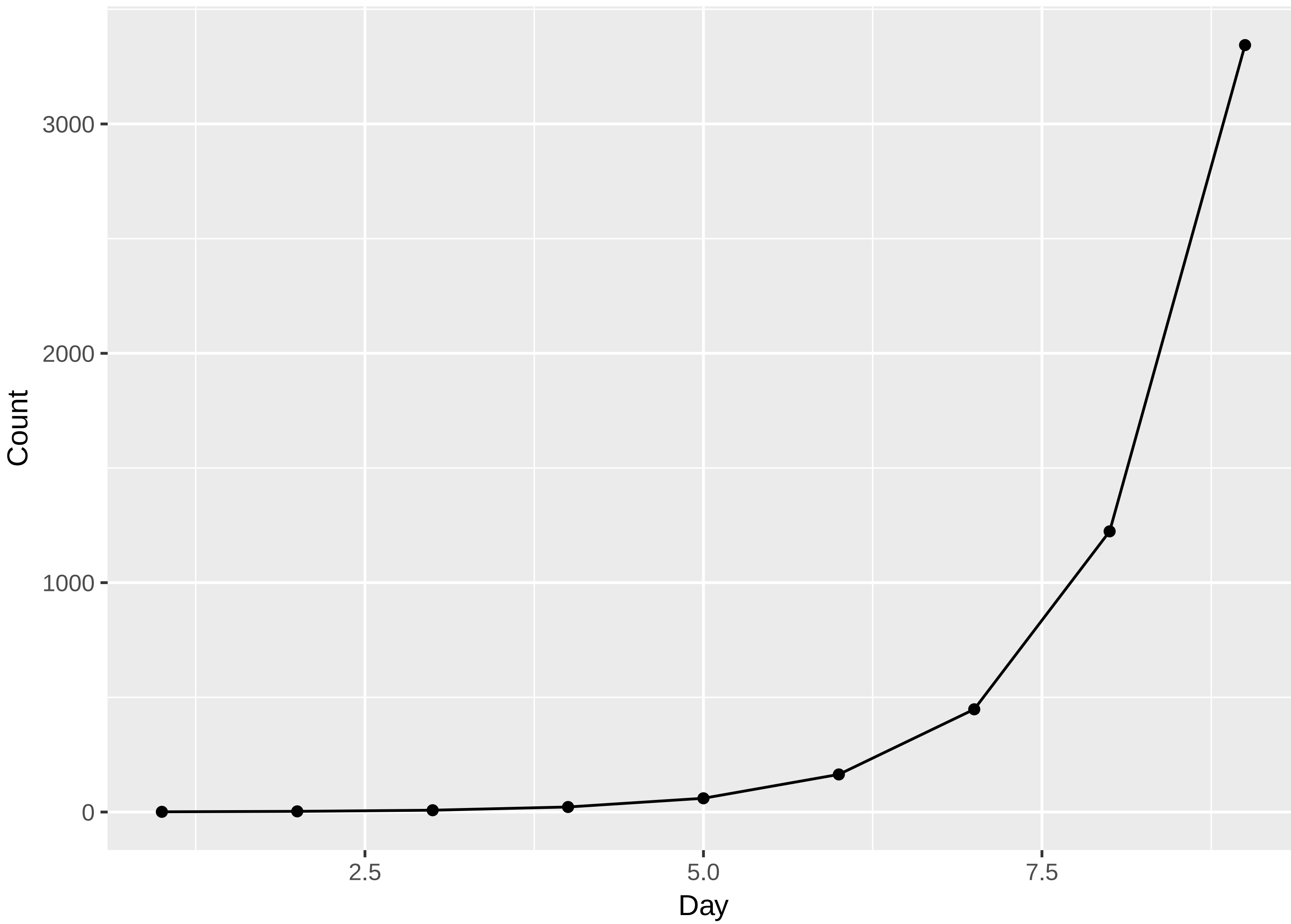
## suppose cases are infectious for 2 days

$$I_{t+1} = 2(I_t + I_{t-1})$$

```
Itm1 = 1
It = 3
for t in 1..9:
  Itp1 = 2*(It+Itm1)
  print t, Itp1
  Itm1 = It
  It = Itp1
```

gives

| Day | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|
| Count | 1 | 3 | 8 | 22 | 60 | 164 | 448 | 1224 | 3344 |




fewer cases, but still out of control..

# Exponential model

Each of those examples above can be represented as an exponential model

$$I_t = I_1 e^{t \log(\mathbb{R}_0)}$$

where $I_{t+1} =$

$$\begin{array}{rcl} 2I_t & \mathbb{R}_0 = 2 & \text{1-day infectious period} \\ 2I_t + 2I_{t-1} & \mathbb{R}_0 = 2.73 & \text{2-day infectious period} \\ I_t + 2I_t & \mathbb{R}_0 = 3 & \text{no recovery} \end{array}$$

$\mathbb{R}_0$ is the “basic reproduction number”

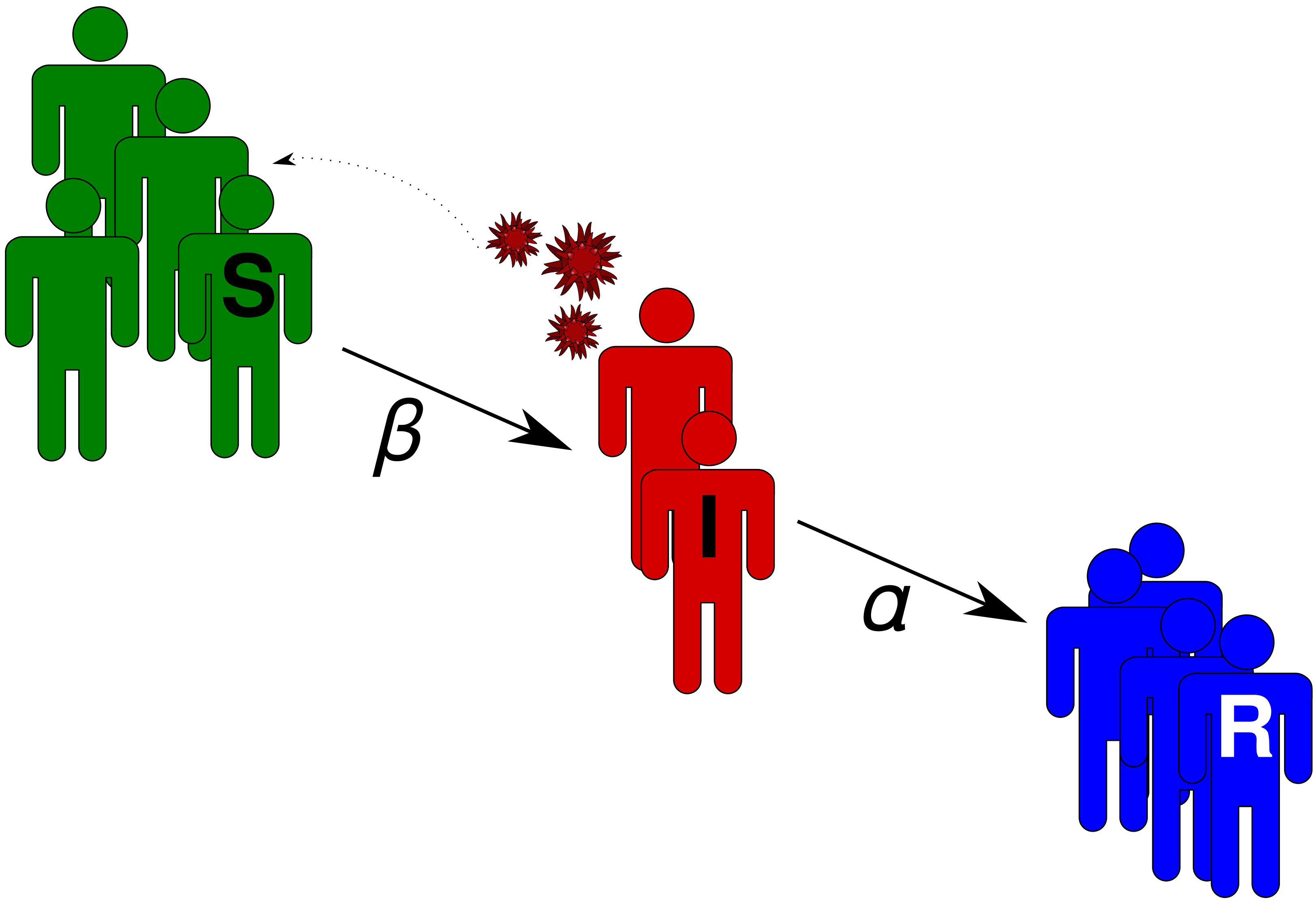
$$\begin{array}{ll} \mathbb{R}_0 < 1 & \text{Decreasing} \\ \mathbb{R}_0 = 1 & \text{Steady-state} \\ \mathbb{R}_0 > 1 & \text{Increasing} \end{array}$$

# Finite Populations - The SIR Model

At any time $t$, we can divide the population into:

- $S_t$ = number of susceptible individuals
- $I_t$ = number of infectious individuals
- $R_t$ = number of removed individuals

Removed refers to individuals who may have contracted the disease at an earlier time, but are no longer infectious and no longer susceptible. Its also called “recovered” and often means “dead”.


S
β
I
α
R

We assume a closed population so that, at any time $t$,

$$S_t + I_t + R_t = N$$

The initial conditions are the values of $S_1, I_1, R_1$.

The epidemic then develops as follows:

- $\alpha$ is the daily fraction of infectious individuals recovering (“death rate”):

$$R_{t+1} = R_t + \alpha \times I_t$$

- $\beta$ is the rate at which infectious individuals infect susceptibles:

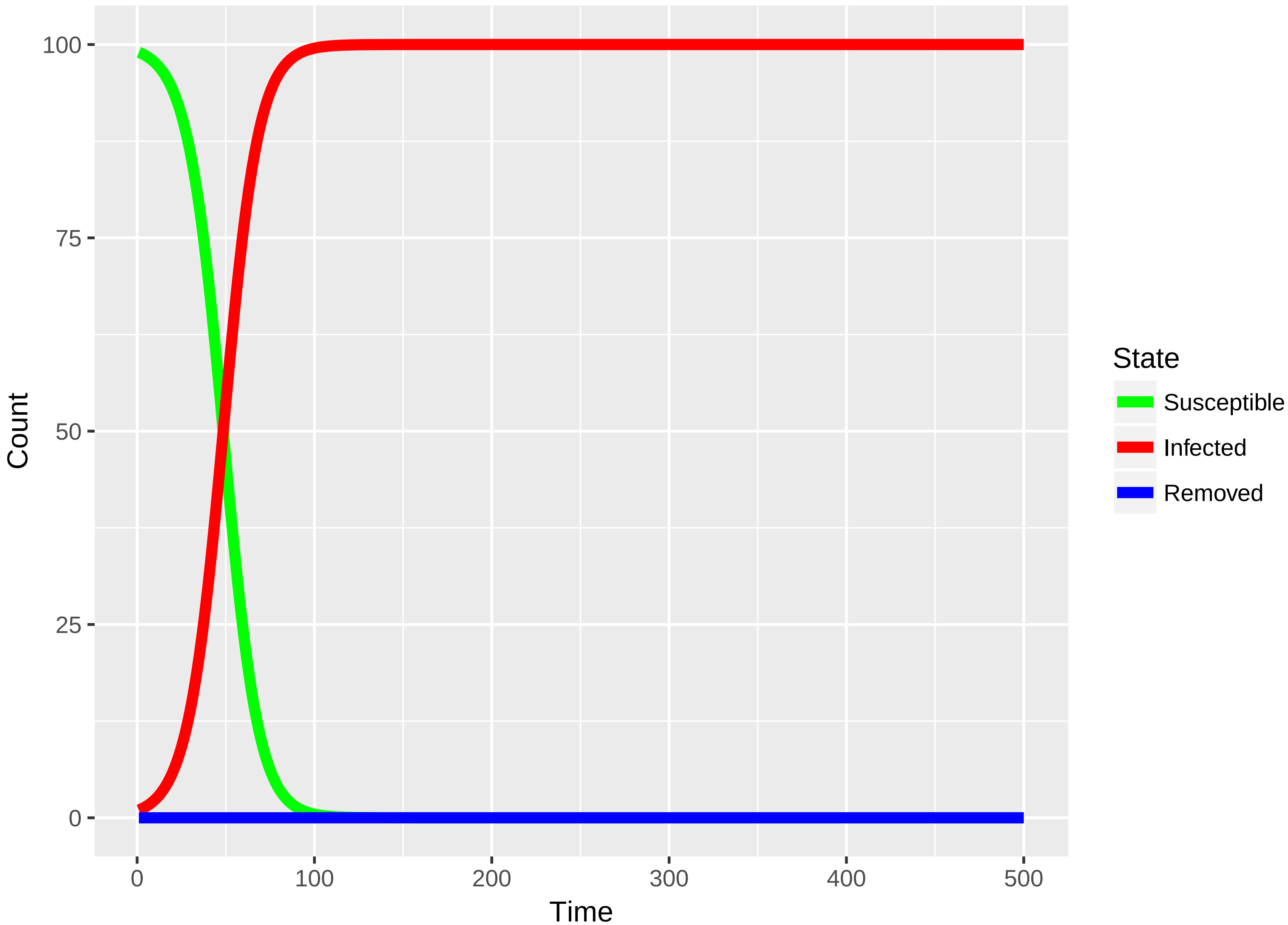
$$S_{t+1} = S_t - \beta \times I_t \times S_t$$

- Number of infectious people updates like this:

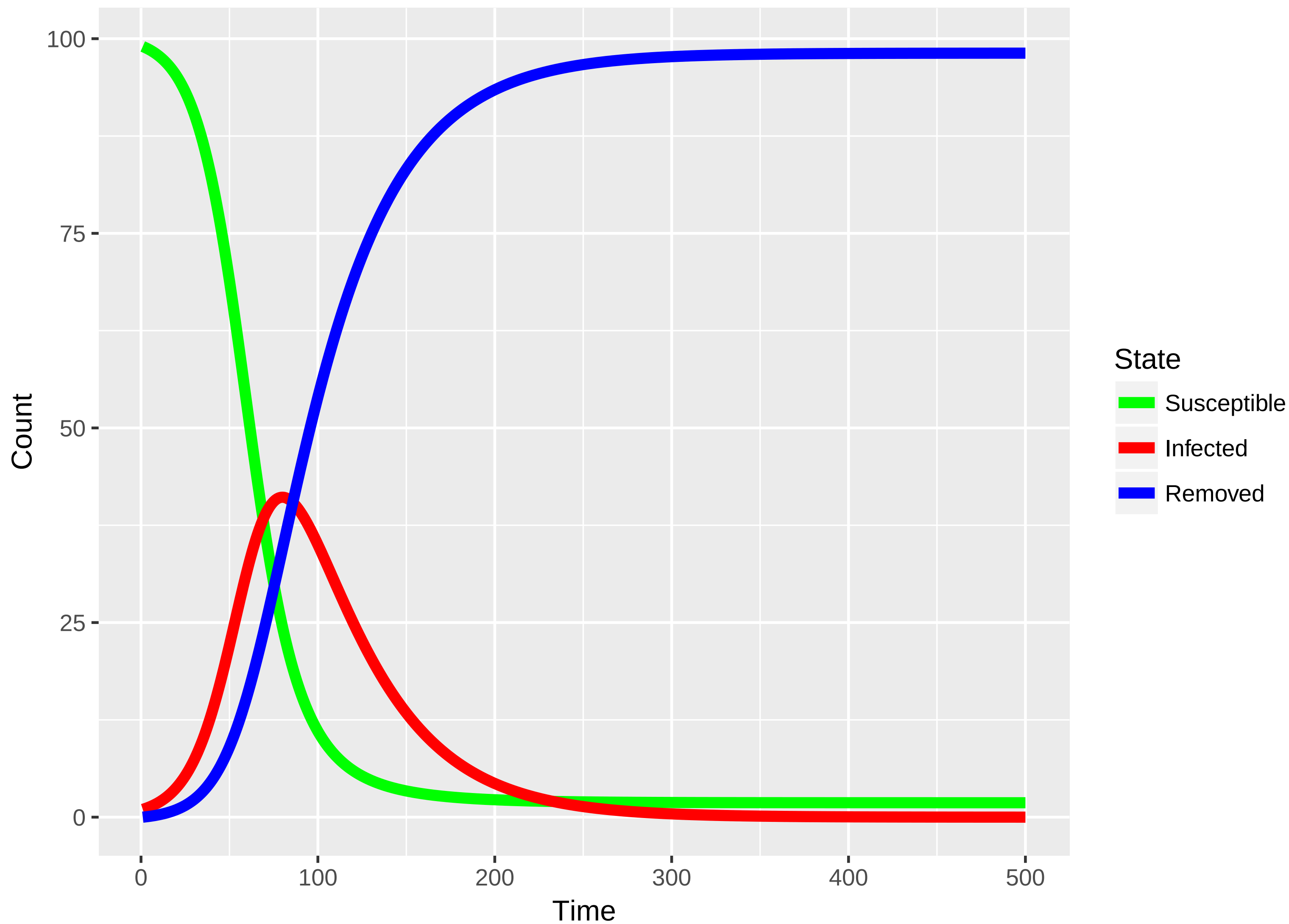
$$I_{t+1} = \beta \times I_t \times S_t - \alpha \times I_t$$

What happens when $I_t = 0$?
What if it’s not?

Example 100 people, 1 infection, $\alpha = 0 \quad \beta = 0.001 \quad N = 100$ (Nobody recovers)

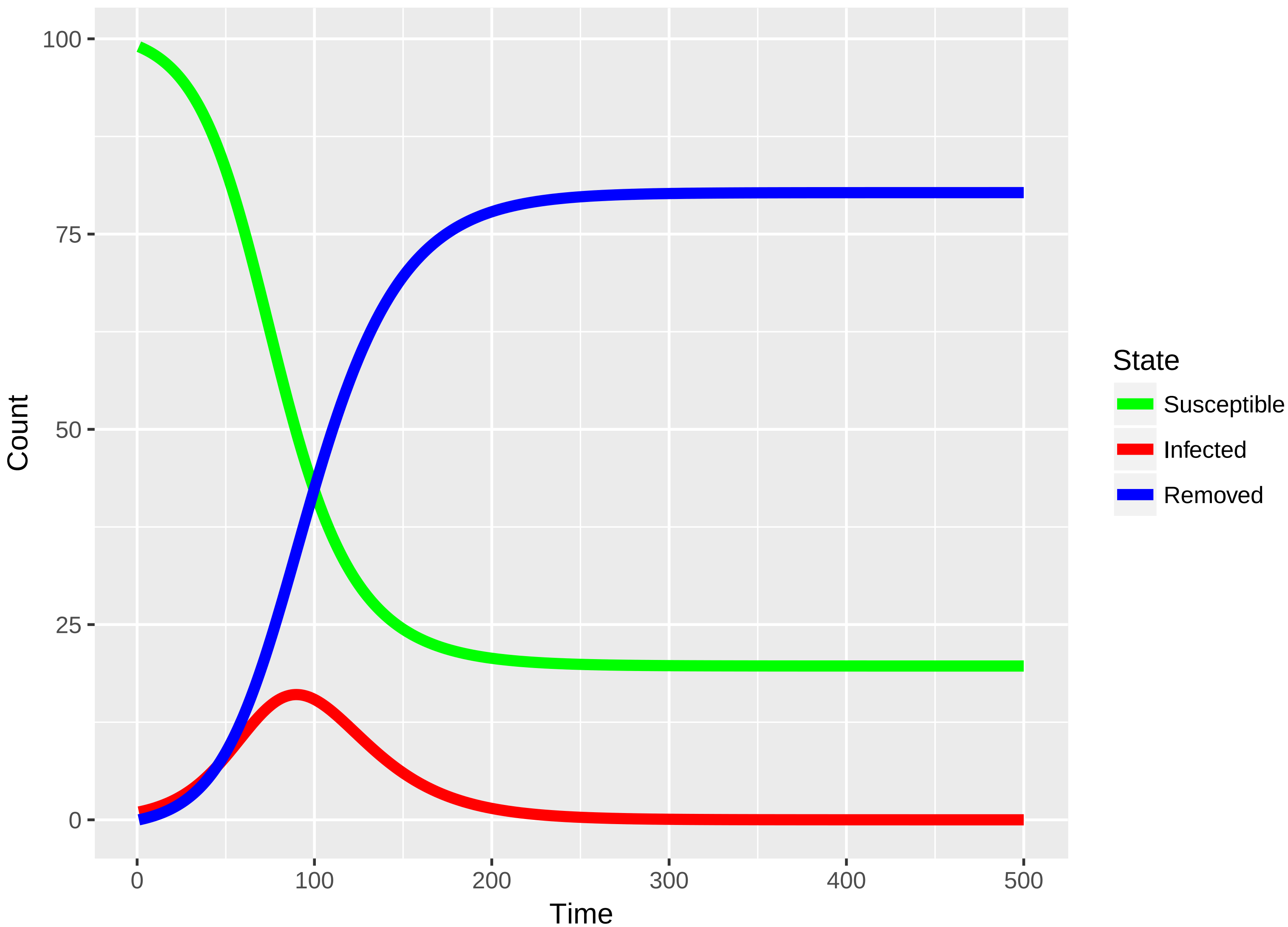


Example $\alpha = 0.025 \quad \beta = 0.001$ (Nearly everyone gets infected)




Only 1.9 people uninfected. Infection peaks on day 80.

Example $\alpha = 0.05 \quad \beta = 0.001$ (Faster recovery)




This time 19.7 people uninfected. Infection peaks on day 90.

# Computational note

What we are actually have here are *differential equations*

$$\begin{aligned}\frac{dS}{dt} &= -\beta SI \\ \frac{dI}{dt} &= \beta SI - \alpha I \\ \frac{dR}{dt} &= \alpha I\end{aligned}$$

which we convert to finite-differences:

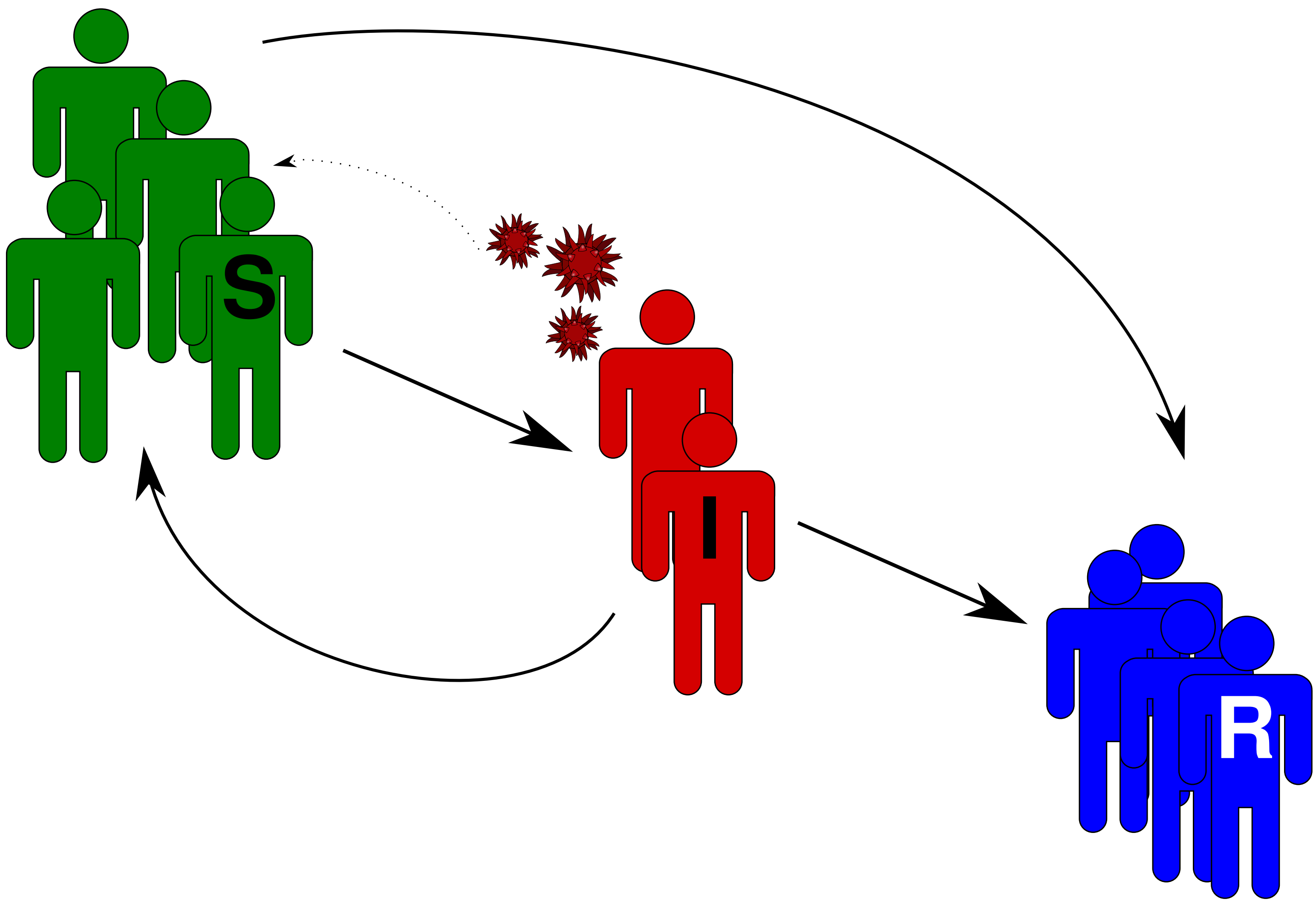
$$\frac{S_{t_2} - S_{t_1}}{t_2 - t_1} = -\beta S_{t_1} I_{t_1}$$

and for a time-step of 1 we get

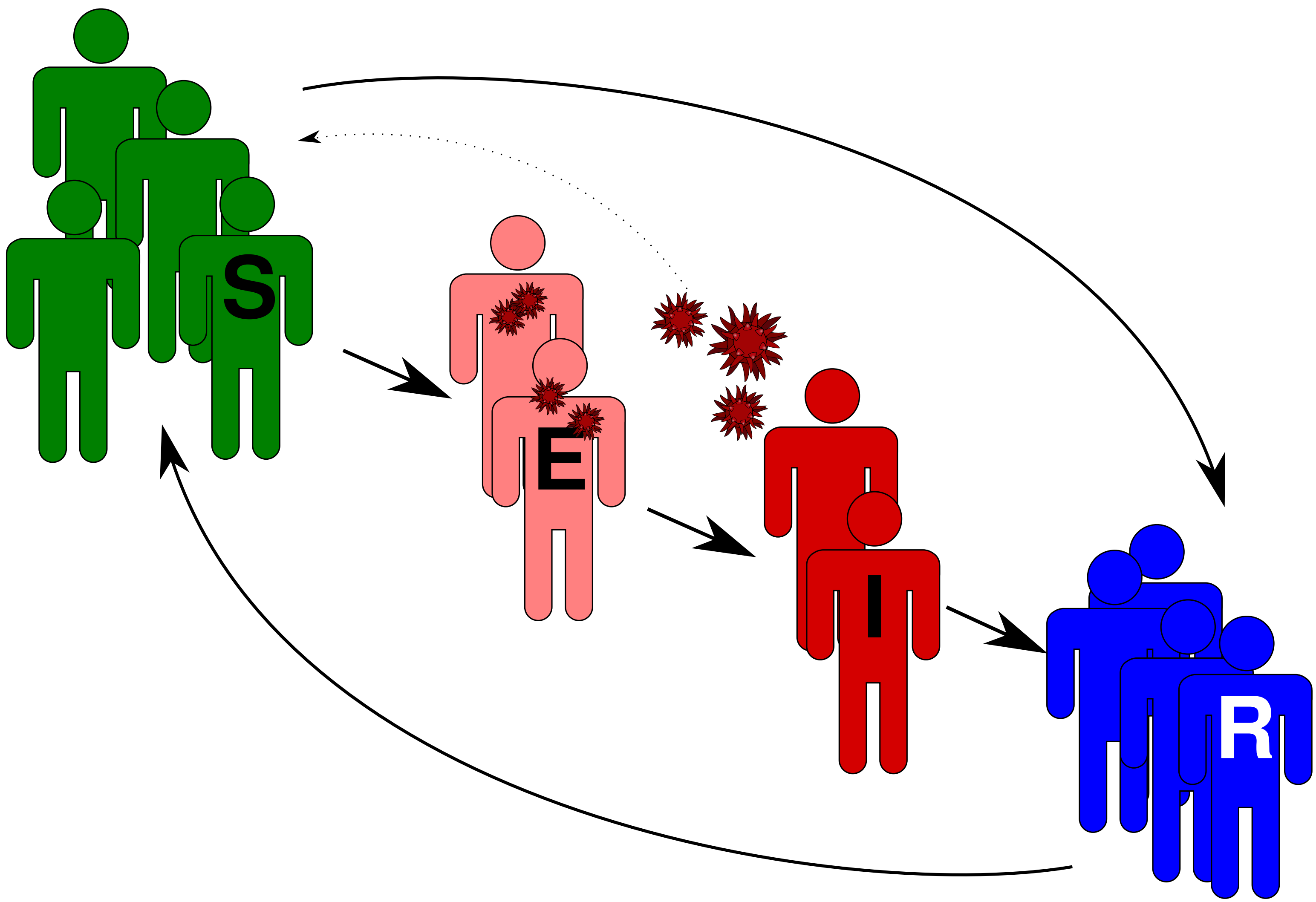
$$S_{t+1} = S_t - \beta S_t I_t$$

but this is an approximation to a continuous process.

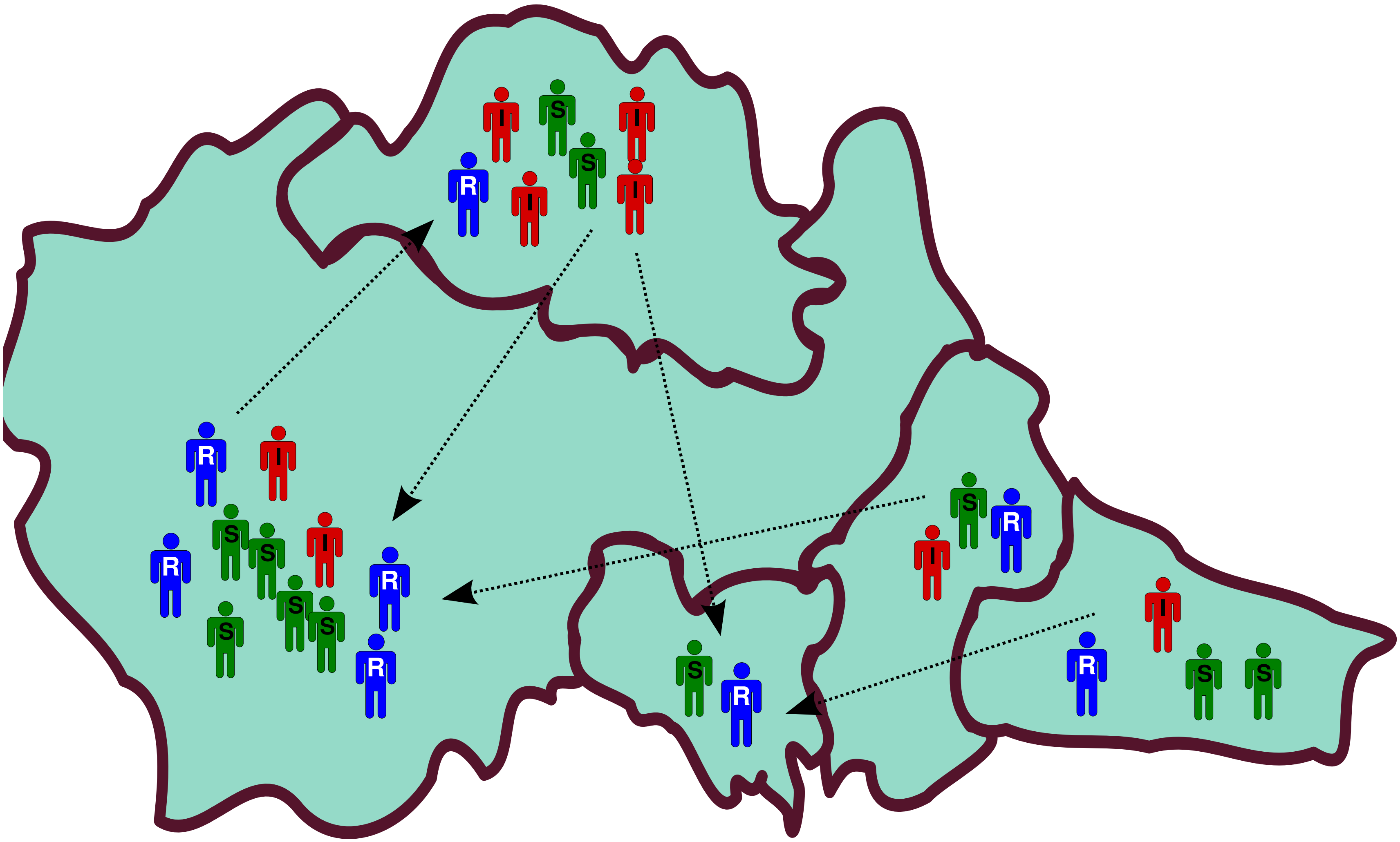
Other models – more transitions:



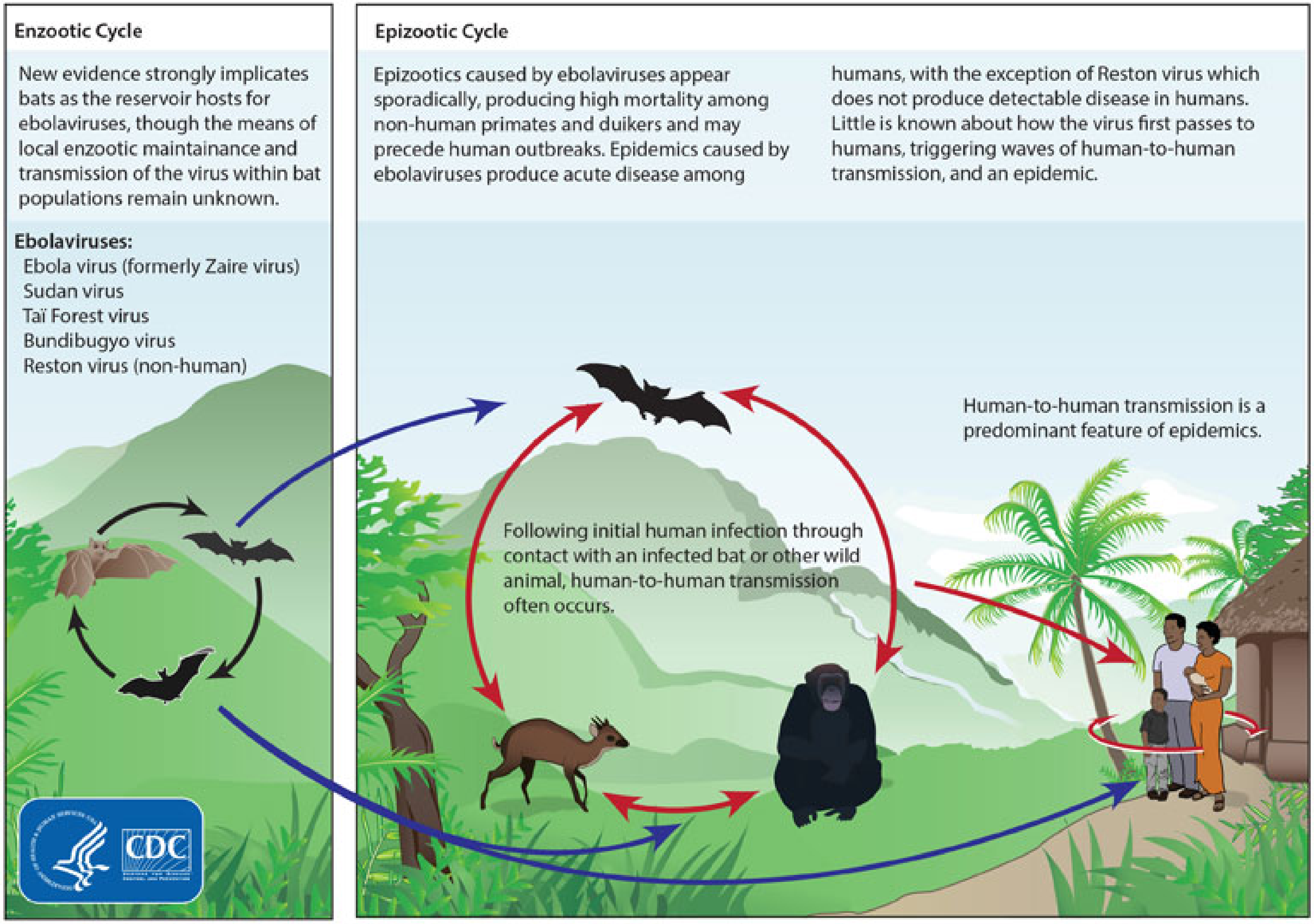
Other models – more states:



# Regional SIR model

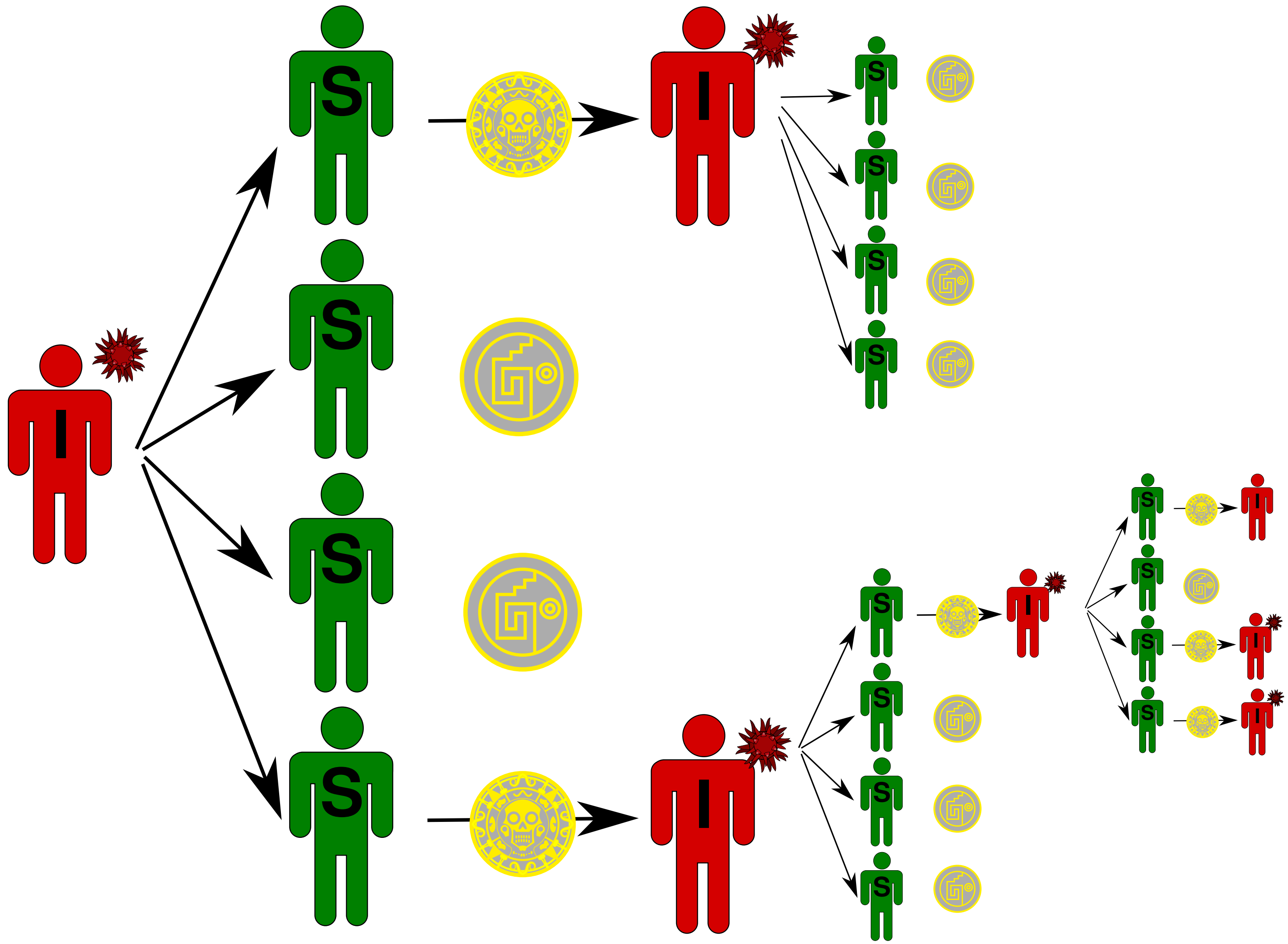


# More Species



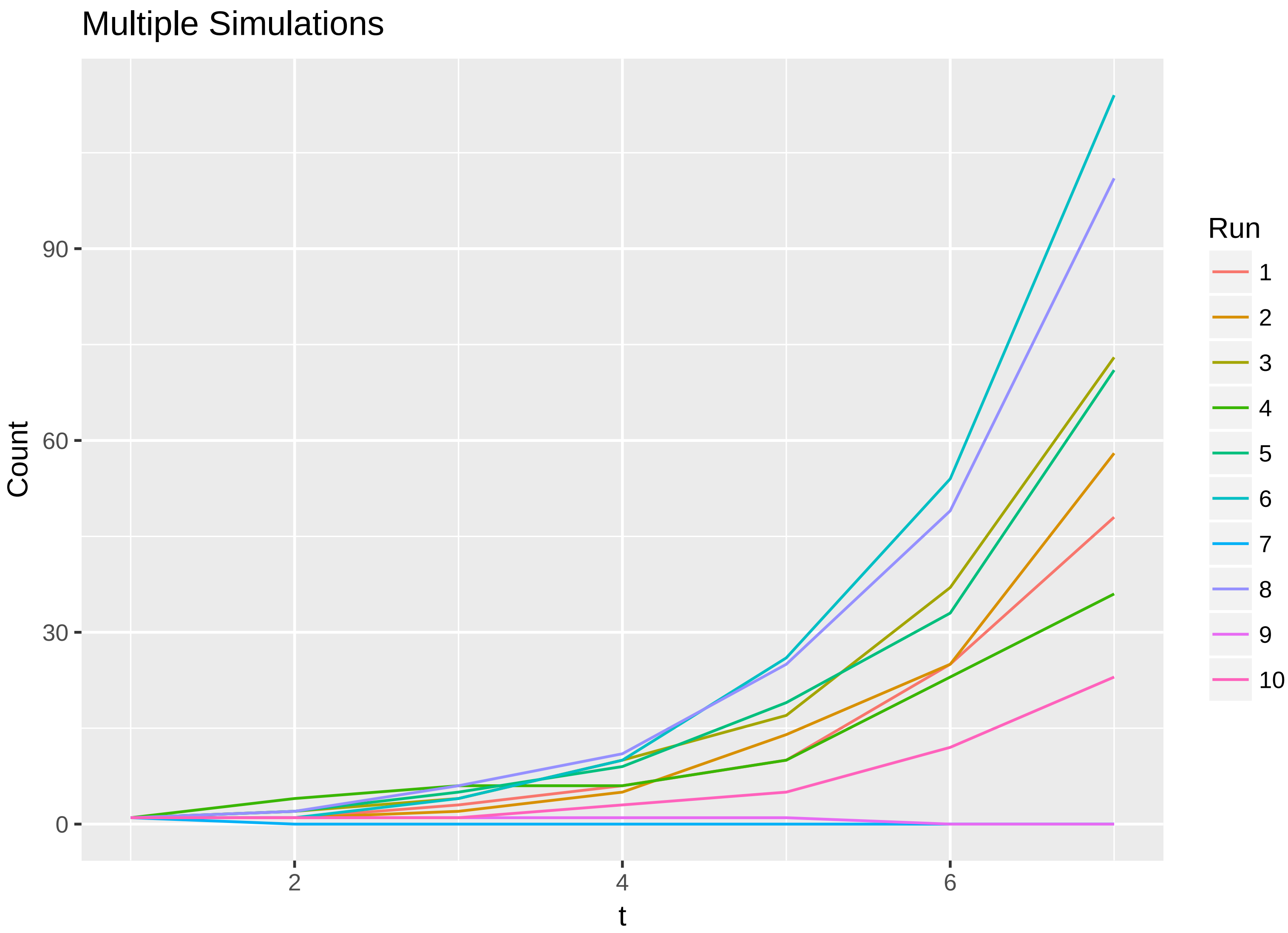
# Reality Is Not Predictable

- Deterministic: 1 case infects 2 new cases
- Stochastic: 1 case infects 4 people with probability $\frac{1}{2}$
- Averages at 1 case infecting 2 new cases
- What happens?


I
S
S
S
S
I
S
S
S
S
I
S
S
S
S
I
S
S
S
S
I
I
I

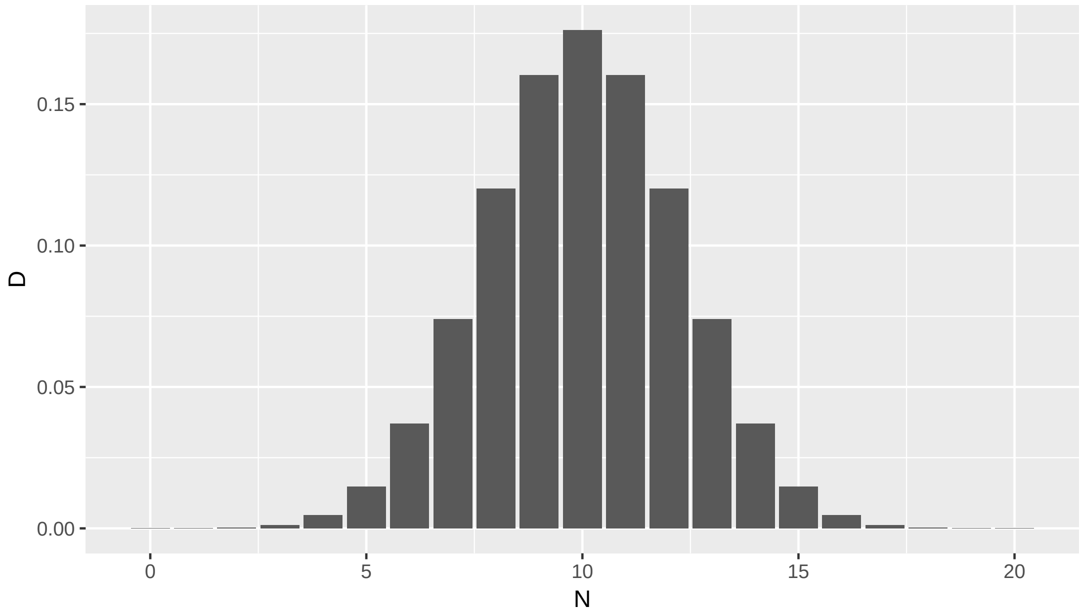
# Multiple Simulations

- One simulation is not enough.
- Need repeated replications
- Results are summaries of the replications properties


Multiple Simulations
Count
90
60
30
0
2
4
6
t
Run
1
2
3
4
5
6
7
8
9
10

# Statistical Theory

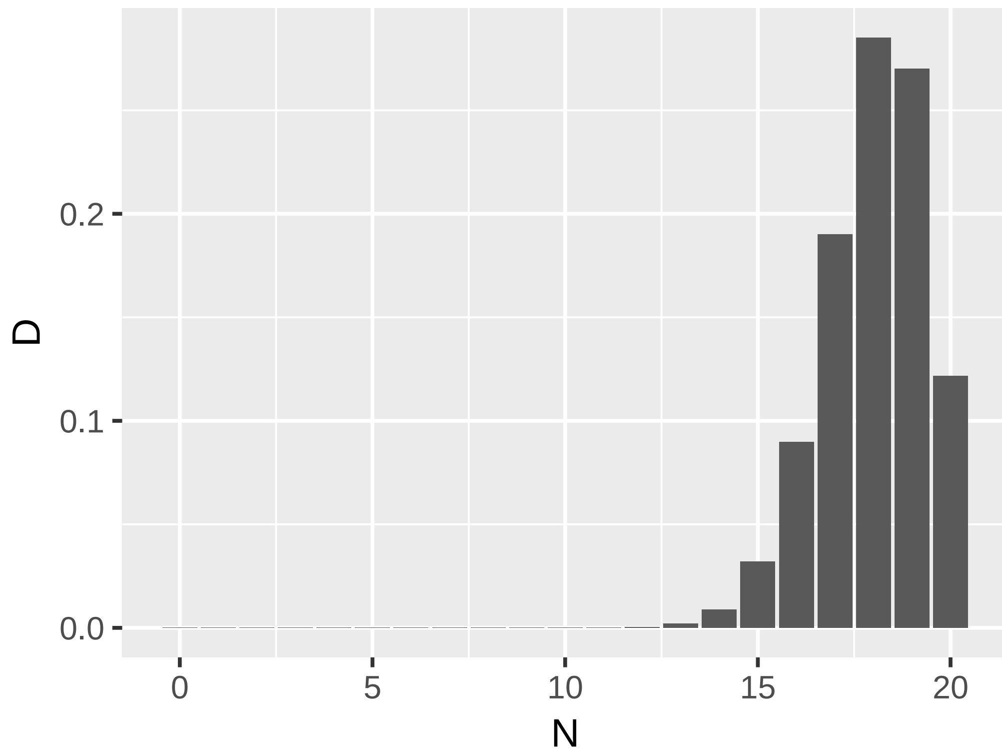
- Is this back to individual, “agent-based” models?
- Can sample directly from a probability density
- Consider 20 infectious cases, probability $\frac{1}{2}$




- Now we can model bulk behaviour

# Changing Probabilities

## 20 Infectious cases, probability = 90%

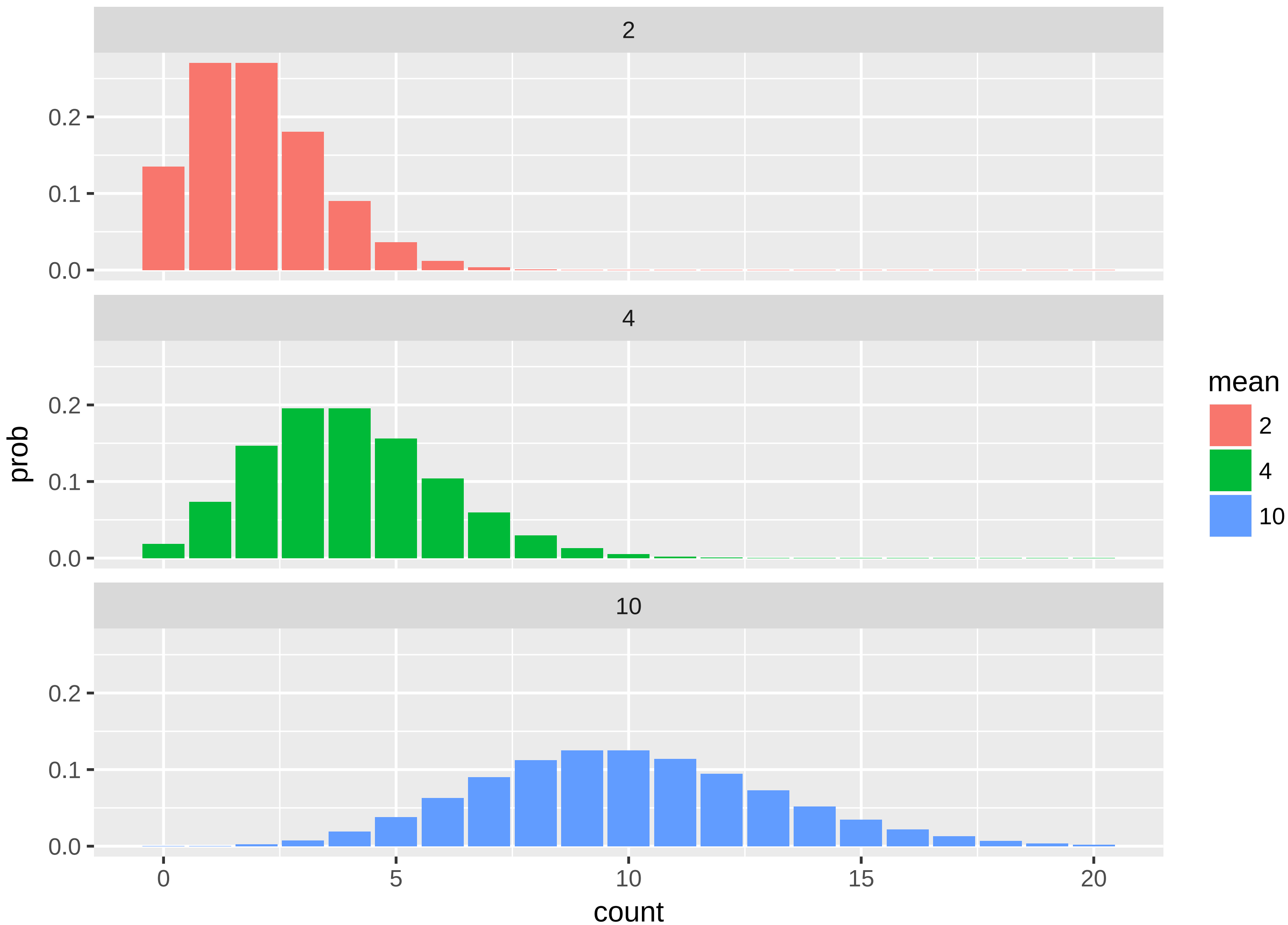


# Changing Numbers

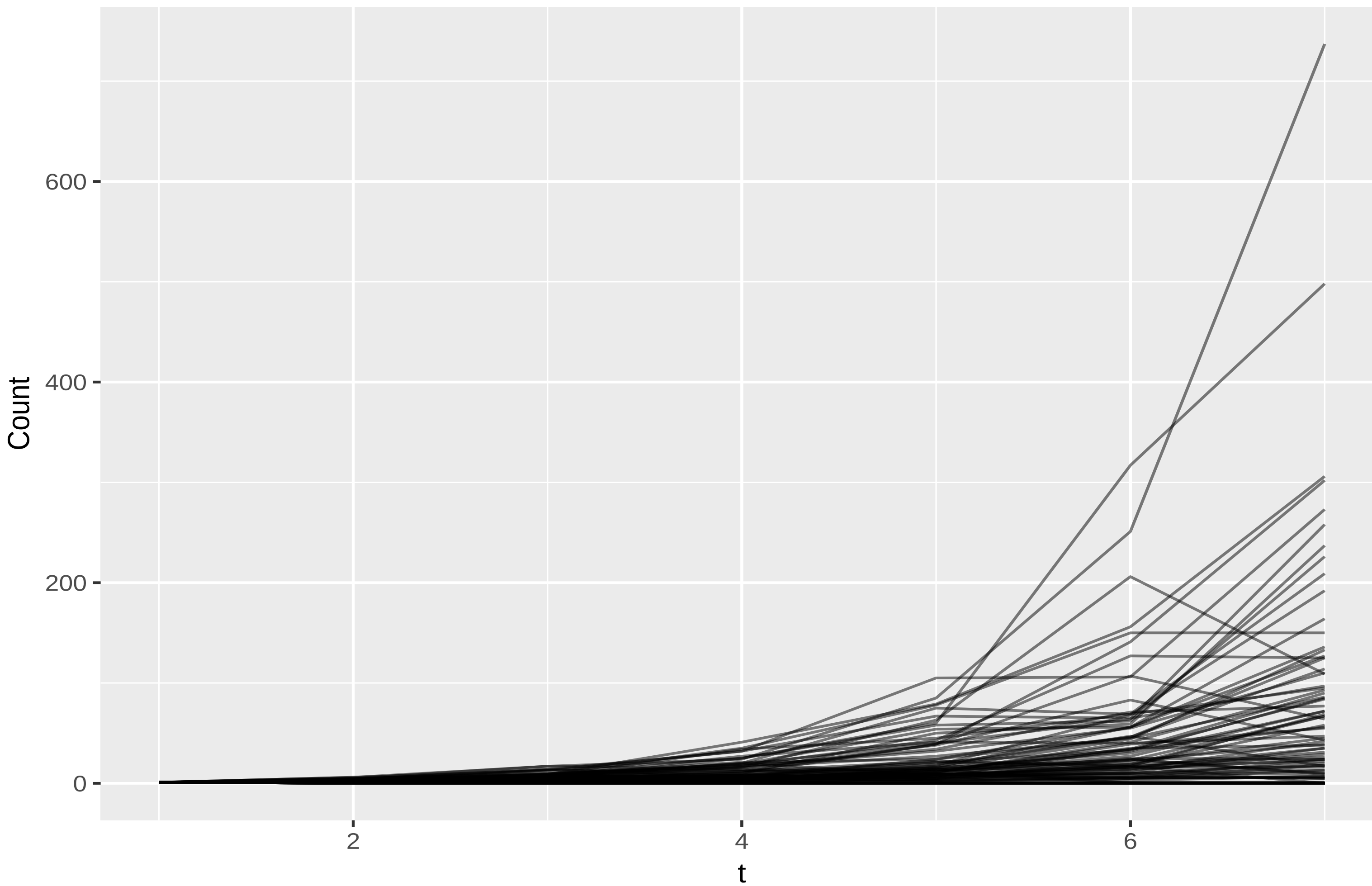
- Each infected person contacts 4 susceptibles
- Seems a bit... deterministic

The “natural” random numbers for count data are “Poisson” random numbers.

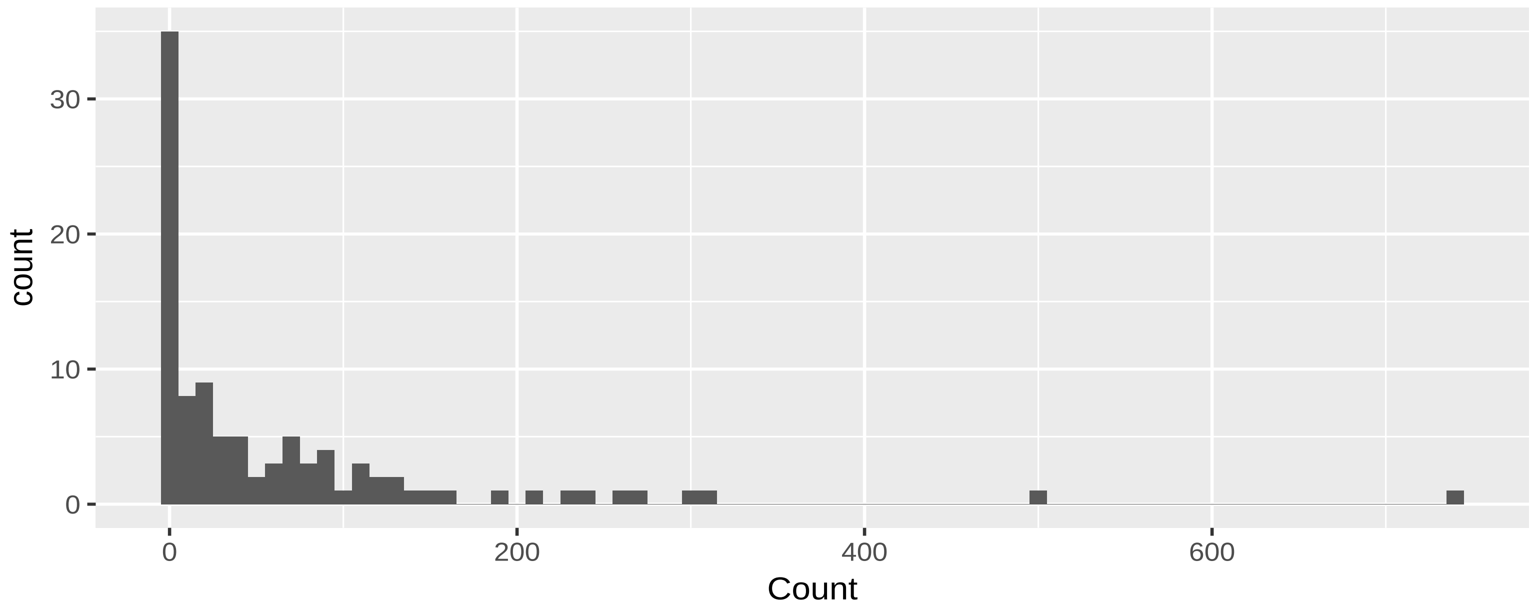
- Integer-valued
- Zero minimum
- Infinite maximum
- Single mean parameter


2
4
10
0.2
0.1
0.0
prob
0
5
10
15
20
count
mean
2
4
10

# Poisson(4) contacts with transmission prob=$\frac{1}{2}$



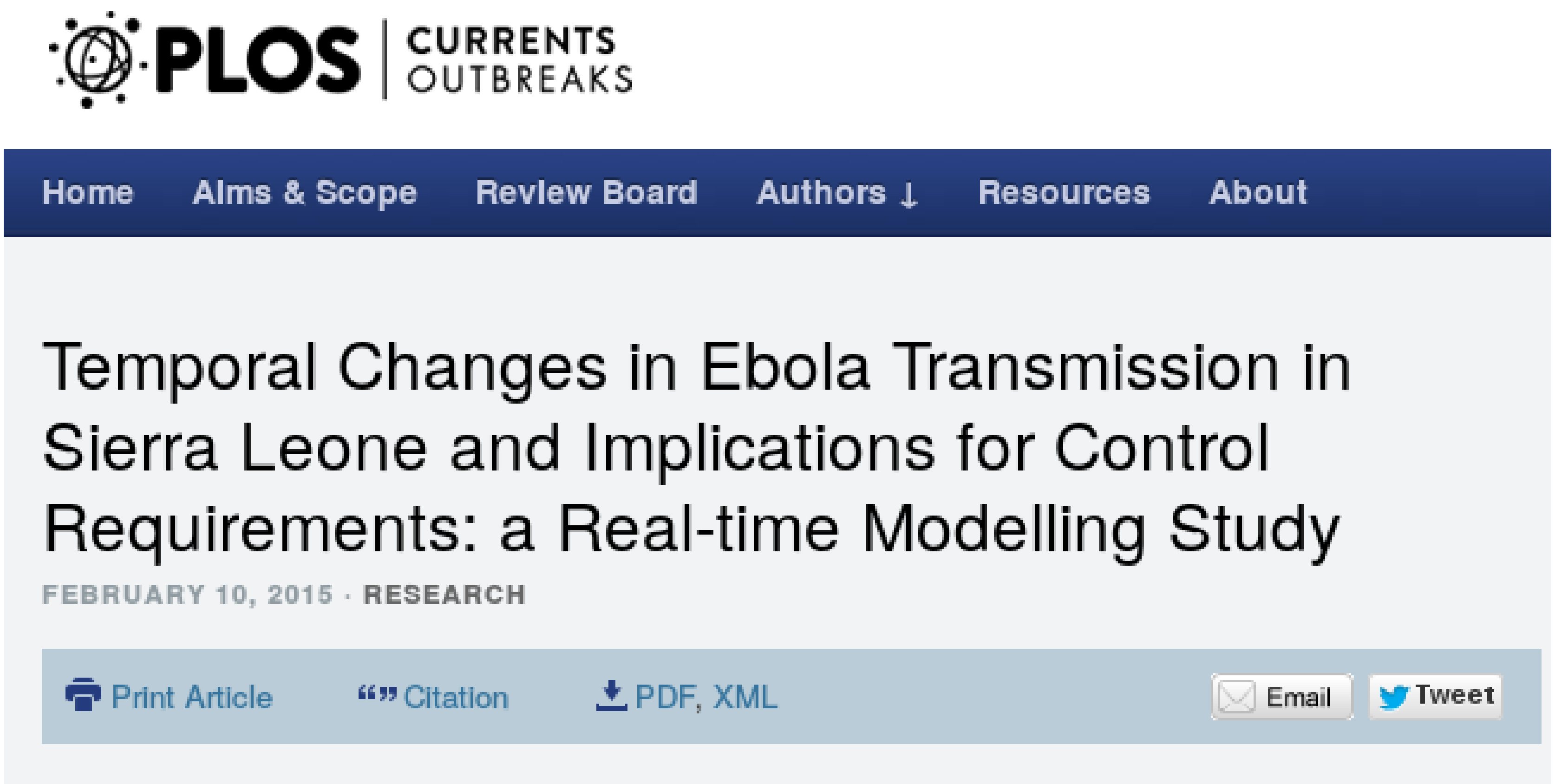
# Summary Statistics on Day 7




- Average count: 65
- Epidemic dies out: 30/100
- Epidemics over 128 cases: 14/100

# The Real World

`http://t.co/pPyHVcZb61`



# Model

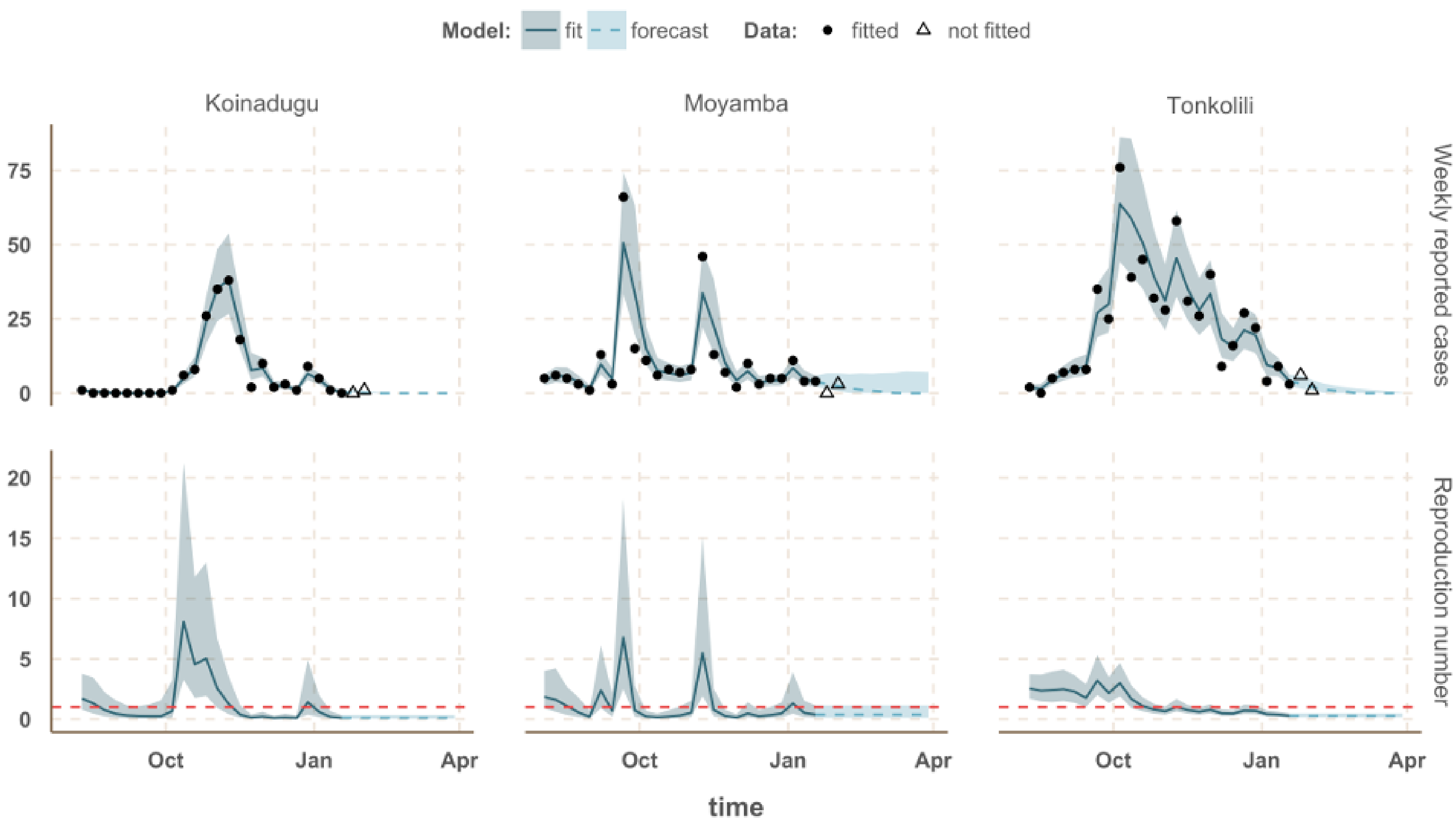
$$S \xrightarrow{\beta_t \frac{(I_c+I_h)}{N}} E_1 \xrightarrow{2\nu} E_2 \xrightarrow{2\nu} I_c \xrightarrow{\tau} I_h \xrightarrow{\gamma} R$$

**Fig. 1: Flowchart of the model**

**Table 2. Description of the transition rates**

| Transition | Description | Rate | Note |
|---|---|---|---|
| $S \to E_1$ | Infection | $\beta_t S(I_c + I_h)/N$ | $\log(\beta_t)$ is a Wiener process[9].<br>$N$ is the population size. |
| $E_1 \to E_2$ | Progression of incubation | $2\nu E_1$ | |
| $E_2 \to I_c$ | Onset of symptoms and infectiousness | $2\nu E_2$ | |
| $I_c \to I_h$ | Hospitalisation and notification | $\tau I_c$ | Includes multiplicative Gamma noise |
| $I_h \to R$ | Removal | $\gamma I_h$ | |

# Predictions



# Some Conclusions

- simple models can be useful
- complex models can be better
- perfect models are probably impossible
- stochastic effects can be counter-intuitive
- if you can’t calculate, simulate!