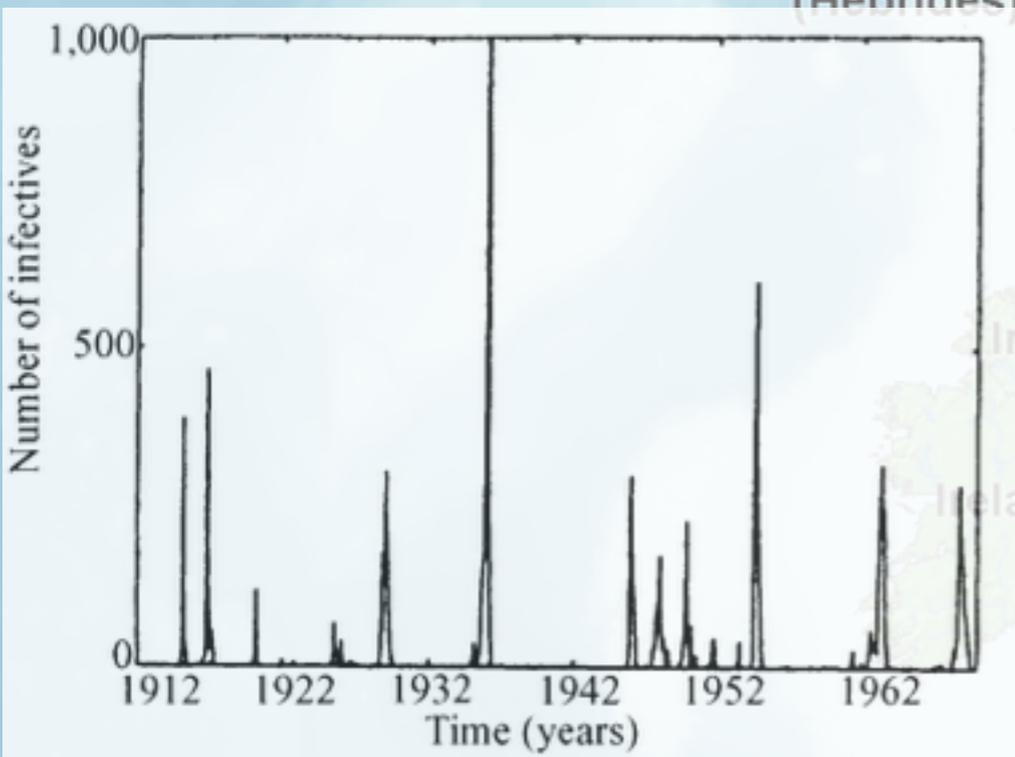


Near-critical dynamics of infectious diseases

Tobias Brett

I) Measles in the Faroe Islands



The Faroe Islands



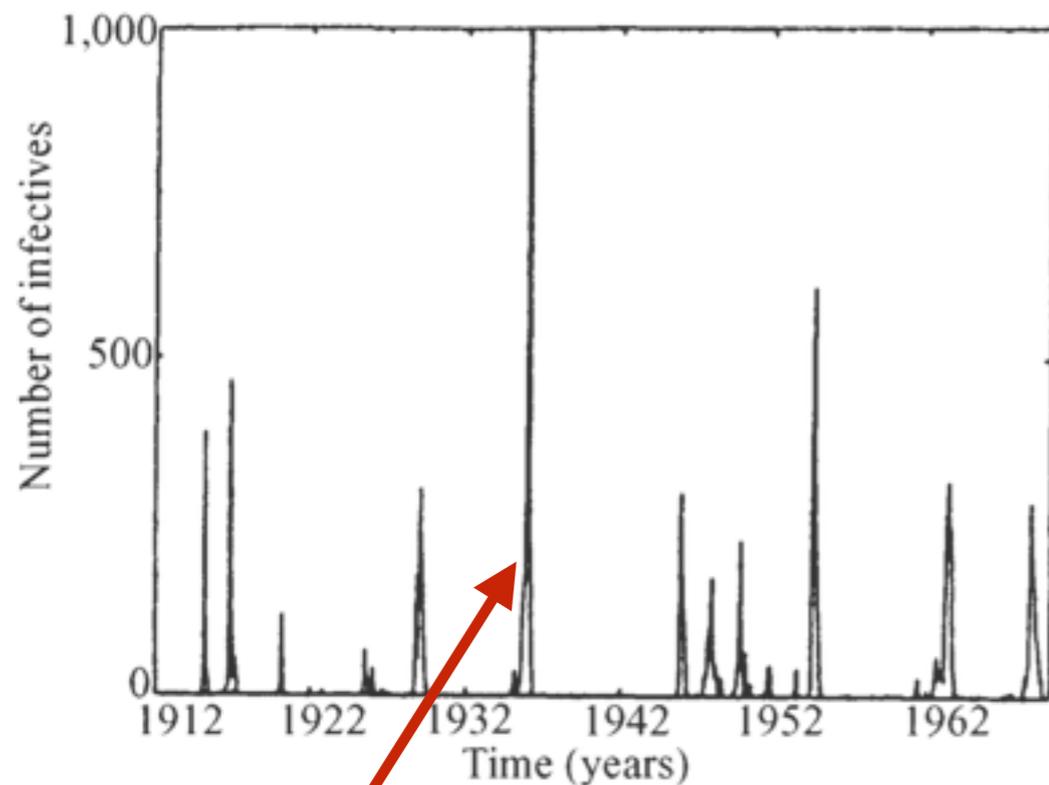
- Isolated islands
- Small population
- Inhabitants scattered across islands

Measles virus

- Morbillivirus, causes measles in humans
- Time from infection to recovery typically less than 3 weeks
- Infection confers lifelong immunity
- Highly contagious, $R_0 \approx 15$

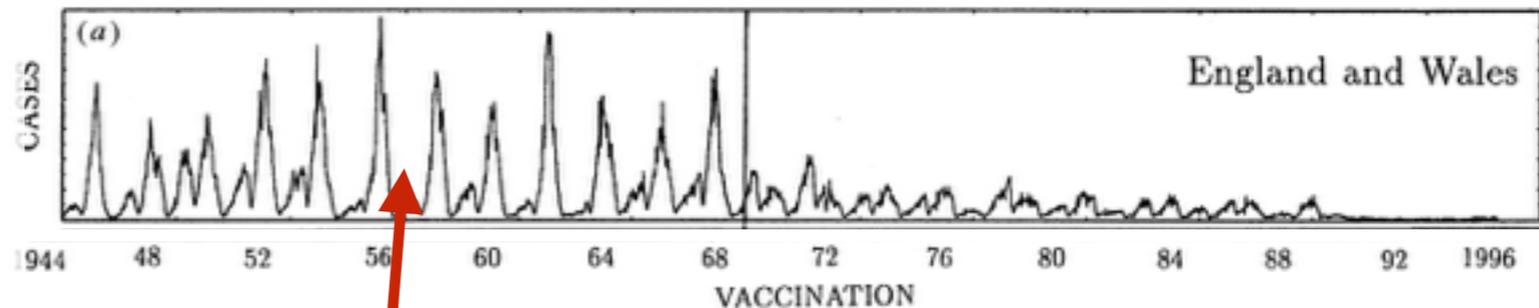
What can we learn about the epidemiology?

Faroe Islands



- Erratic, infrequent outbreaks
- Highly variable sizes
- Long periods with no reported cases

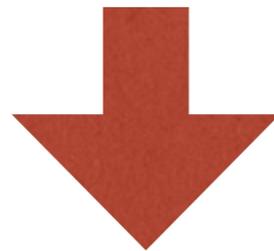
England and Wales



- Regular, periodic outbreaks
- Variable size, but comparable
- Cases reported every month

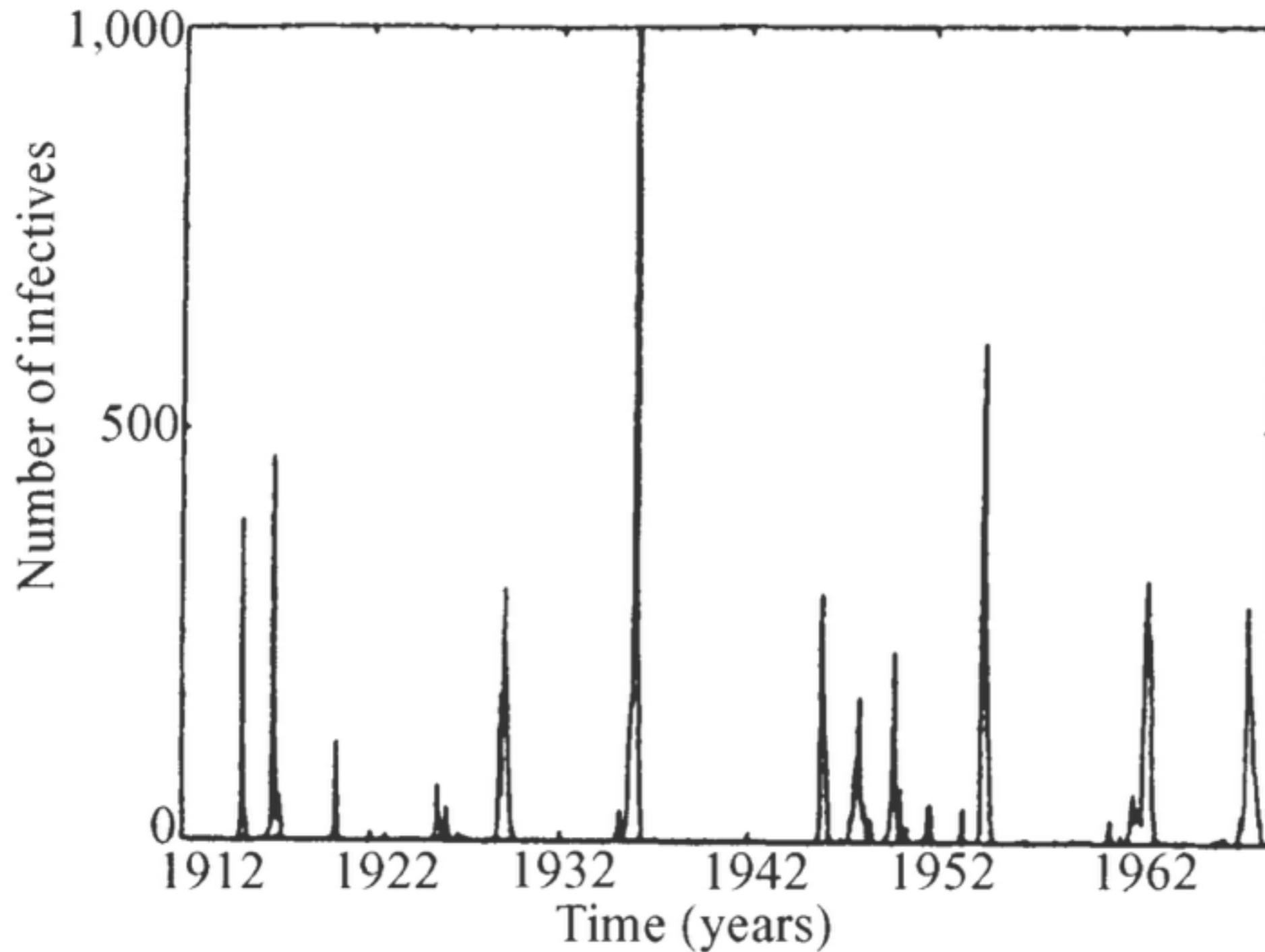
Purpose of the lecture

- Stochasticity in infectious disease dynamics can change the outcomes of an epidemic
- Explore how outbreak size depends on population size through fade-out
- Further look at the epidemic transition at $R_0 = 1$ and introduce the concept of critical slowing down
- Show how critical slowing down is manifest in the outbreak size distribution



use this to understand measles transmission in the Faroe Islands

What is a disease outbreak?



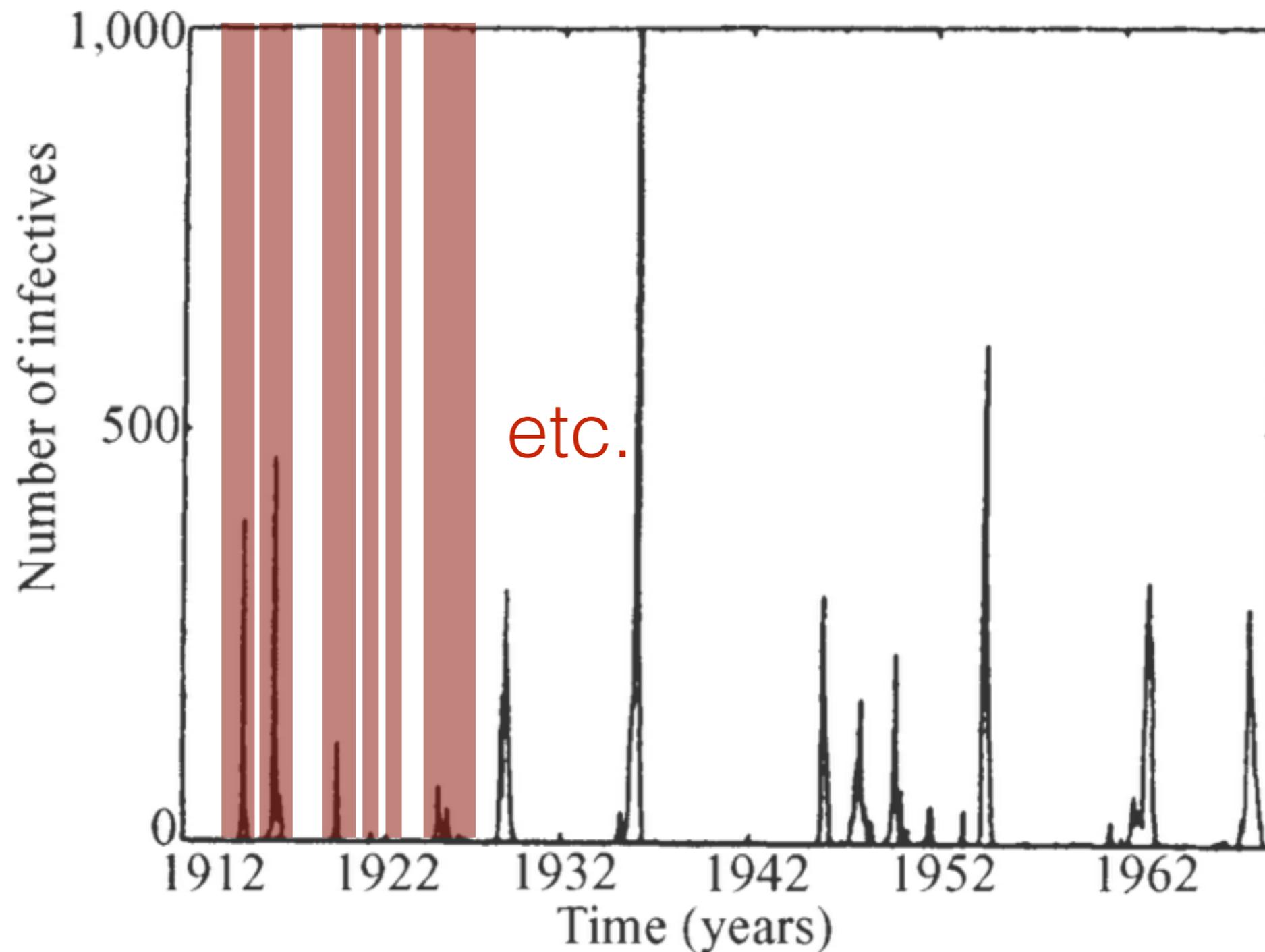
What is a disease outbreak?

A disease outbreak is the occurrence of cases of disease *in excess of what would normally be expected* in a defined community, geographical area or season.
WHO definition

For measles in the Faroe islands:

- Outbreak started by an index case
- Outbreak consists of connected chains of transmission
- Outbreaks ends when there are no longer any infected individuals in the population

Identifying disease outbreaks



The outbreak size distribution

```
43  ##Calculate epidemic size
44  epidemic_size <- function(data){
45    i = 2
46    l = length(data$Time)
47    epi_data <- data.frame(matrix(ncol = 2, nrow = 0)) %>%
48      rename("start_time" = X1,"size" = X2)
49
50  while(i < l){
51    if(data$Infected[i] !=0){
52      t_epidemic = data$Time[i]
53      epidemic_size = 0
54    while(data$Infected[i] !=0 && i < l){
55      if(data$Infected[i] - data$Infected[i-1] == 1) epidemic_size = epidemic_size + 1
56      i = i + 1
57    }
58    epi_data <- rbind(epi_data, list("start_time" = t_epidemic,"size" =epidemic_size) )
59  }
60  else i = i + 1
61  }
62  return(epi_data)
63 }
```

How can we understand these violent outbreaks? (1)

Simple SIR model with birth and death

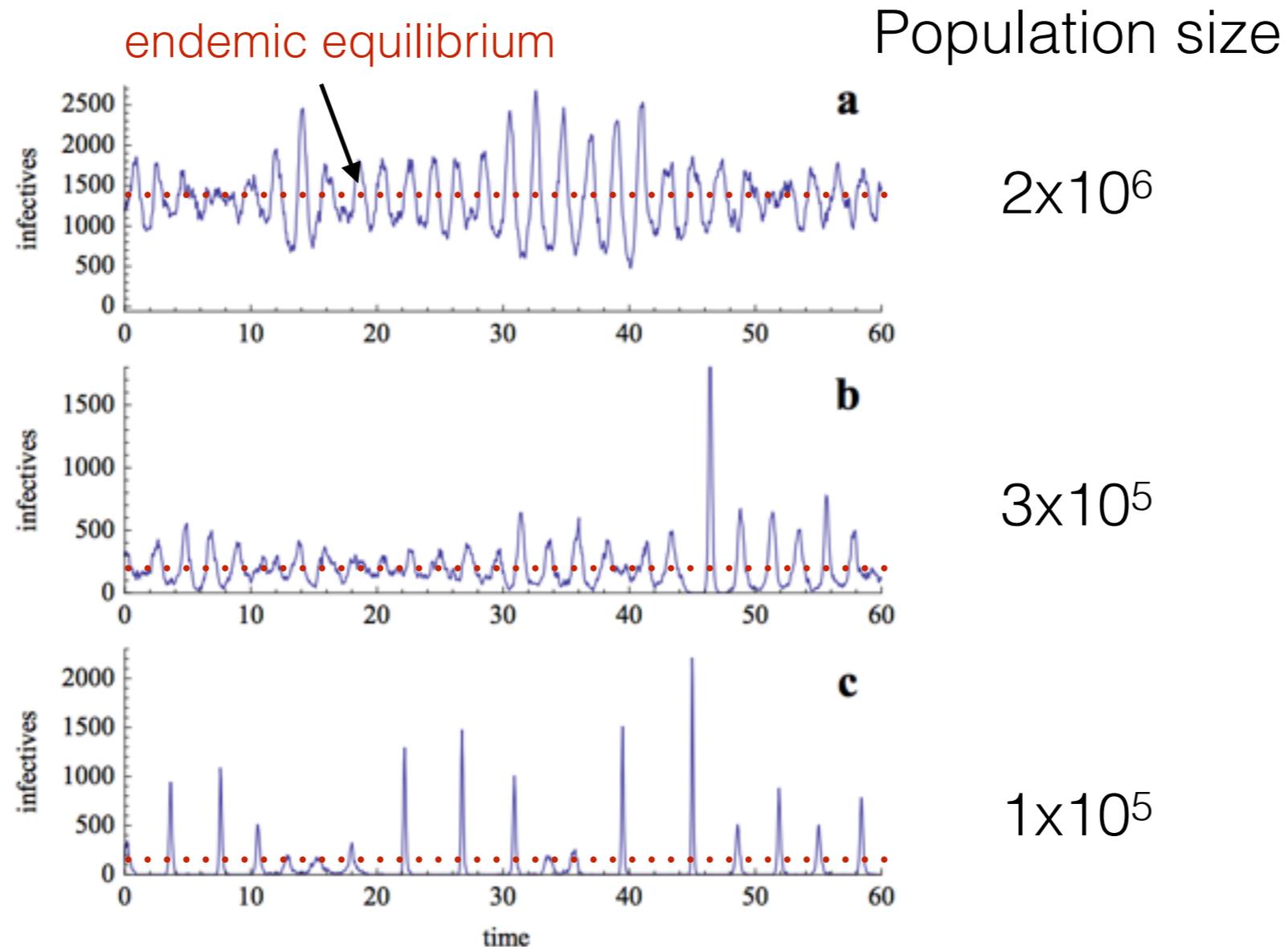
$$\begin{aligned}\frac{dS}{dt} &= \mu - \beta SI - \mu S, \\ \frac{dI}{dt} &= \beta SI - \gamma I - \mu I, \\ \frac{dR}{dt} &= \gamma I - \mu R.\end{aligned}$$

Equilibrium solution gives the ***fraction*** of the population infected

$$I^* = \frac{\mu}{\beta}(R_0 - 1).$$

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

How can we understand these violent outbreaks? (2)



- Fluctuations cause the number of infected individuals to drop to zero. This is known as fade out. **Fade out is a stochastic event**
- Time series simulated using SIR model with frequency dependent transmission, Black McKane (2011)

How can we understand these violent outbreaks? (3)

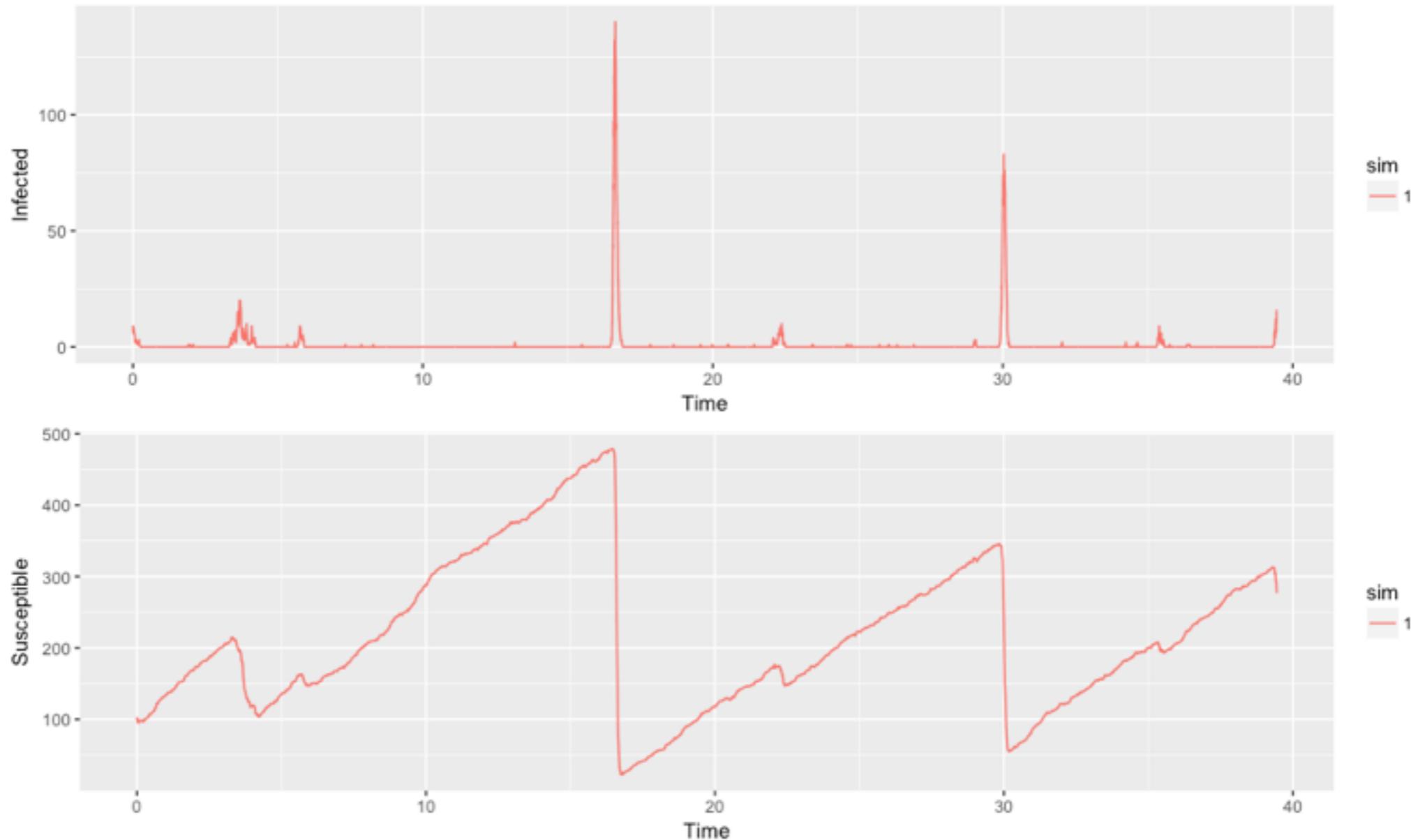
What happens after fade-out? Deterministic behaviour is:

$$\frac{dS}{dt} = \mu - \mu S,$$

$$\frac{dR}{dt} = -\mu R.$$

In the absence of infectious individuals population slowly becomes fully susceptible via birth and death

How can we understand these violent outbreaks? (3)



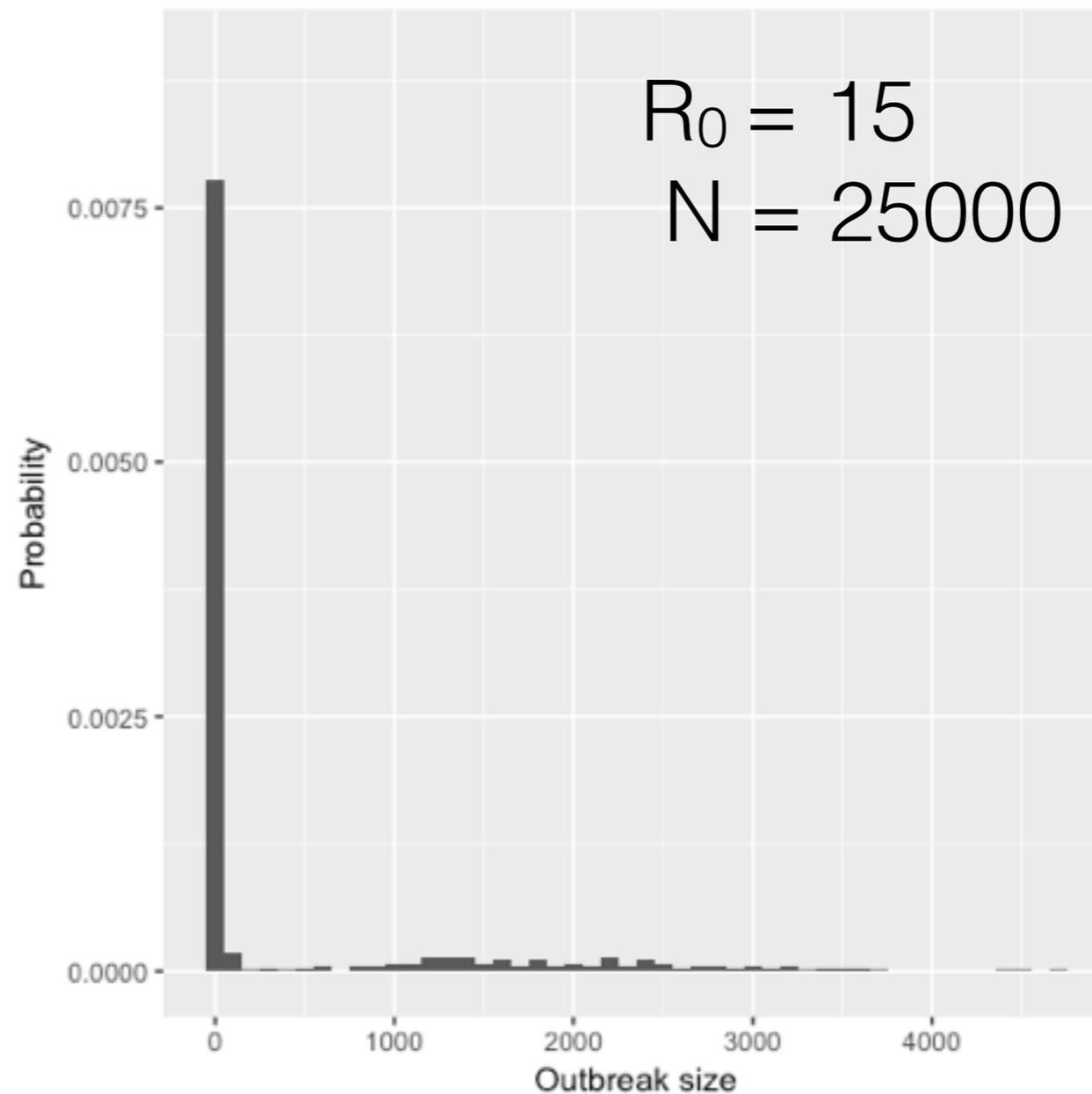
```
96 set.seed(38495) #set seed
97 nsims <- 1 #number of simulations
98 pop.size <- 2500 #total population size
99 Y0 <- 8 #initial number infected
100 X0 <- 100 #round(0.1*pop.size) #initial number susceptible (~98% of population)
101 nstep <- 5000#2500*50 #50*pop.size #number of events to simulate
102 xstart <- c(time=0,X=X0,Y=Y0,Z=pop.size-X0-Y0) #initial conditions
103 params <- list(mu=1.0/70.0,beta=420,gamma=365/13, eta = 1) #parameters
104 #data <- vector(mode='list',length=nsims) #initialize list to store the output
```

What does the outbreak distribution look like?

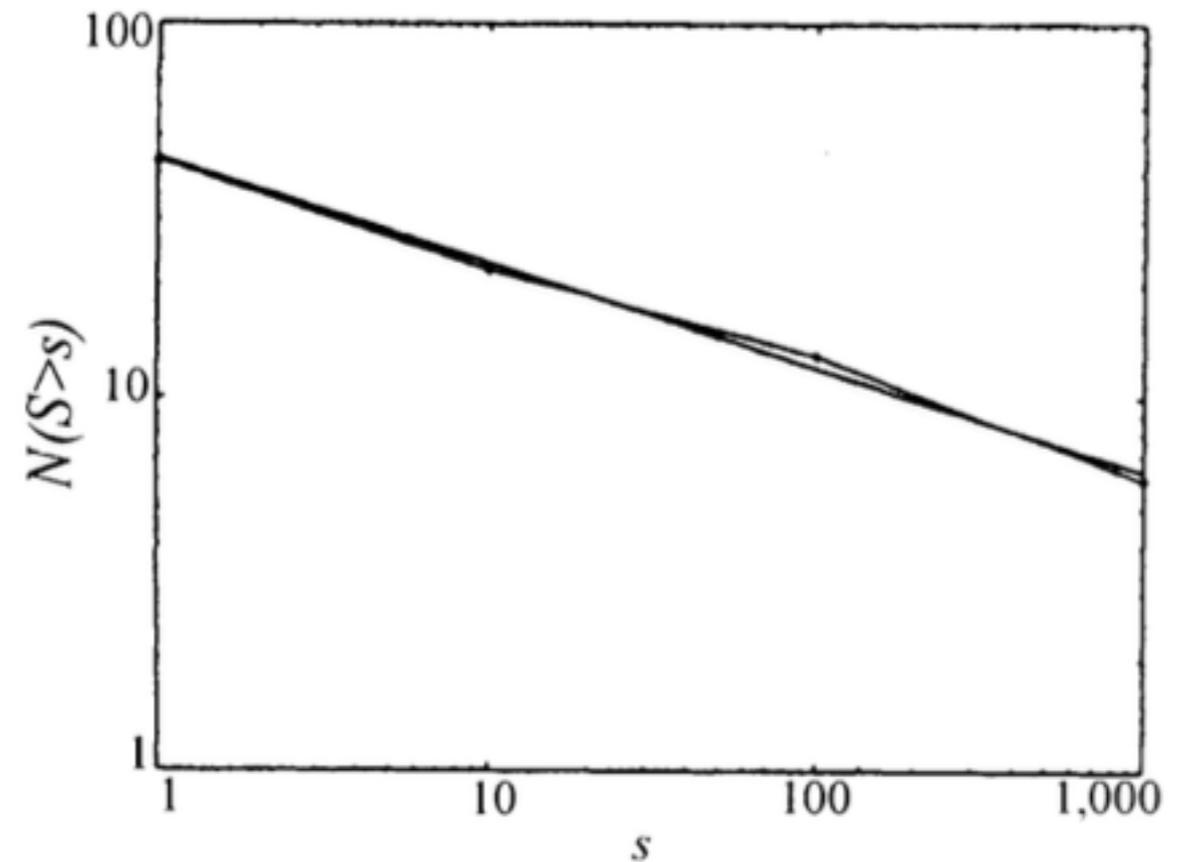
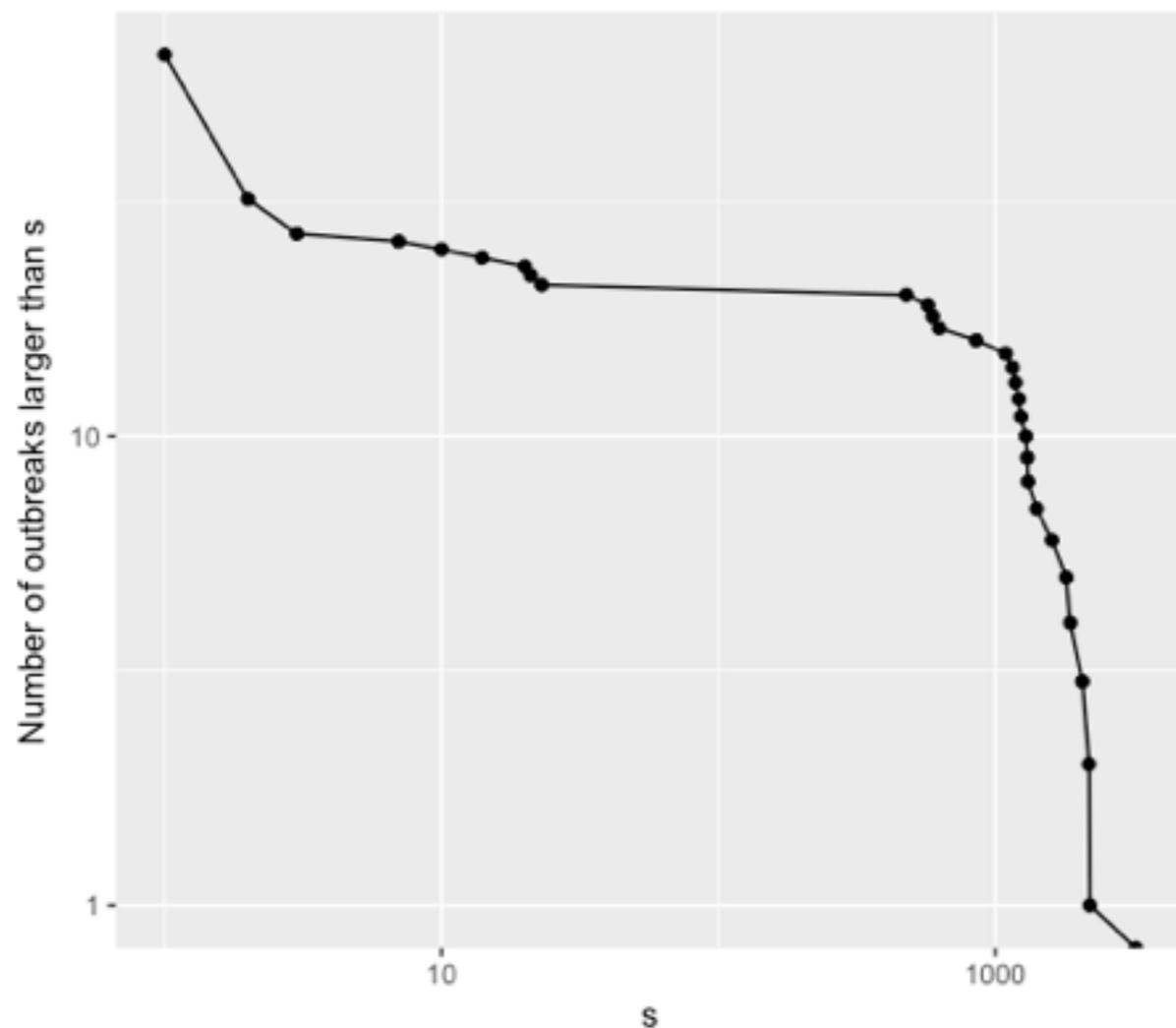
Simulate the SIR model with birth, death and repeated introductions

```
96  set.seed(38495) #set seed
97  nsims <- 1 #number of simulations
98  pop.size <- 25000 #total population size
99  Y0 <- 8 #initial number infected
100 X0 <- 100 #initial number susceptible
101 nstep <- 1250000 #number of events to simulate
102 xstart <- c(time=0,X=X0,Y=Y0,Z=pop.size-X0-Y0) #initial conditions
103 params <- list(mu=1.0/70.0,beta=420,gamma=365/13, eta = 1) #parameters
104 #data <- vector(mode='list',length=nsims) #initialize list to store the output
```

What does the outbreak distribution look like?



How does the outbreak size distribution for the SIR model compare with the Faroe Islands?



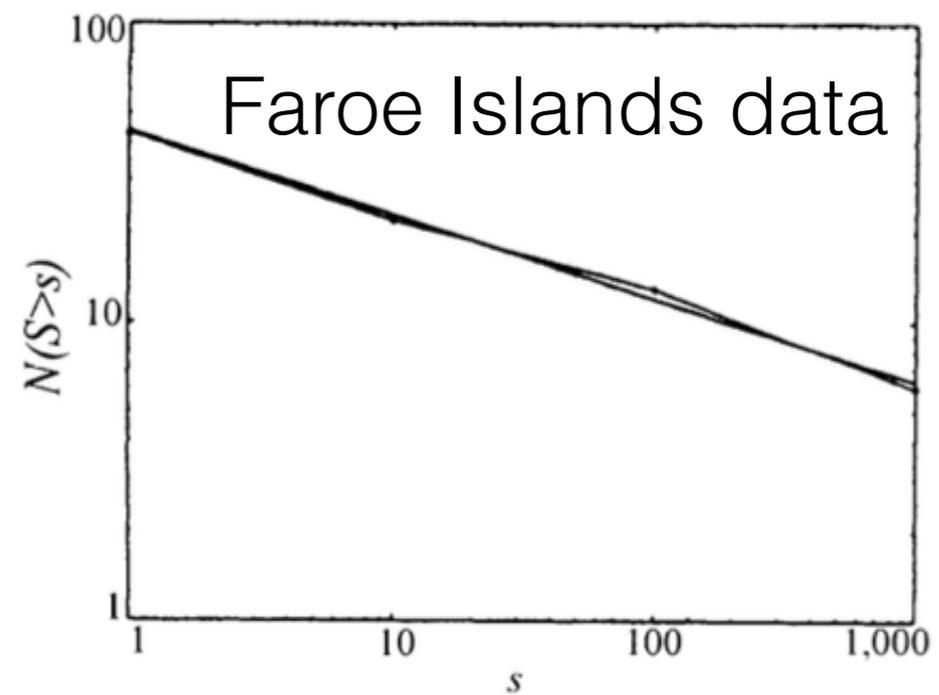
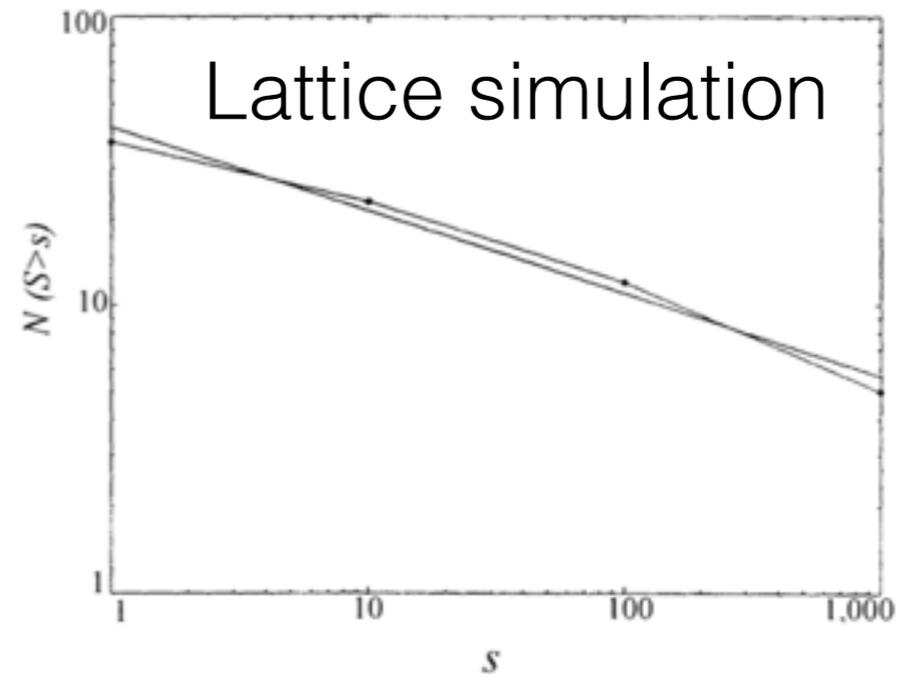
Rhodes and Anderson (1996)

Although qualitatively similar, the stochastic SIR model is incapable of reproducing the data

The hidden ingredient: spatial separation

- The stochastic SIR model was helpful: we now understand how the the small population of the Faroe Islands leads to disease fadeout
- Fadeout drives the violent outbreaks in the data
- However small population size alone is not enough to explain the power law outbreak size distribution
- Another demographic feature of the Faroe Islands is needed: spatial separation of the population

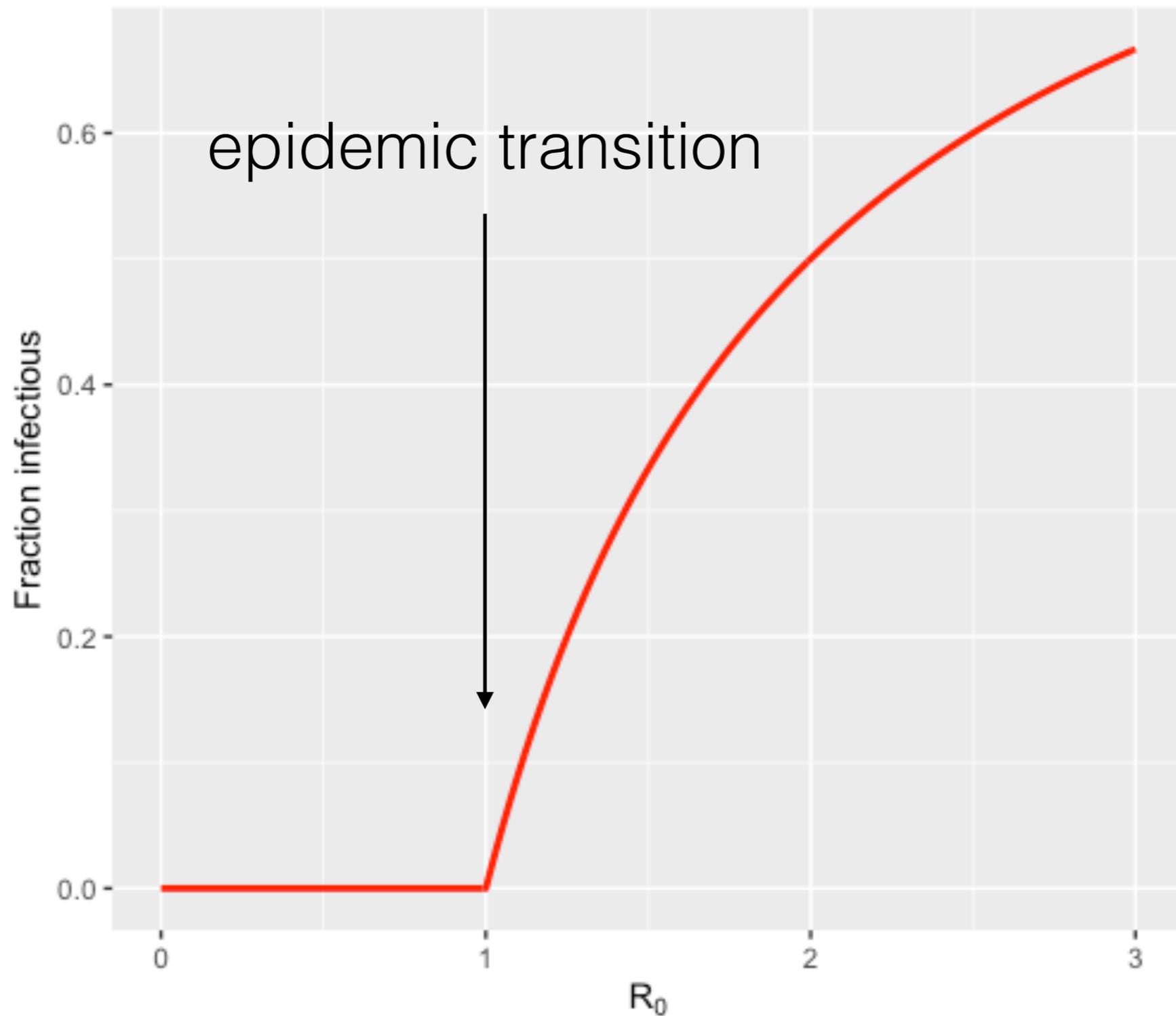
Lattice models of spatial separation



II Critical slowing down



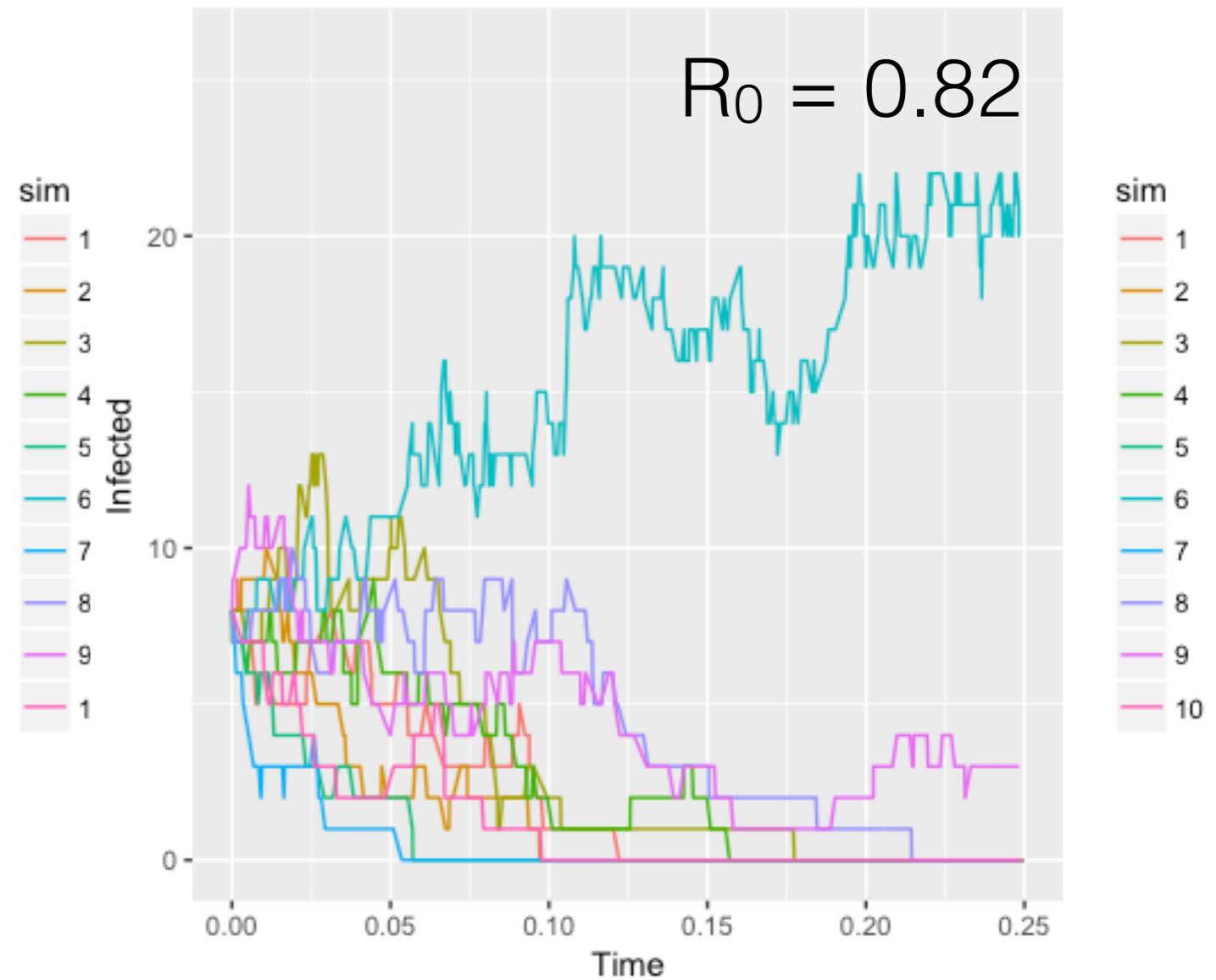
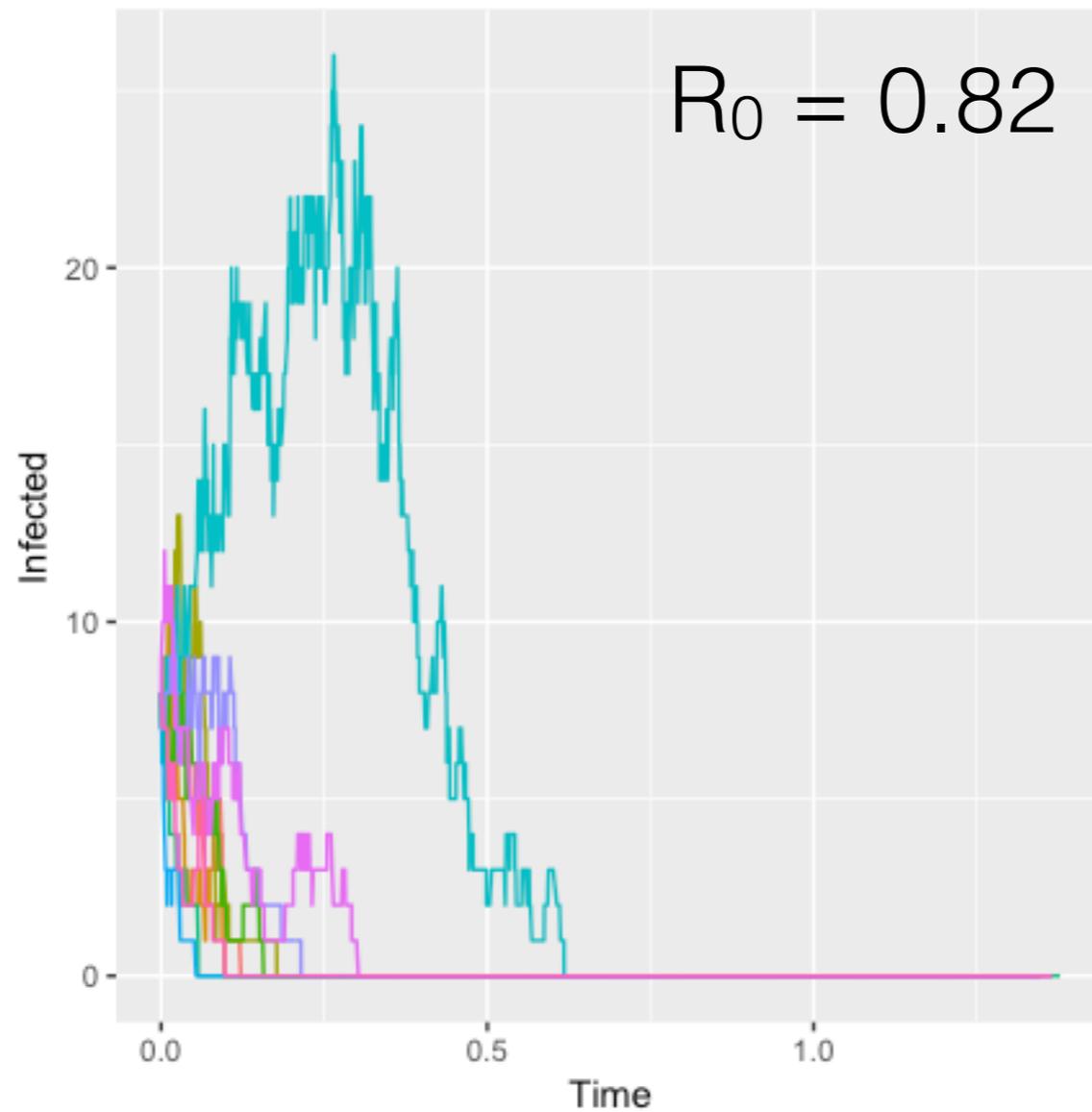
The epidemic transition



What is the epidemic transition?

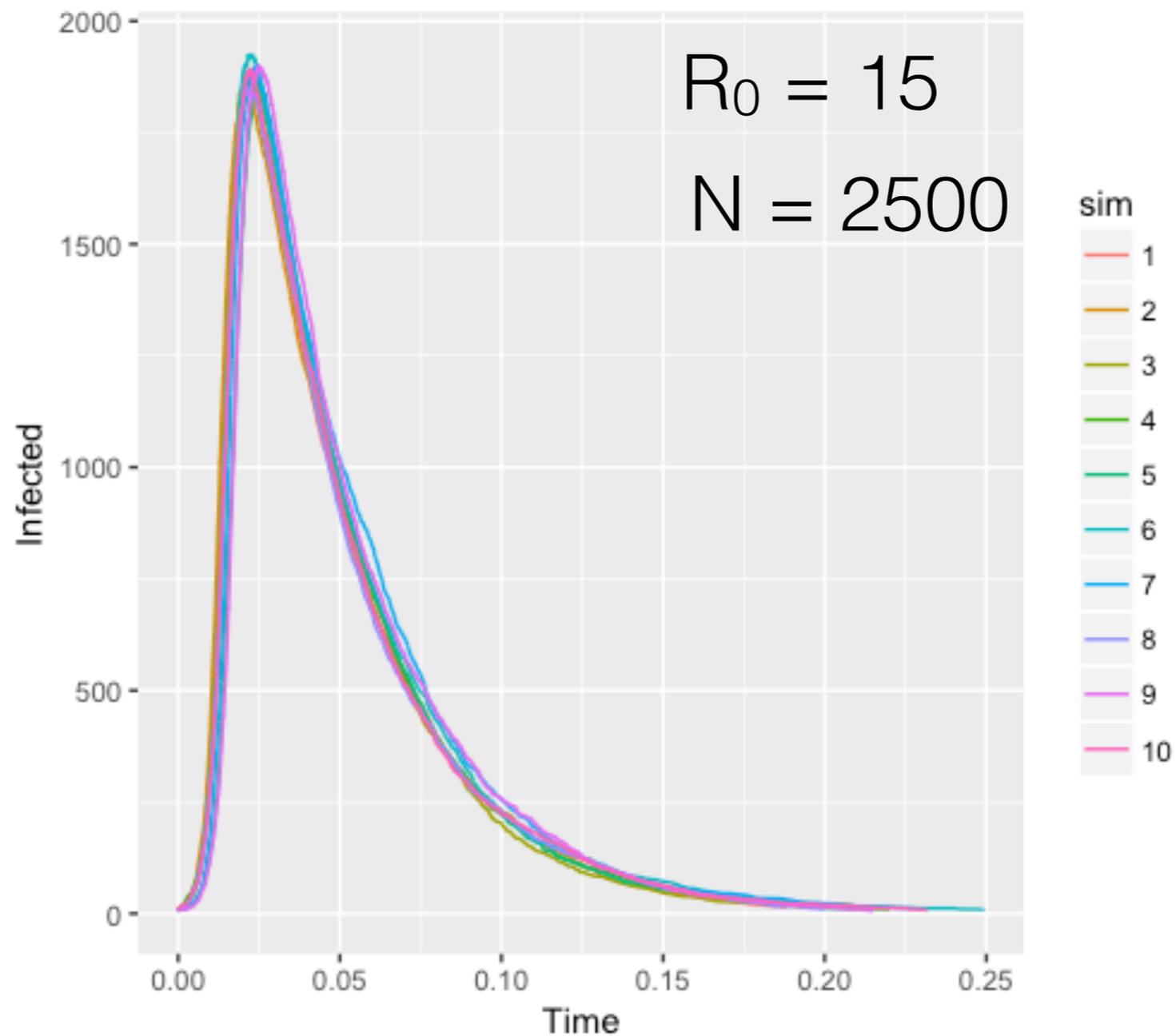
- The epidemic transition separates two distinct regions of parameter space, example of a *critical transition*
- Below the epidemic transition ($R_0 < 1$) the disease cannot establish itself in the population. Dynamics are characterized by short, stuttering chains of transmission. Sustained prevalence is only possible due to external introduction.
- Above the epidemic transition ($R_0 > 1$) the disease is capable of sustained transmission: large scale outbreaks are possible, and the disease may become endemic.

Subcritical dynamics: $R_0 < 1$



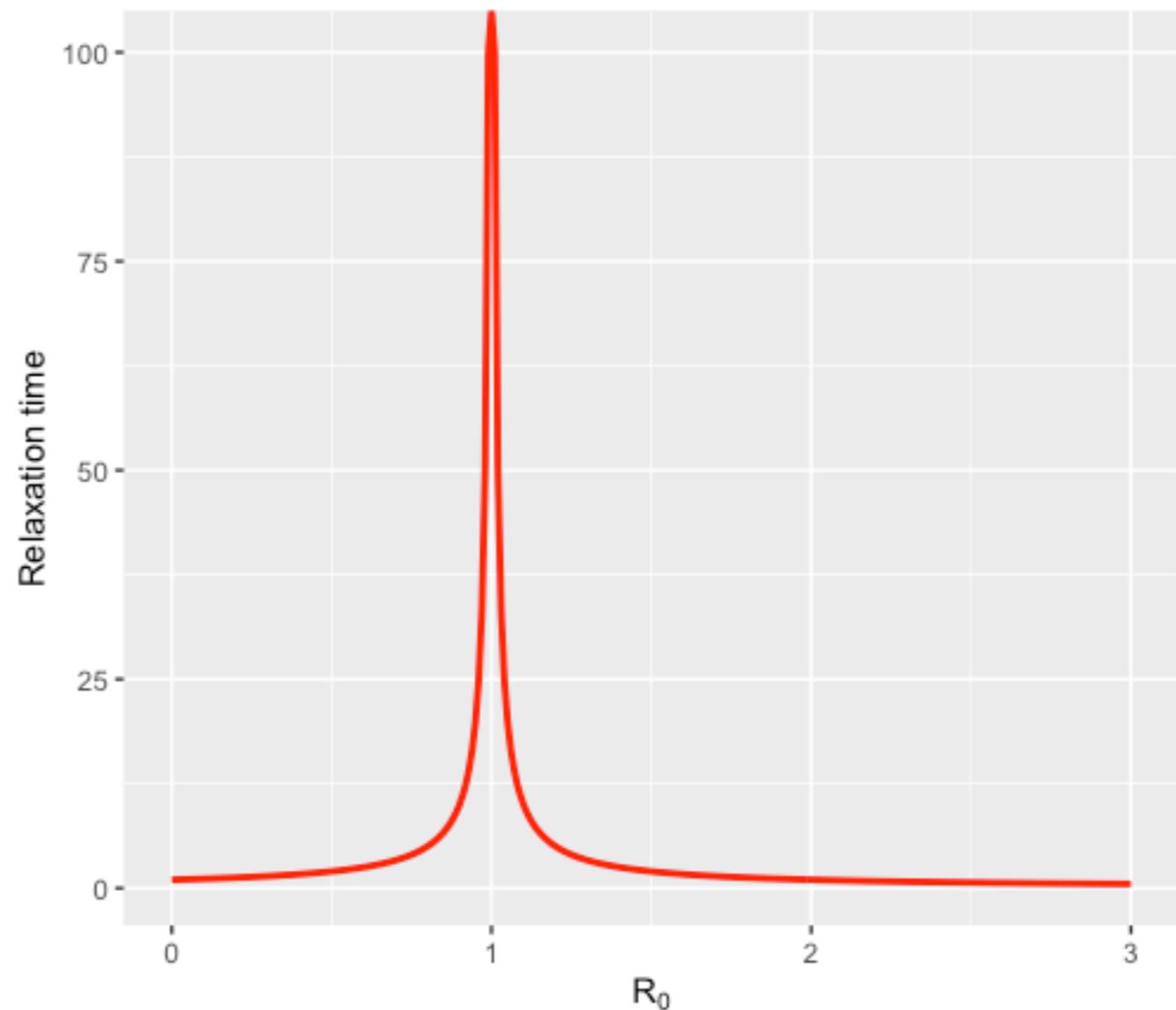
Supercritical dynamics:

$$R_0 > 1$$



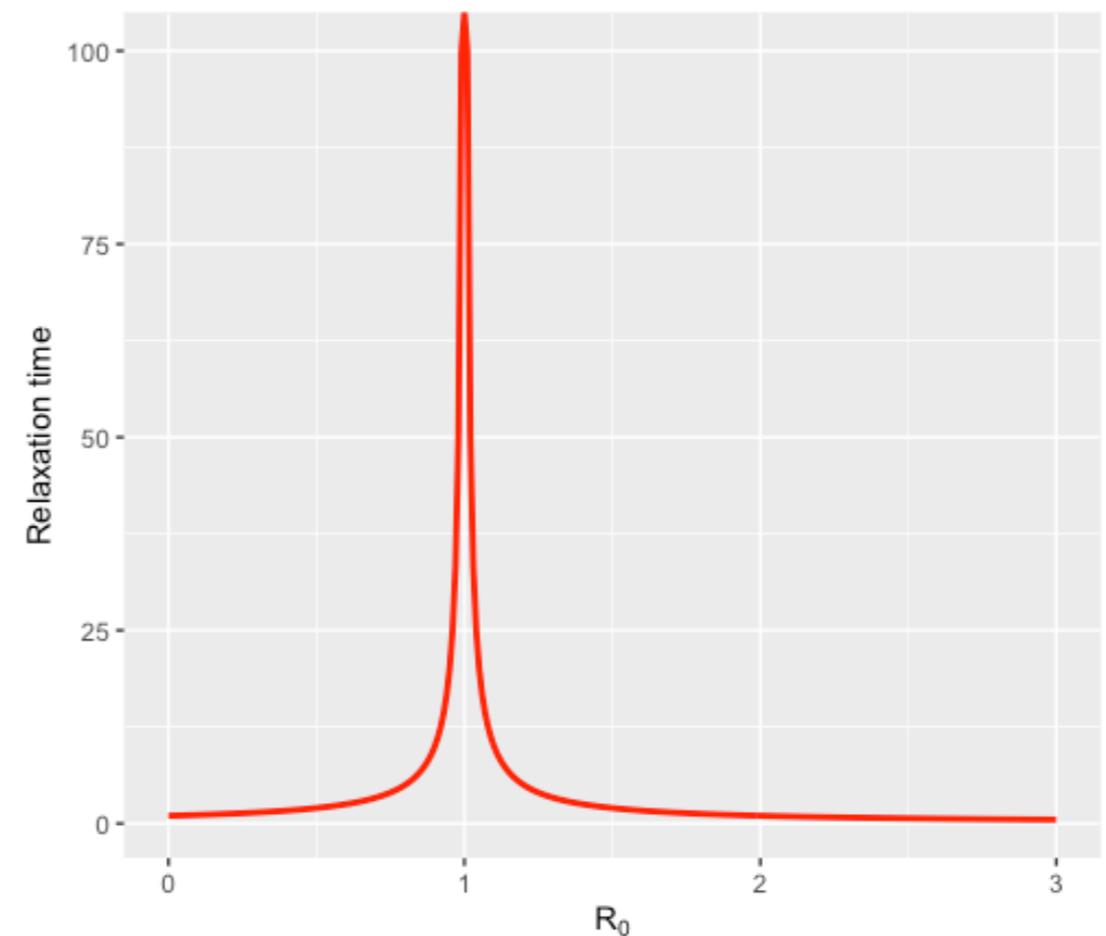
What happens near the transition?

- Near the transition the largest *eigenvalue* of the *dynamical system* goes to zero
- This means that the relaxation time (how long a system needs to recover from perturbations) becomes increasingly large
- This phenomenon is known as *critical slowing down*



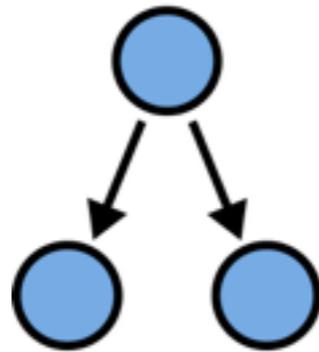
What does critical slowing down mean for emerging diseases?

- A disease is emerging if it is increasing in incidence in a population
- The increased relaxation time comes from the *increased probability of long chains of transmission*

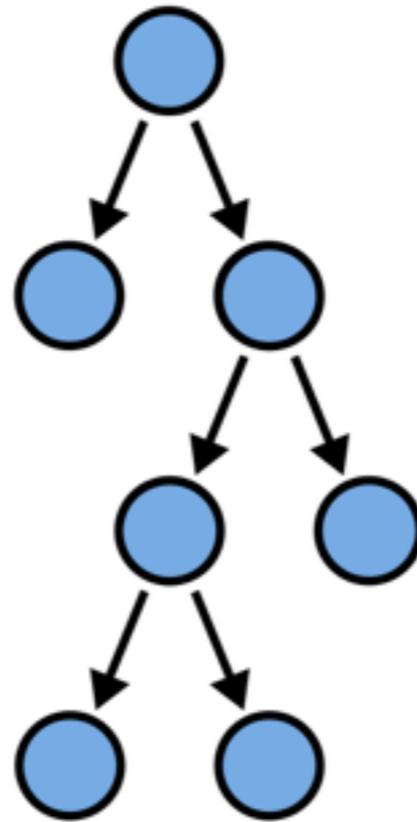


Transmission chains

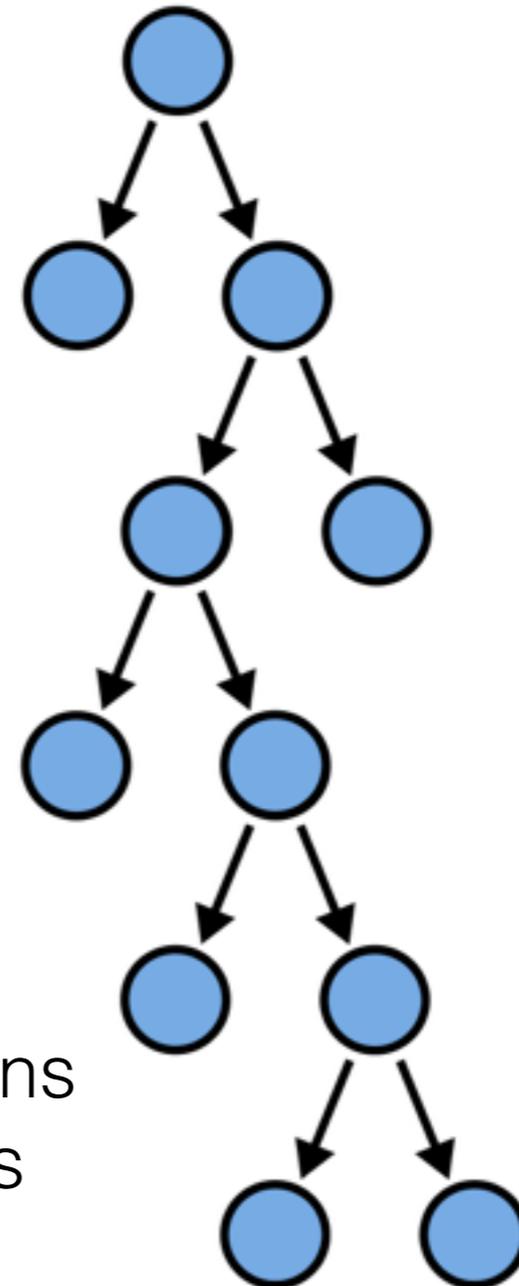
$R_0=0.1$



$R_0=0.5$



$R_0=0.9$

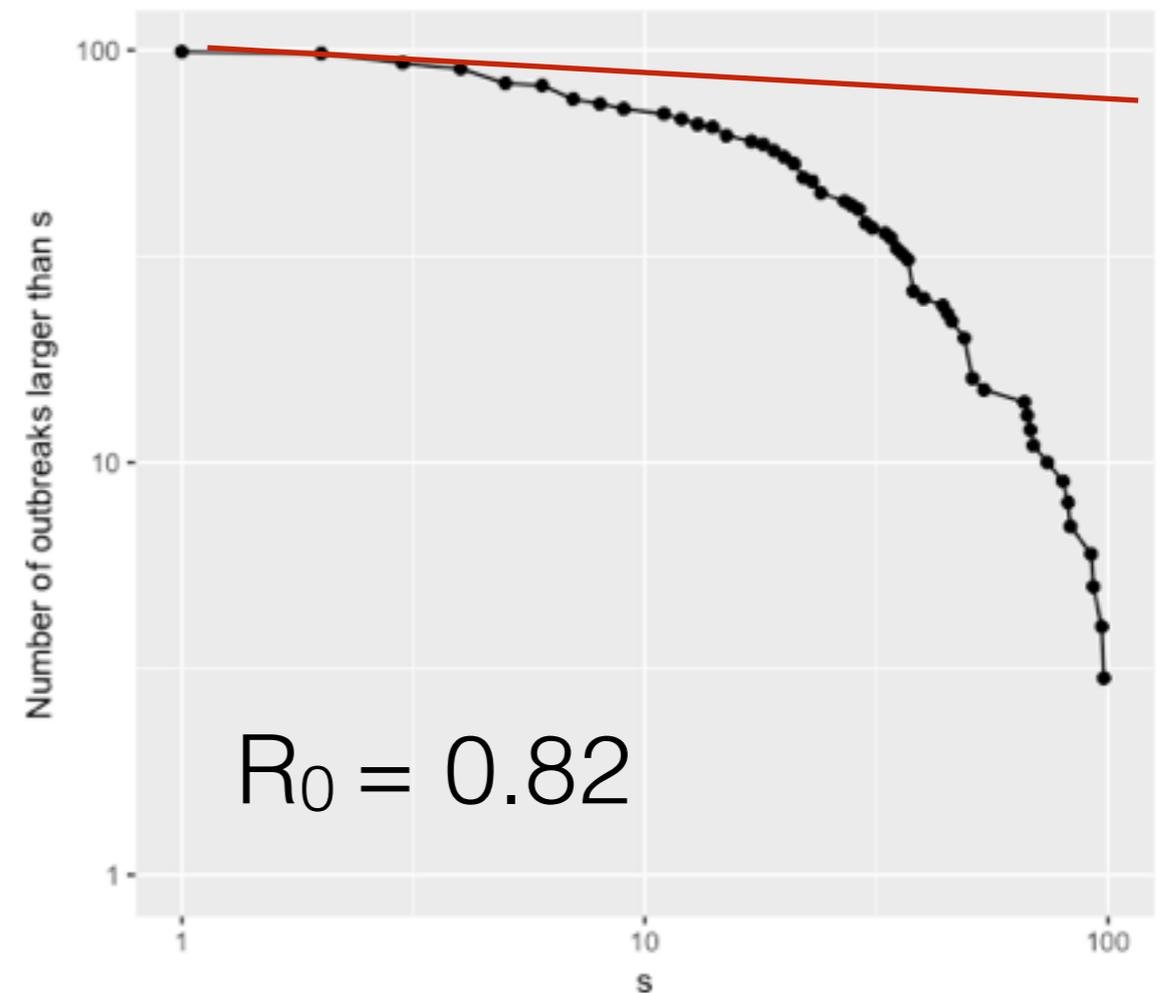
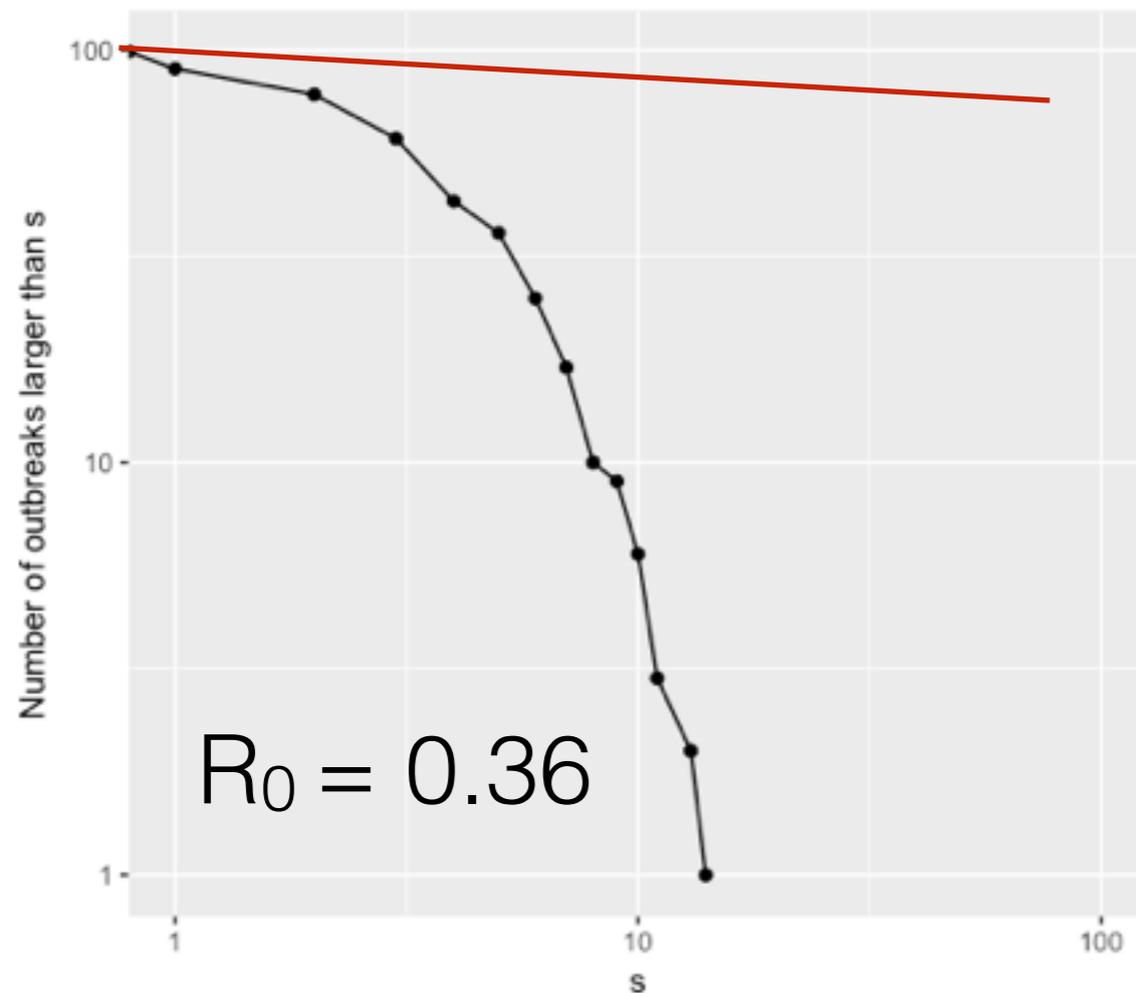


Increased probability of large transmission chains implies increased probability of larger outbreaks

Outbreak size distribution for subcritical disease

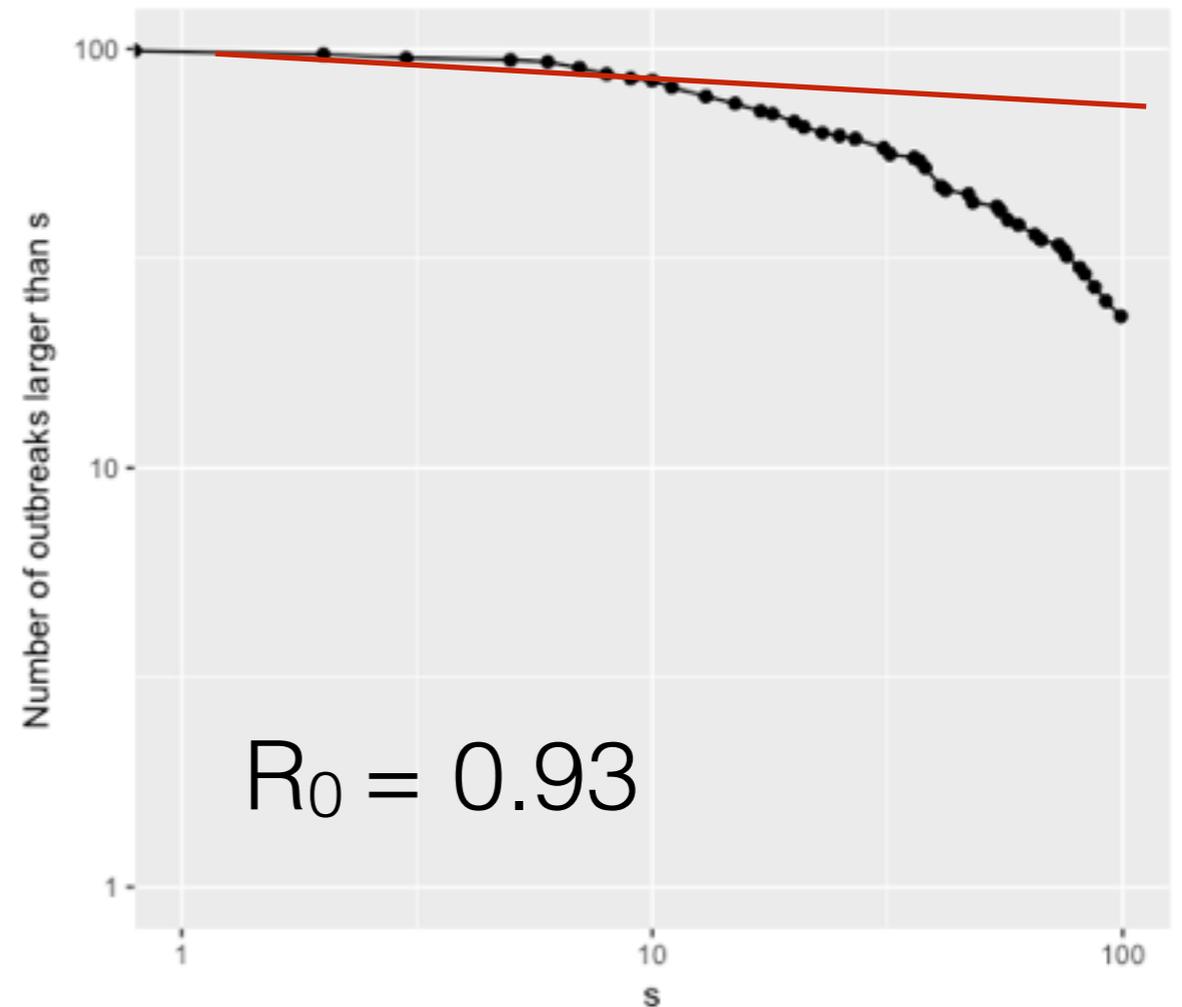
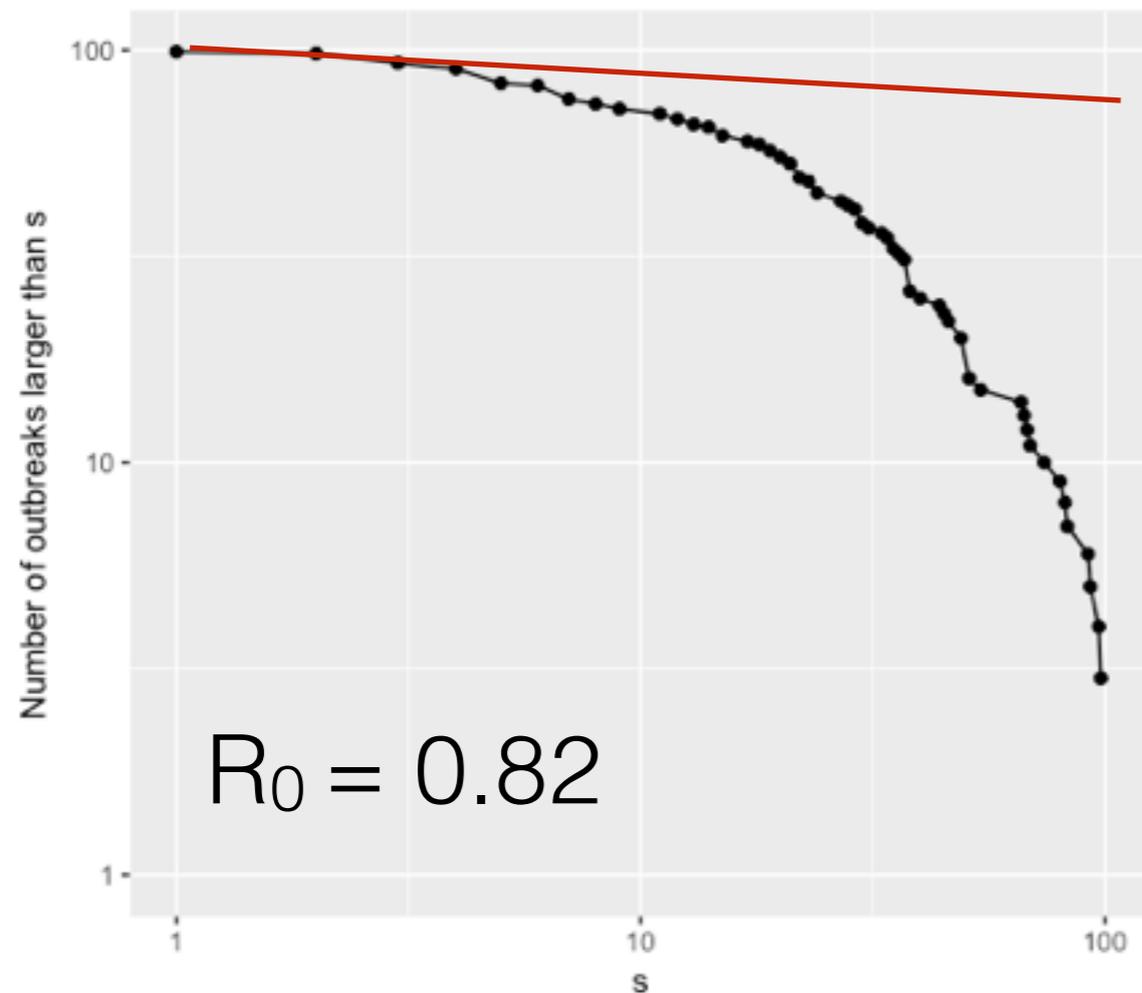
```
113 set.seed(38495) #set seed
114 nsims <- 100 #number of simulations
115 pop.size <- 25000 #total population size
116 Y0 <- 8 #initial number infected
117 X0 <- pop.size-Y0 #initial number susceptible
118 nstep <- 5000 #number of events to simulate
119 xstart <- c(time=0,X=X0,Y=Y0,Z=pop.size-X0-Y0) #initial conditions
120 params <- list(mu=1.0/70.0,beta=16,gamma=365/13, eta = 0) #parameters
121 #data <- vector(mode='list',length=nsims) #initialize list to store the output
122 R0 <- params$beta/(params$mu + params$gamma)
123 print(R0)
```

What happens to the outbreak size distribution?



As R_0 approaches one the outbreak size distribution approaches a power law

What happens to the outbreak size distribution?



As R_0 approaches one the outbreak size distribution approaches a power law

Conclusions

- Demographic stochasticity can lead to fade out of infectious diseases in smaller populations
- Combined with replenishment of the susceptible population, this provides a mechanism for repeated epidemics as seen with measles in the Faroe Islands
- Critical slowing down occurs as R_0 gets closer to one. The outbreak size distribution becomes a power law
- Insight into outbreaks is gained through studying the outbreak size distribution