# Why do we need mathematical models?

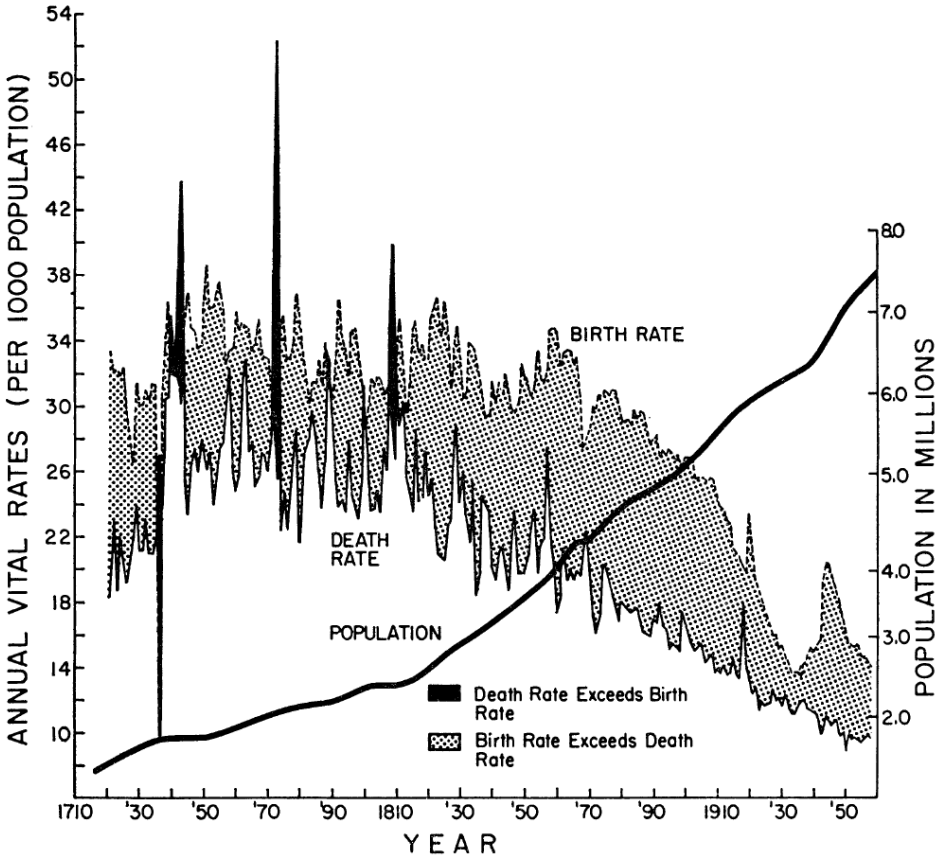
MATHEMATICAL MODELING FOR INFECTIOUS DISEASE PLANNING IN AFRICA

(30 minutes)

Births
Population size
Deaths

The Epidemiologic Transition: A Theory of the Epidemiology of Population Change
Author(s): Abdel R. Omran
Source: *The Milbank Memorial Fund Quarterly*, Vol. 49, No. 4, Part 1 (Oct., 1971), pp. 509-538

FIGURE I. THE TRANSITION IN SWEDEN




*Source:* Vielrose, E., ELEMENTS OF THE NATURAL MOVEMENT OF POPULATIONS, Oxford, Pergamon Press, Inc., 1965.

DIFFERENCE EQUATION

Pop size (t+1) = Pop size (t) + births*Pop size(t) – deaths* Pop size (t)

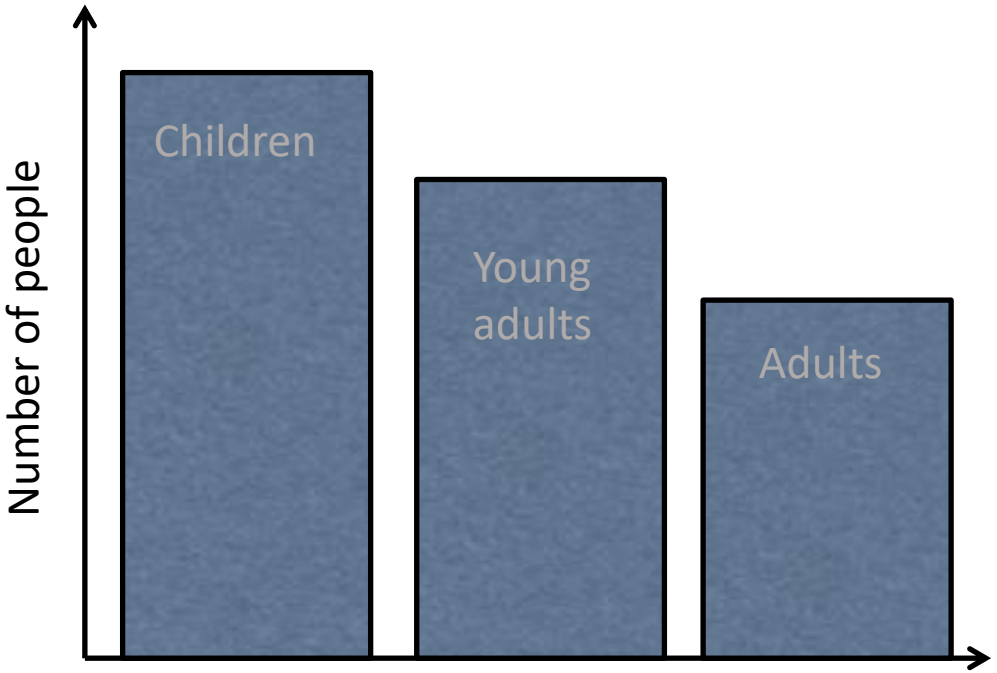
= Pop size (t) + (births – deaths)*Pop size(t)

P(t+1) = P(t) + (births – deaths)*P(t)

ORDINARY DIFFERENTIAL EQUATION

dP/dt = (births – deaths)*P

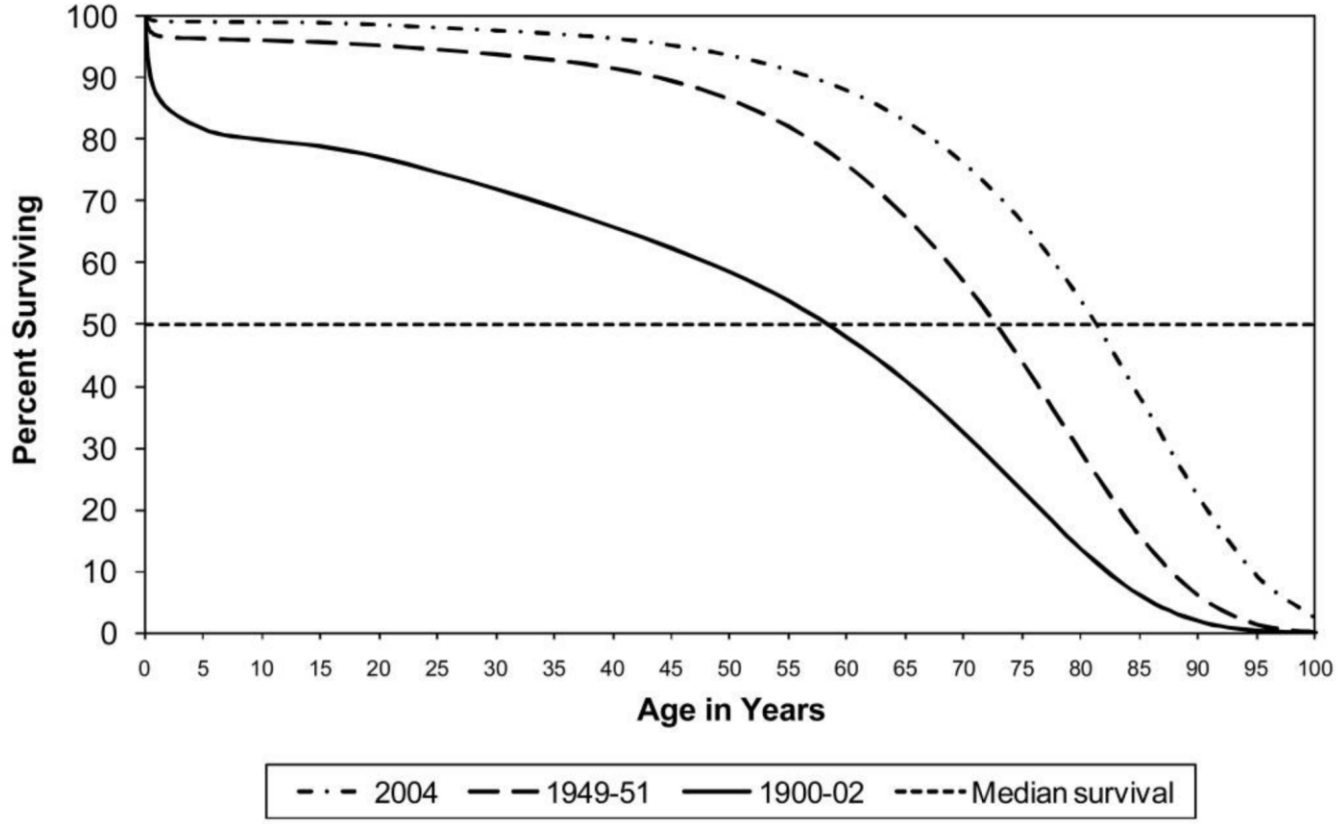
Births
Children
Deaths
Ageing
Young adults
Deaths
Ageing
Adults
Deaths

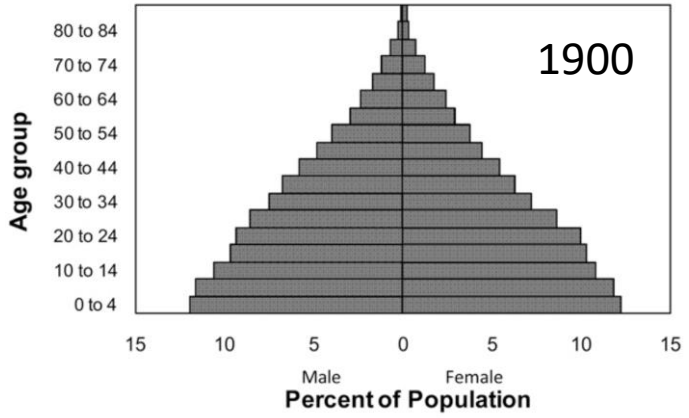

Number of people
Children
Young adults
Adults

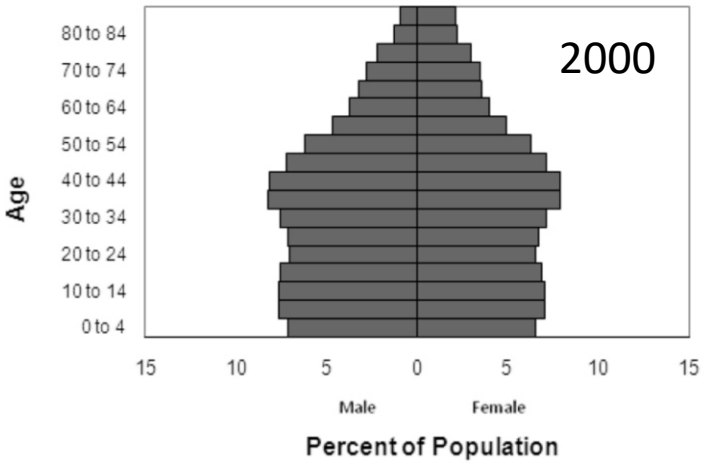
*Am J Lifestyle Med*. 2009 July 1; 3(1 Suppl): 19S–26S. doi:10.1177/1559827609335350.

## The Epidemiologic Transition: Changing Patterns of Mortality and Population Dynamics

**Robert E. McKeown, PhD, FACE [Professor and Chair]**

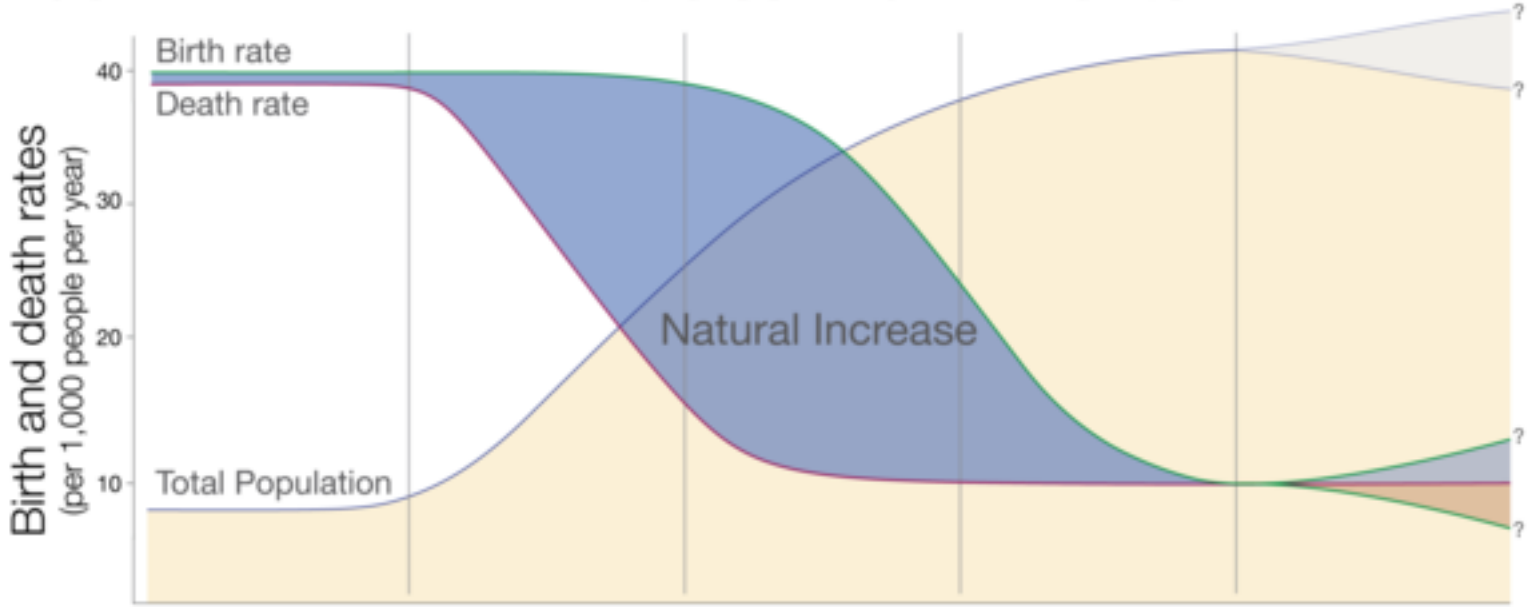


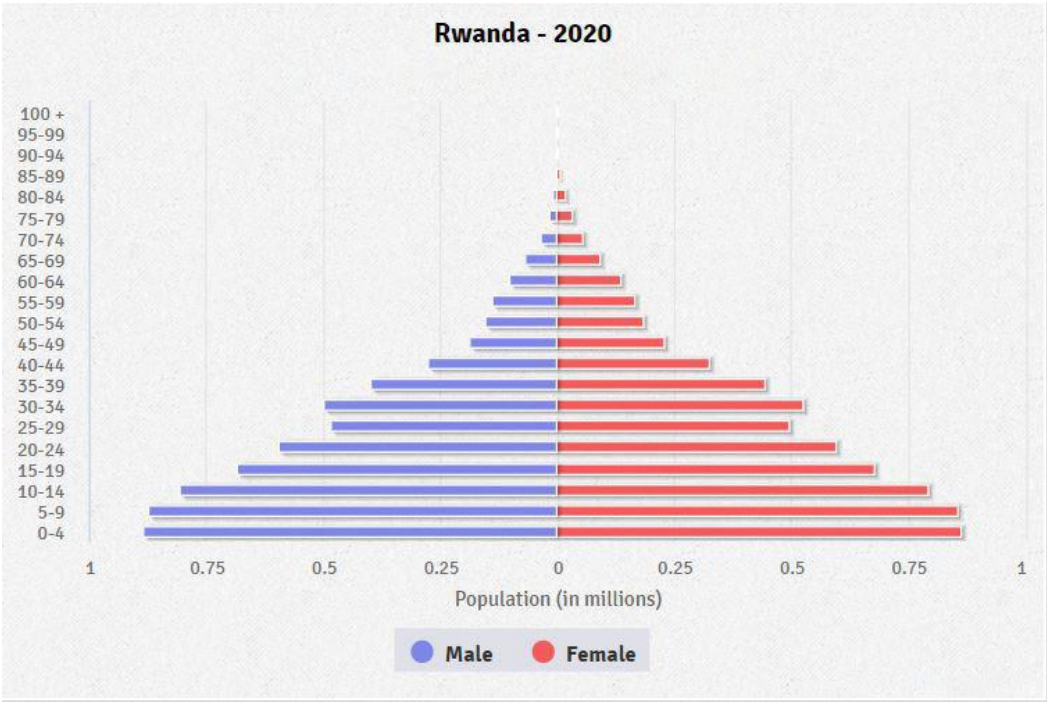



# The five stages of the demographic transition

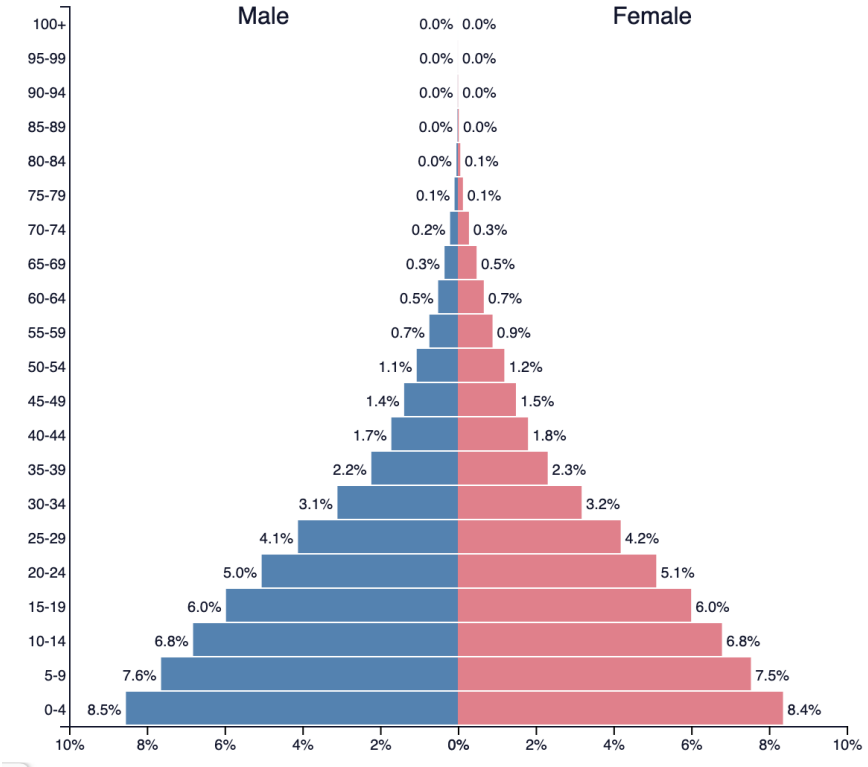
The demographic transition is a model that describes why rapid population growth is a temporary phenomenon.




| | Stage 1 | Stage 2 | Stage 3 | Stage 4 | Stage 5 |
|---|---|---|---|---|---|
| Birth rate | High | High | Falling | Low | Yet to be seen (Possibly falling further, possibly rising again) |
| Death rate | High | Falls rapidly | Falls more slowly | Low | Low |
| Natural increase | Stable or slow increase | Rapid increase | Increase slows down | Falling and then stable | Little change |
| Population Pyramid | | | | | |


Rwanda - 2020
100 +
95-99
90-94
85-89
80-84
75-79
70-74
65-69
60-64
55-59
50-54
45-49
40-44
35-39
30-34
25-29
20-24
15-19
10-14
5-9
0-4
1
0.75
0.5
0.25
0
0.25
0.5
0.75
1
Population (in millions)
Male
Female

# Uganda 2020


Male
Female
100+ 0.0% 0.0%
95-99 0.0% 0.0%
90-94 0.0% 0.0%
85-89 0.0% 0.0%
80-84 0.0% 0.1%
75-79 0.1% 0.1%
70-74 0.2% 0.3%
65-69 0.3% 0.5%
60-64 0.5% 0.7%
55-59 0.7% 0.9%
50-54 1.1% 1.2%
45-49 1.4% 1.5%
40-44 1.7% 1.8%
35-39 2.2% 2.3%
30-34 3.1% 3.2%
25-29 4.1% 4.2%
20-24 5.0% 5.1%
15-19 6.0% 6.0%
10-14 6.8% 6.8%
5-9 7.6% 7.5%
0-4 8.5% 8.4%
10%
8%
6%
4%
2%
0%
2%
4%
6%
8%
10%

# Headaches

Healthy: no headache

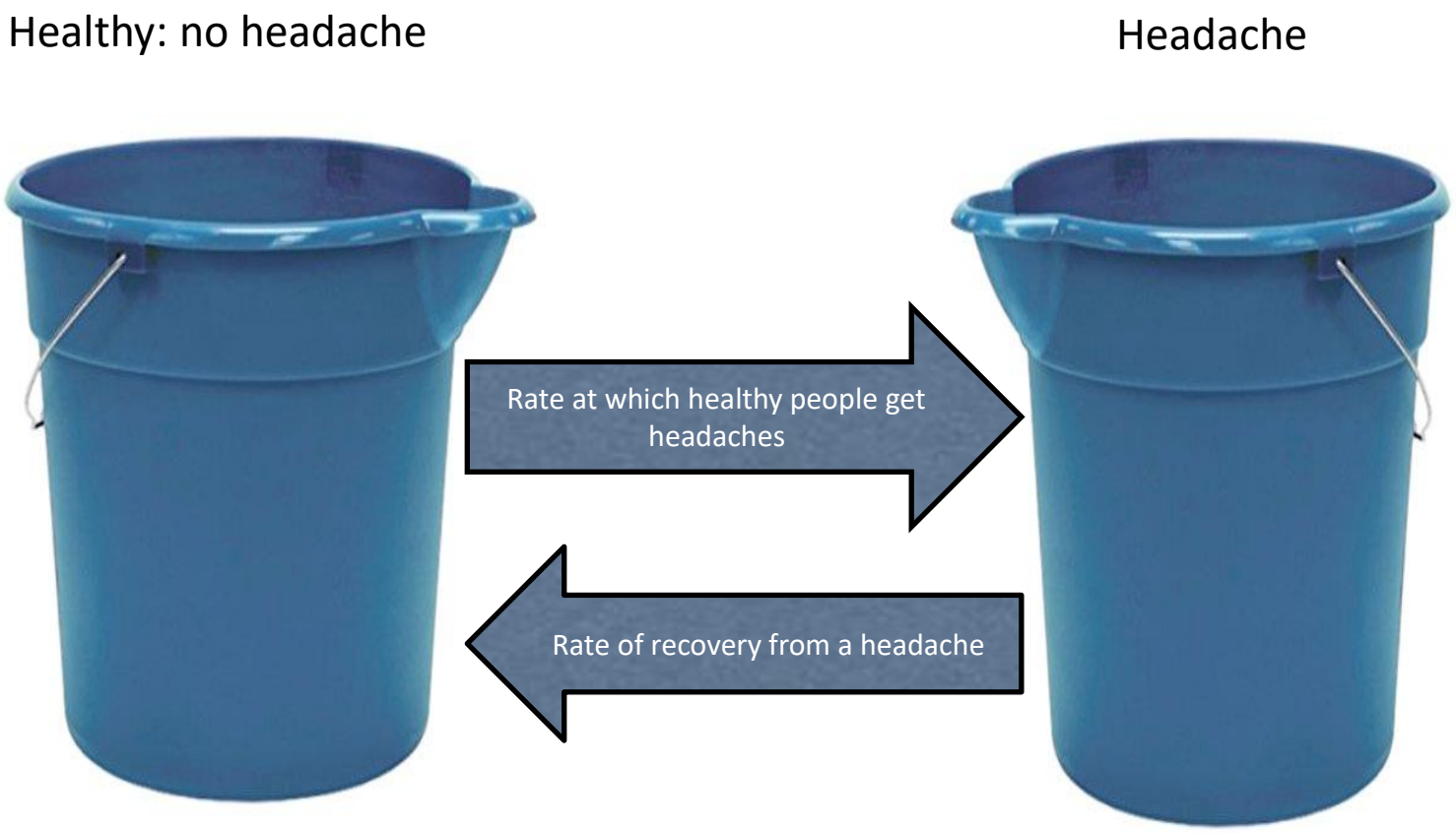
Lady Agnew of Lochnaw
*John Singer Sargent 1892-3*

Rate at which healthy people get headaches

Rate of recovery from a headache

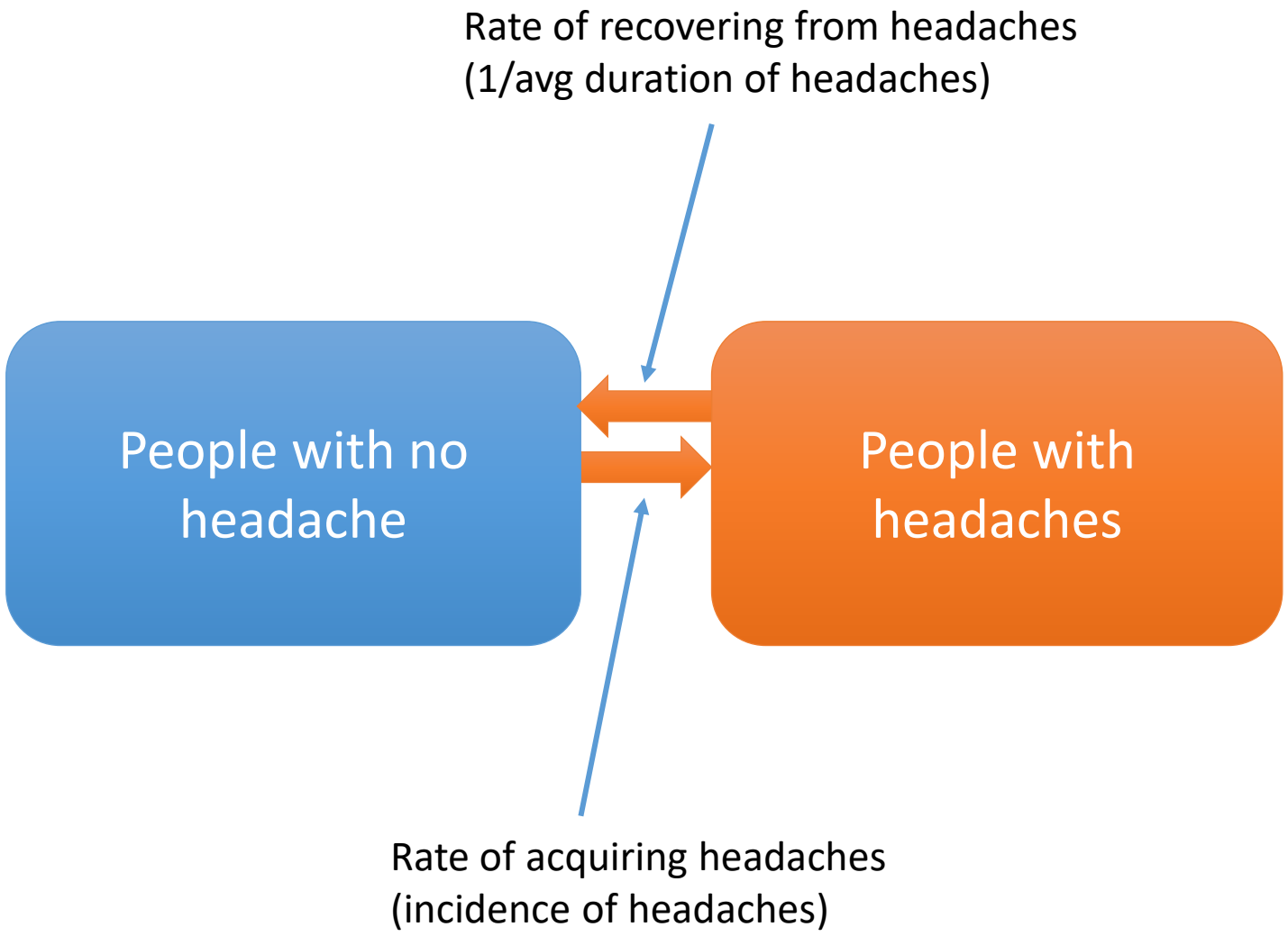
Headache

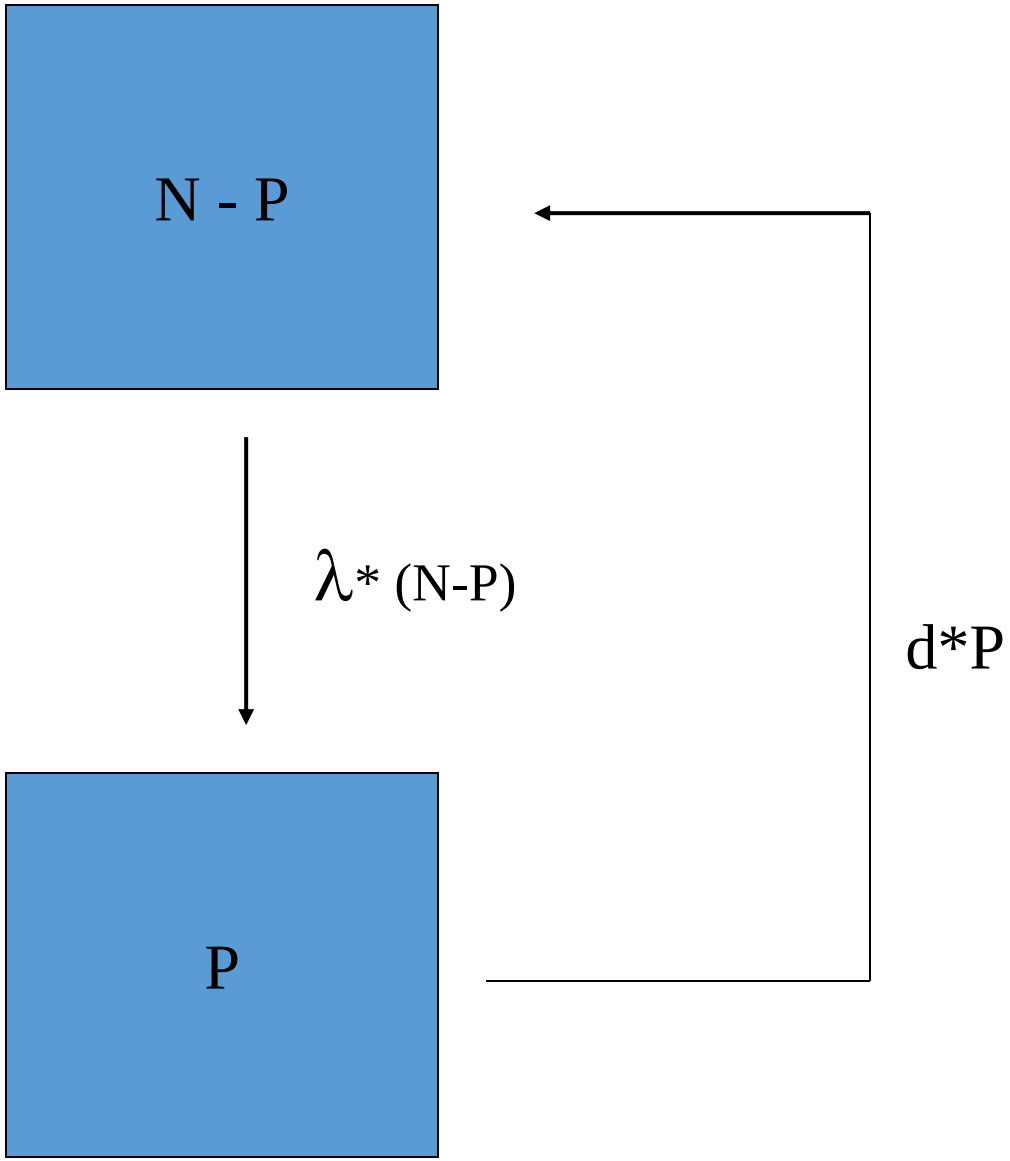
Self-portrait during cluster headache
*Catherine Graffam*


Healthy: no headache
Headache
Rate at which healthy people get headaches
Rate of recovery from a headache

# Definitions

- Prevalence
  - Proportion of cases at any specific time
- Incidence
  - Number of new cases over some time period
- Steady state
  - State in which numbers in compartments do not change


Rate of recovering from headaches
(1/avg duration of headaches)
People with no headache
People with headaches
Rate of acquiring headaches
(incidence of headaches)

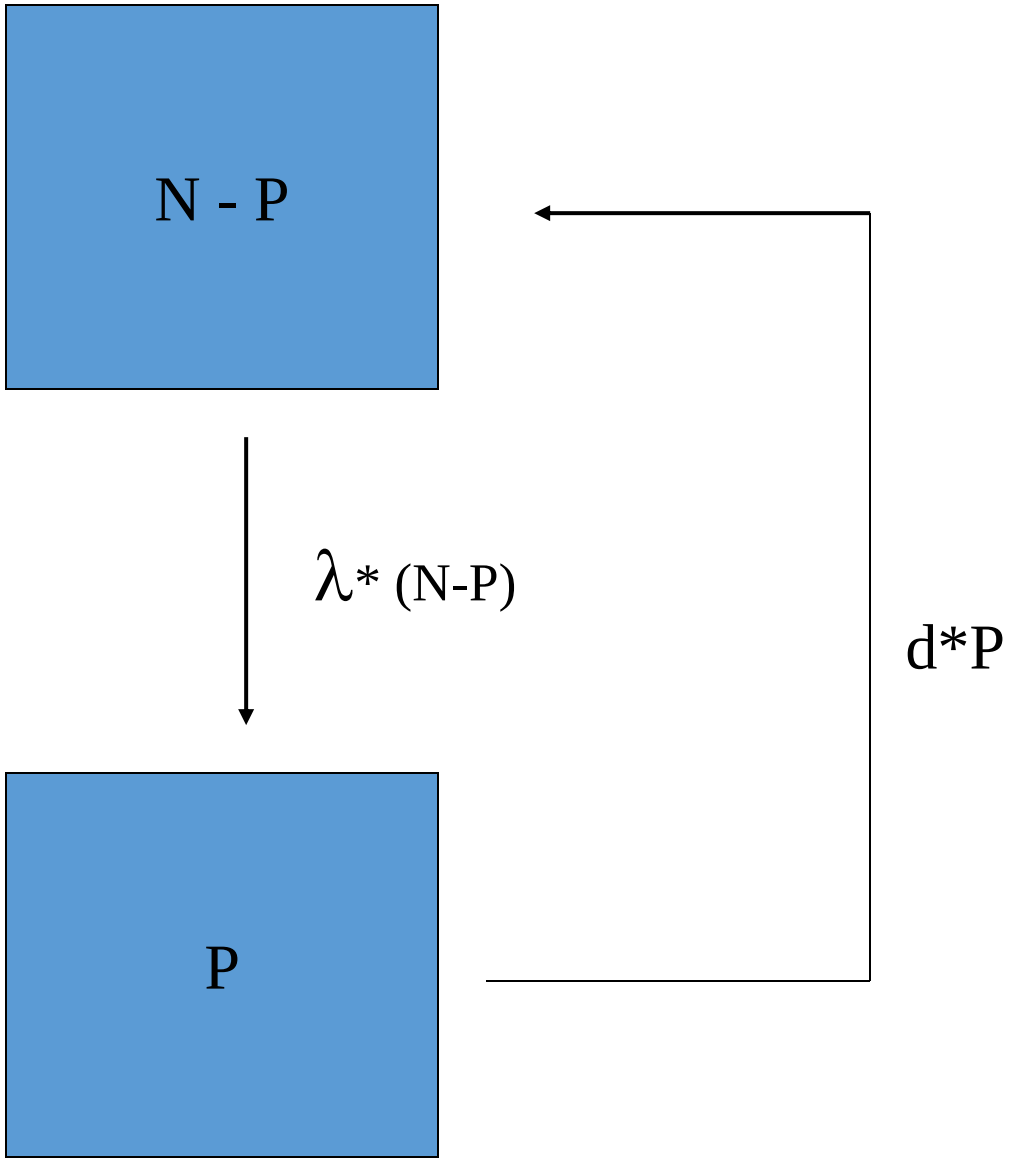



N= population size

P = # of sick

λ = per capita rate of getting a headache

d = recovery rate




N= population size

P = # of sick

λ = headache rate

d = recovery rate

# Chronic diseases versus infectious diseases

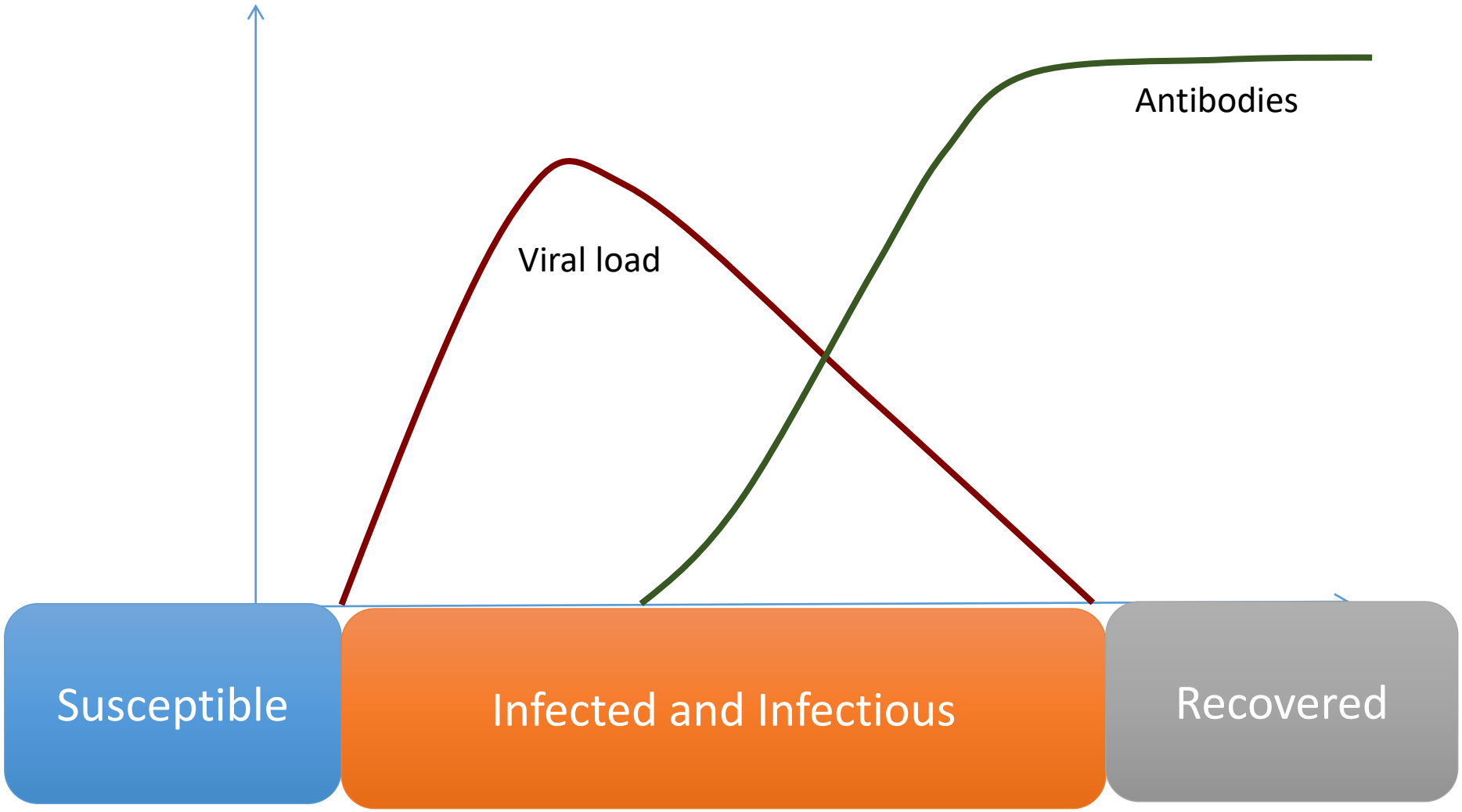
**Chronic diseases:** Population outcome is the average of many individual outcomes considered in isolation.

Four pinball machines
*Wayne Thiebaud, 1962*

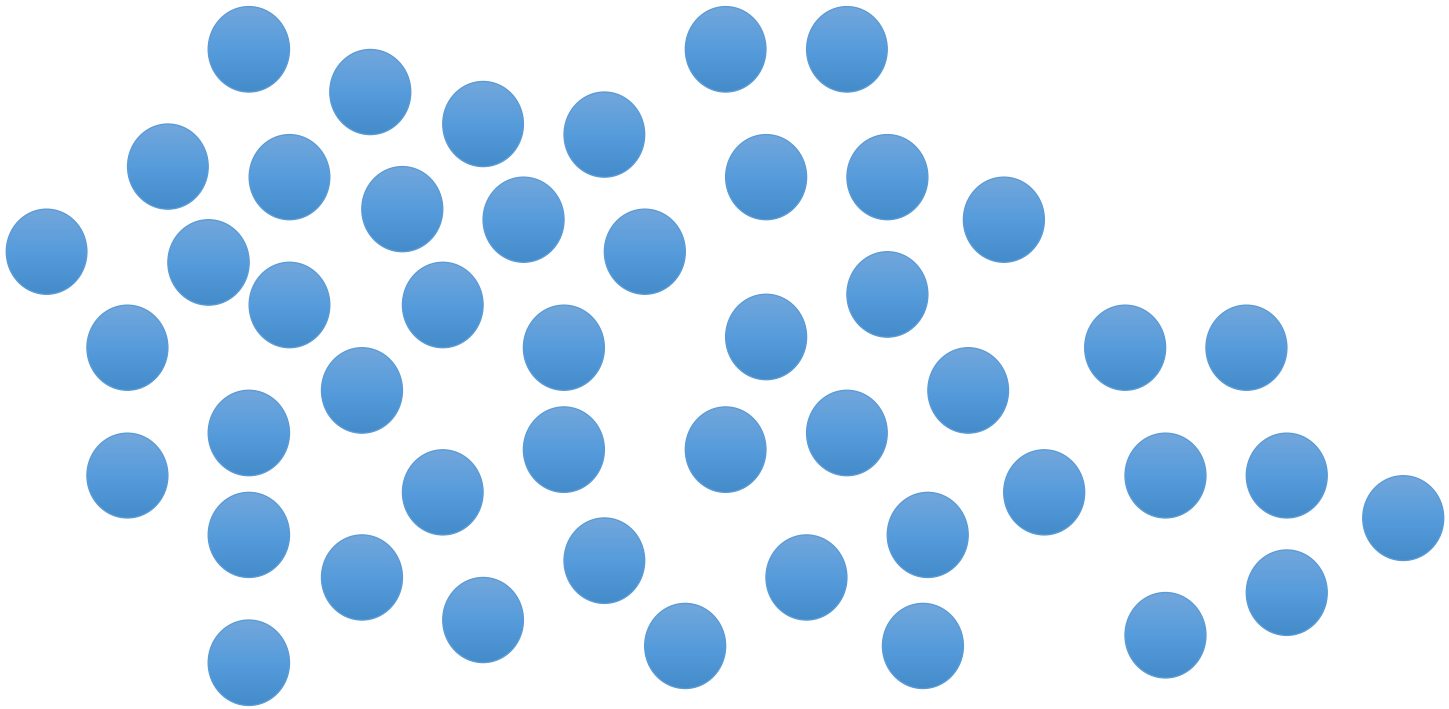
**Infectious diseases:** Individual outcomes depend on others. Individual risks require an understanding of the dynamics of the population.

Pool parlor
*Jacob Lawrence, 1942*

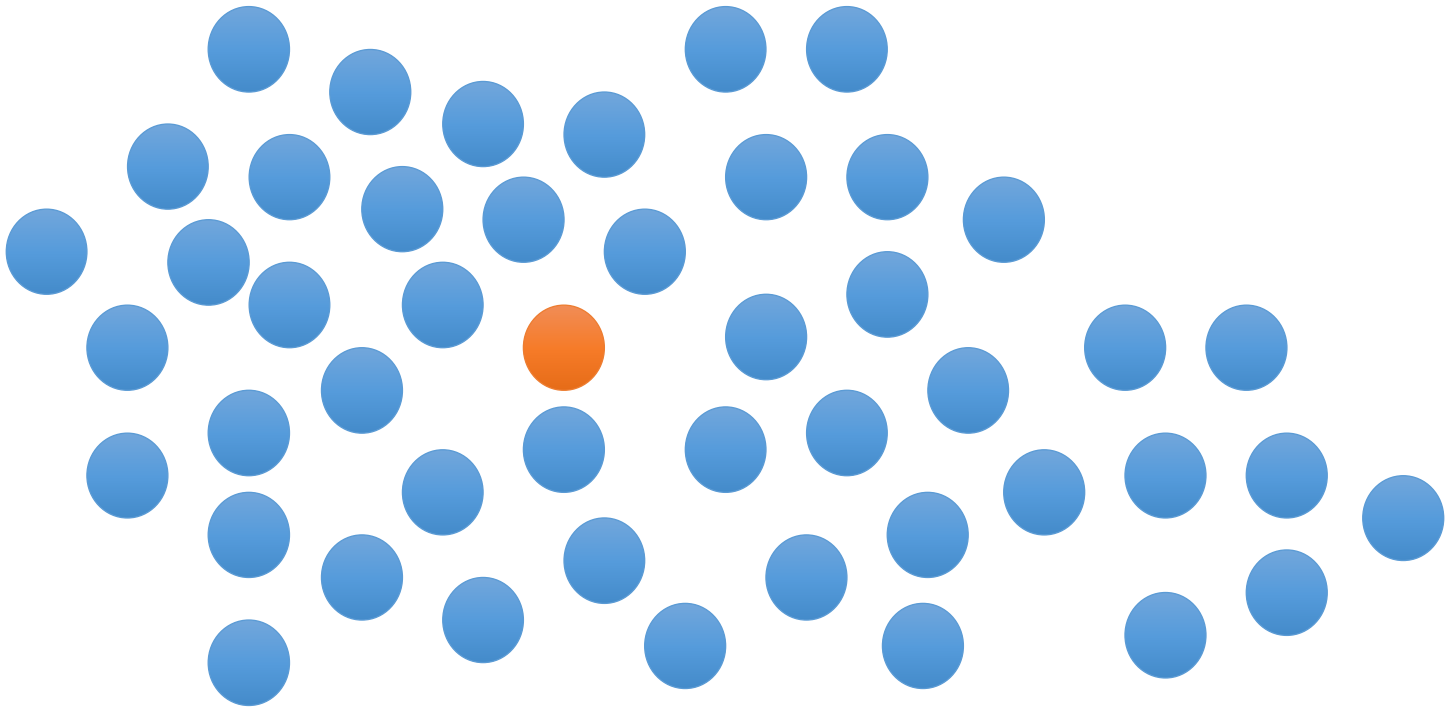
# What compartments are needed in our model?

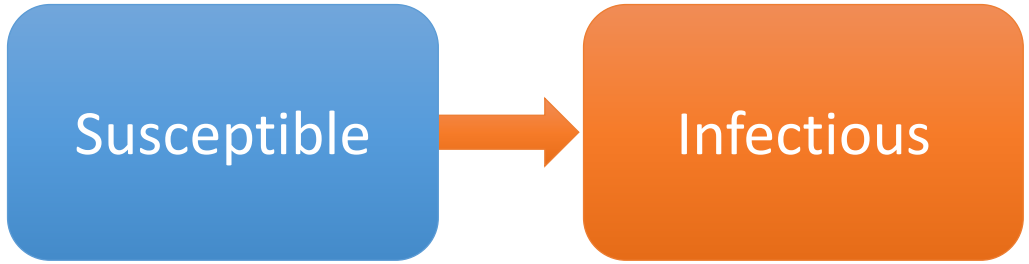


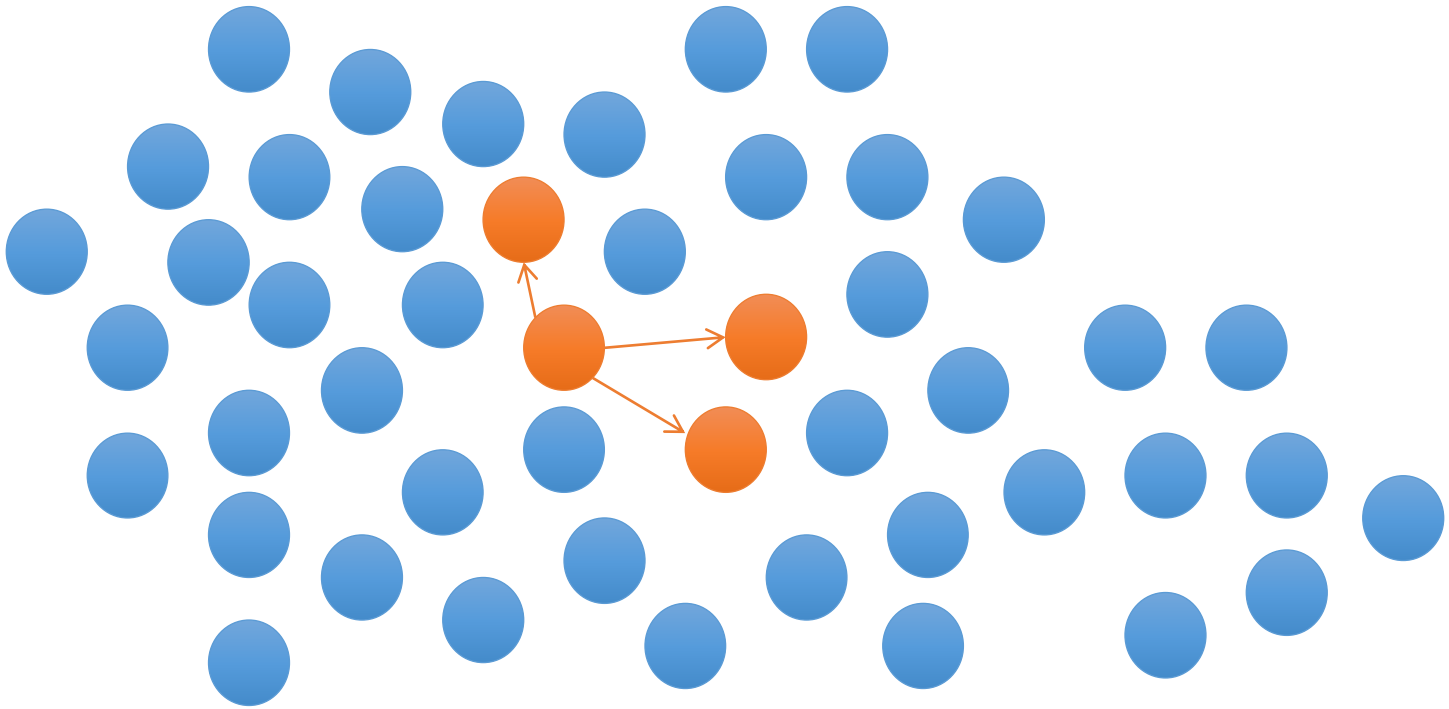
Entirely susceptible population

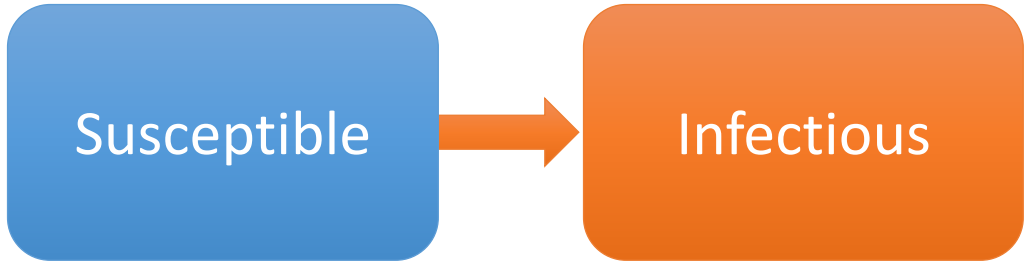


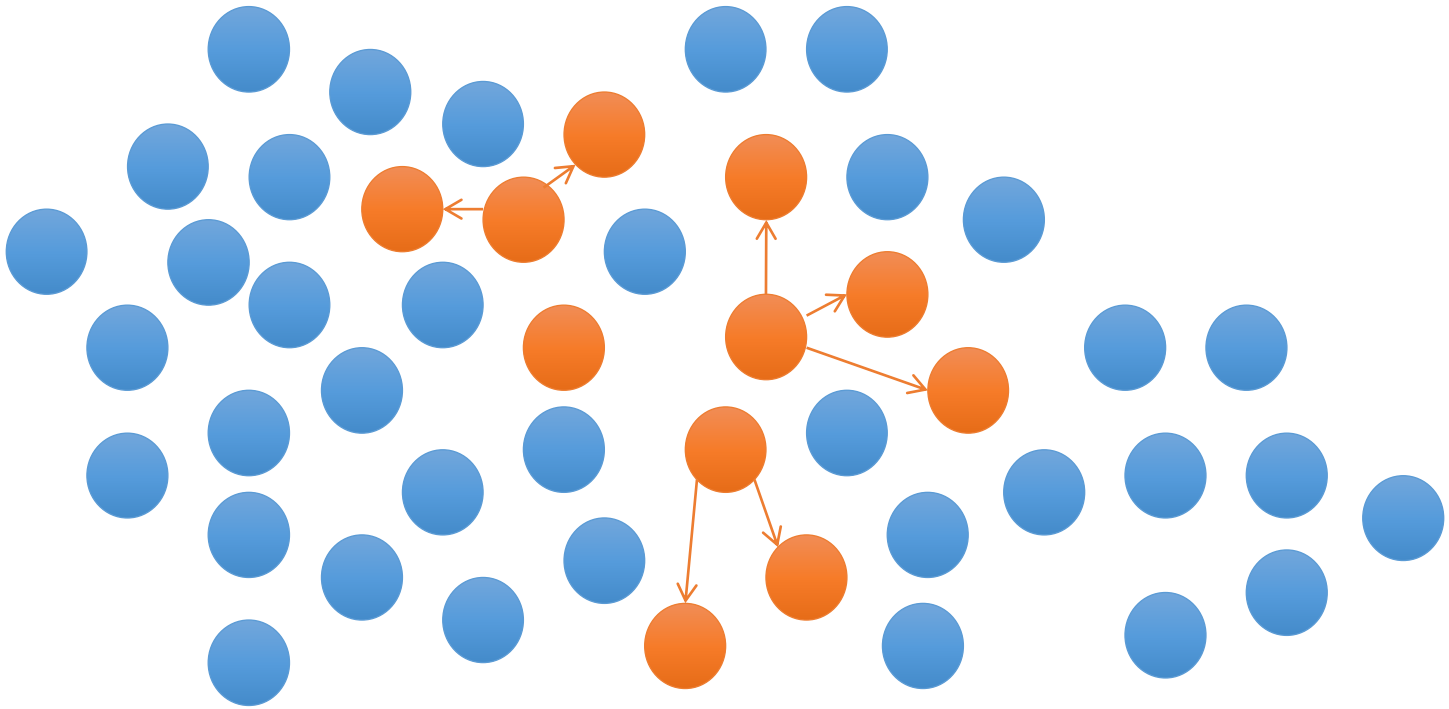
Susceptible

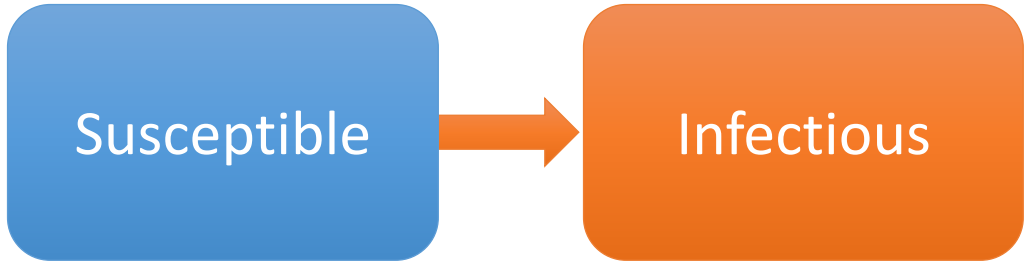


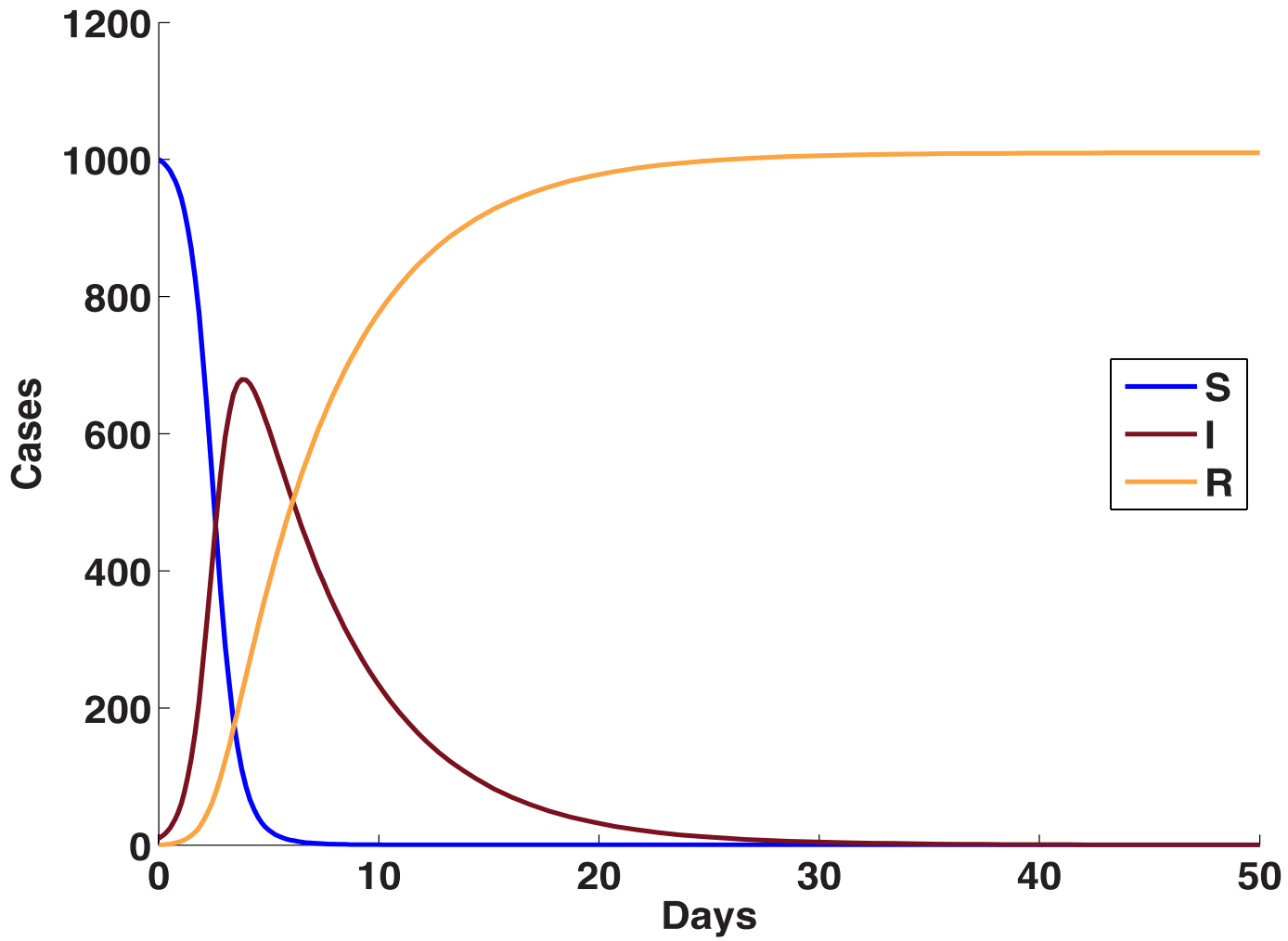

Susceptible
Infectious




Susceptible
Infectious

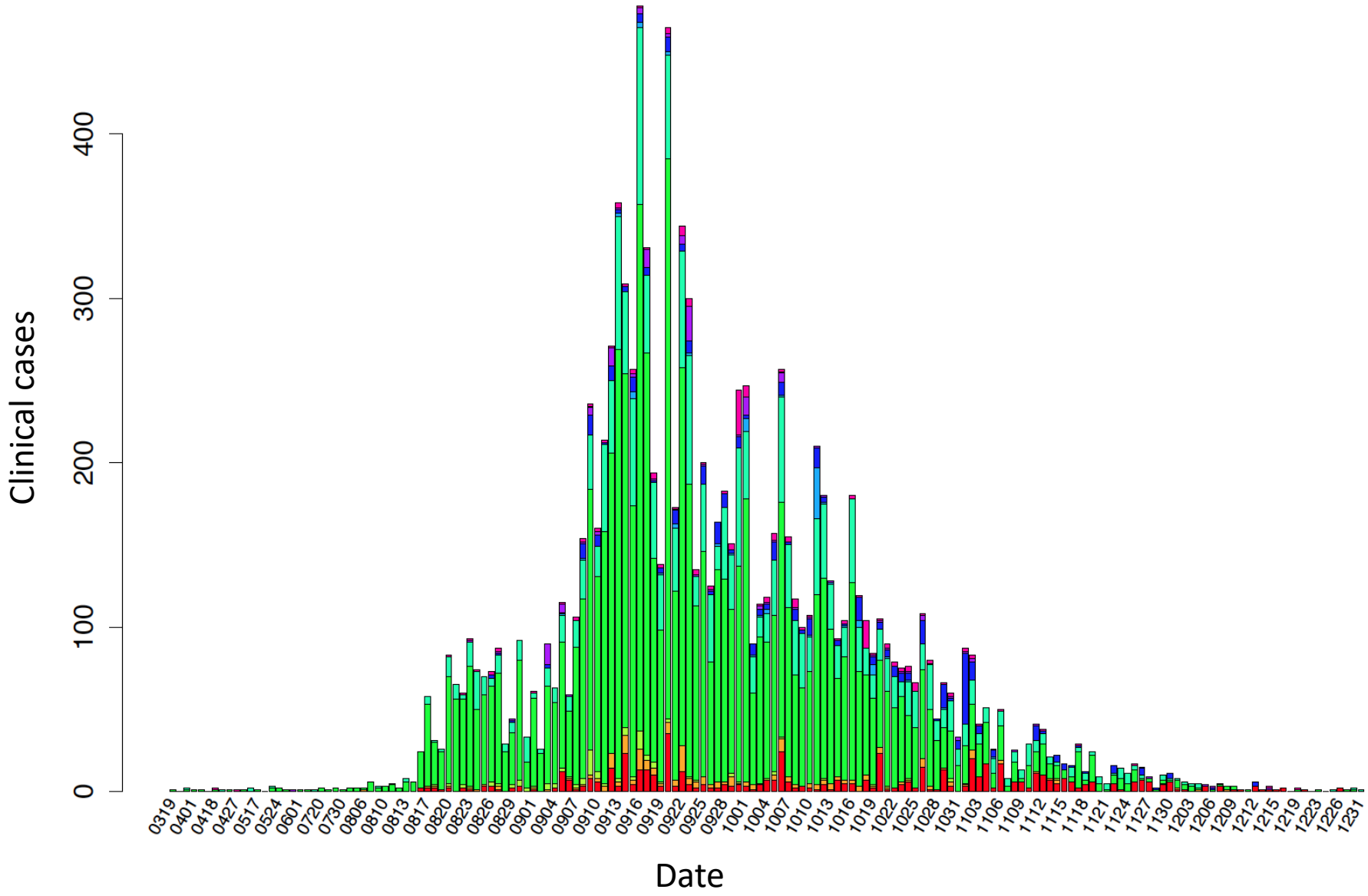



Susceptible
Infectious

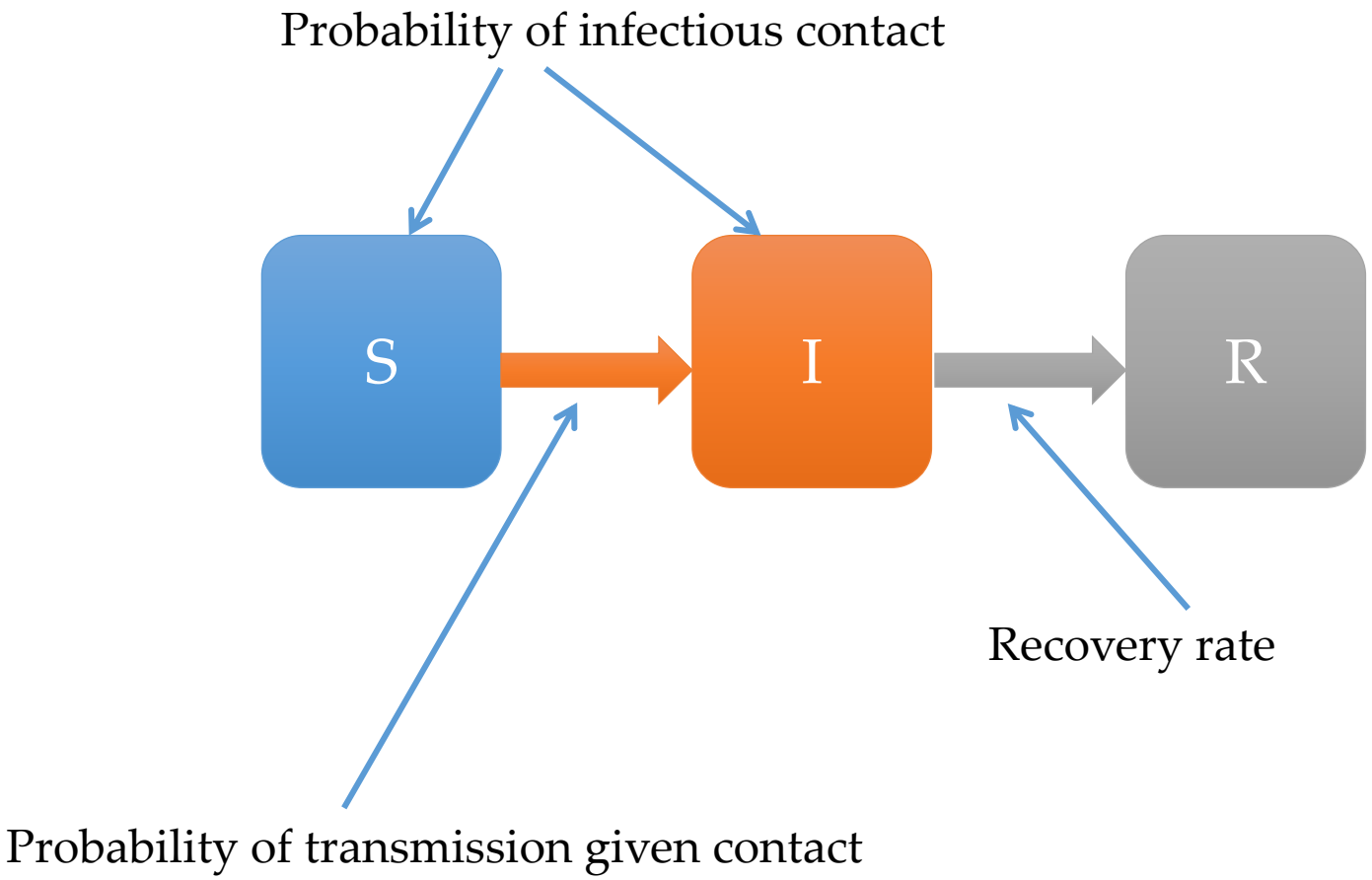

1200
1000
800
600
400
200
0
Cases
0
10
20
30
40
50
Days
S
I
R

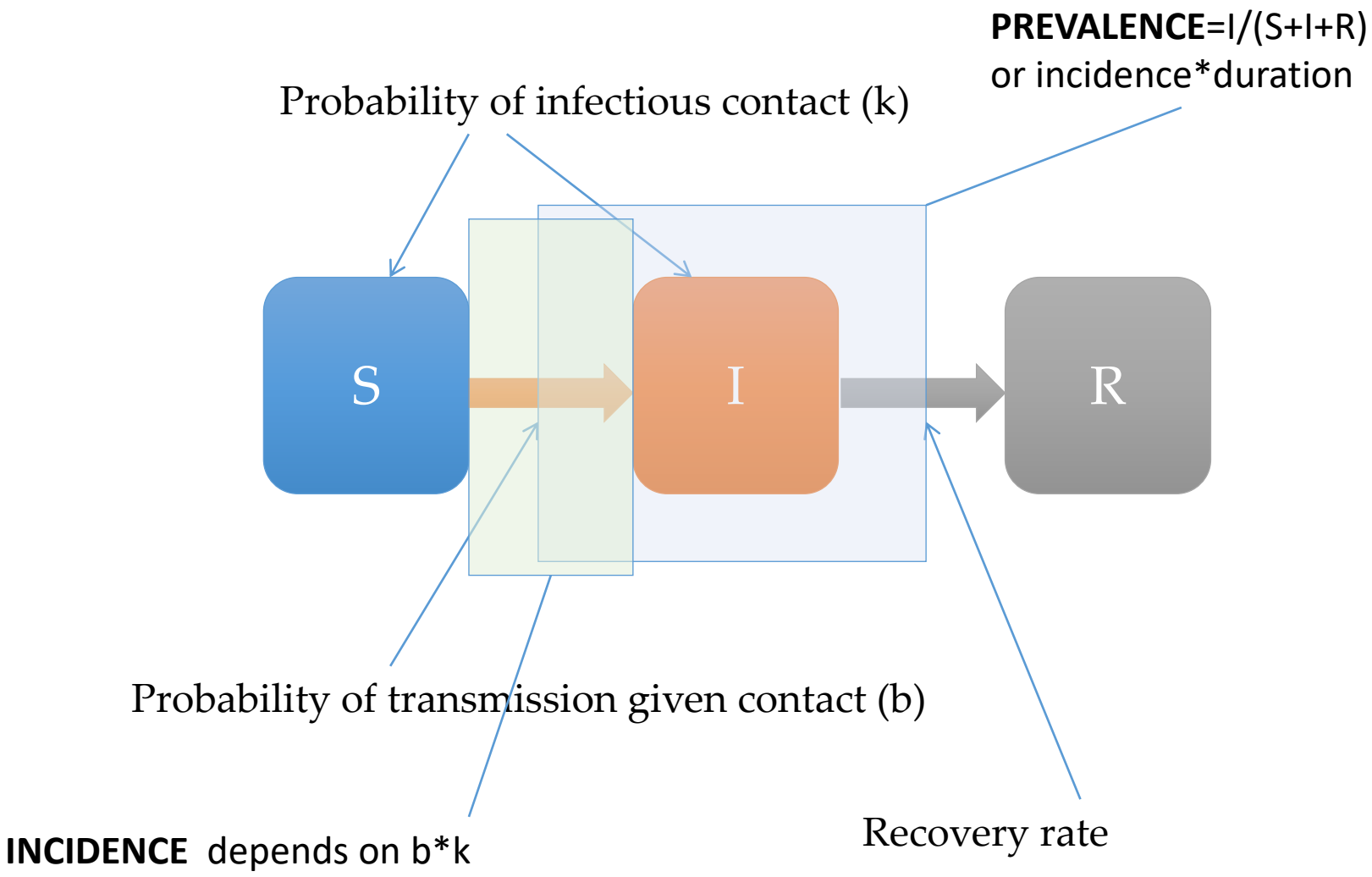
Susceptible
Infectious
Recovered

# Dengue epidemic in Pakistan 2011



# Interventions: how can we reduce transmission?




PREVALENCE=I/(S+I+R)
or incidence*duration
Probability of infectious contact (k)
S
I
R
Probability of transmission given contact (b)
INCIDENCE depends on b*k
Recovery rate

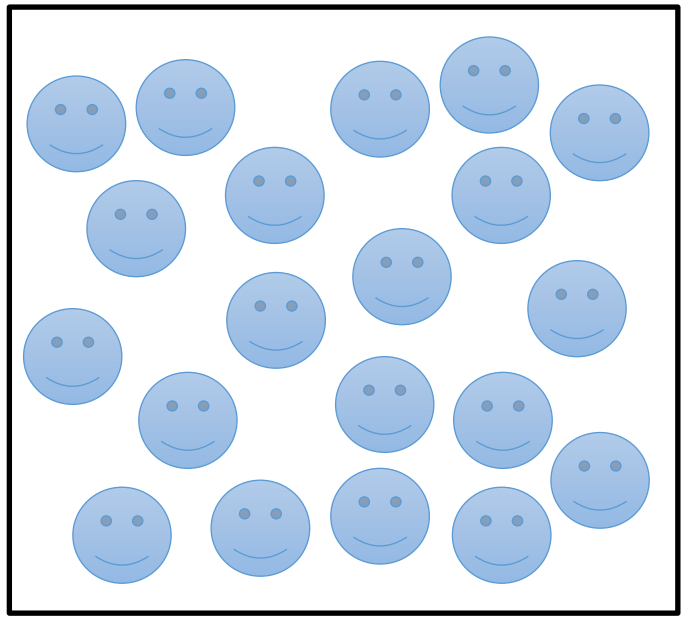
# Definitions

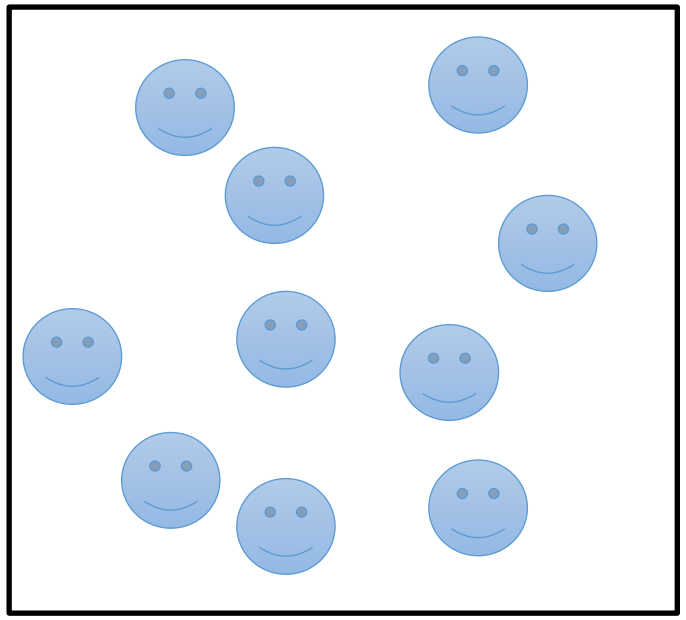
- Force of infection (λ): the per capita rate at which susceptible individuals contract infection

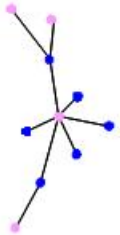
  Therefore, the rate of new infections in the population is λ*number of susceptible individuals

- Transmission coefficient (β): composite measure of probability of infectious contact (k) and transmission probability given contact (b)

# Population at risk: how to think about the contact rate

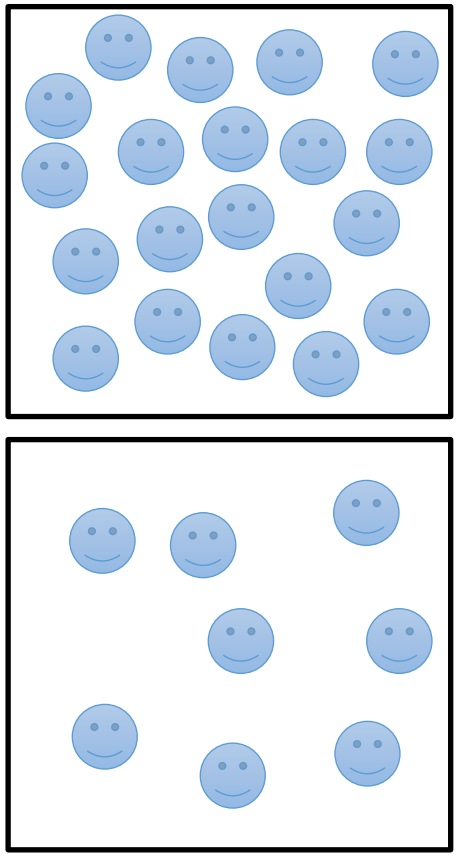


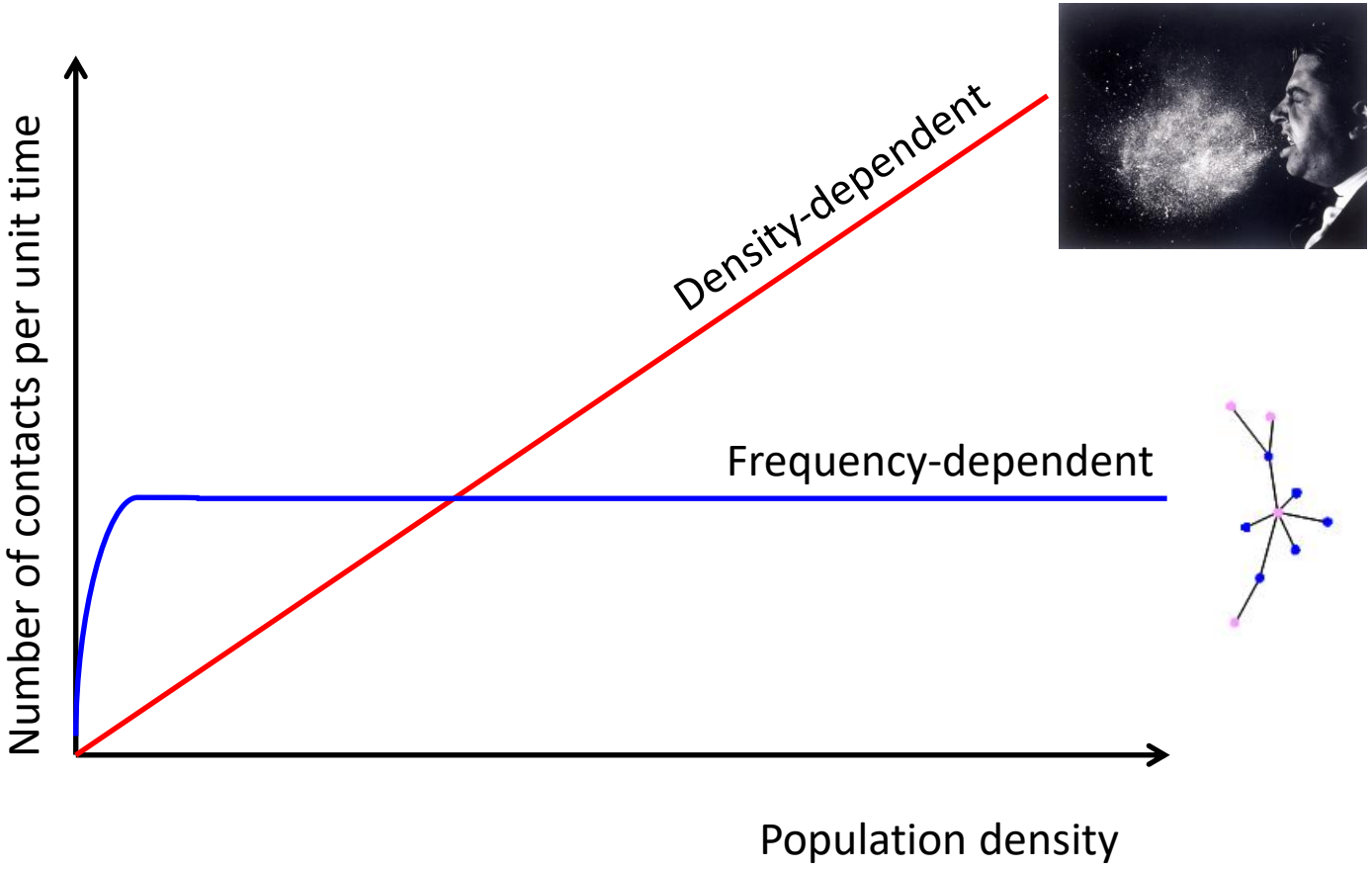




For a nice explanation see: https://parasiteecology.wordpress.com/2013/10/17/density-dependent-vs-frequency-dependent-disease-transmission/

# Population at risk: how to think about the contact rate





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# Density vs Frequency dependence

How do we formulate λ with respect to I?

$\beta = b * k$

Number of contacts (k) does not change with population size

$\lambda = \beta I/N$, where N is the population size

FREQUENCY DEPENDENT

$\lambda = \beta I$

DENSITY DEPENDENT

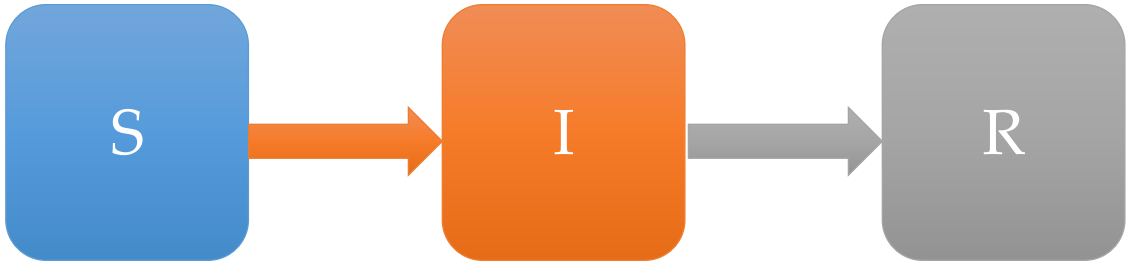
Number of contacts (k) scales with population size

# How would you write down **difference equations** to describe this process?

Difference equations are in the form:

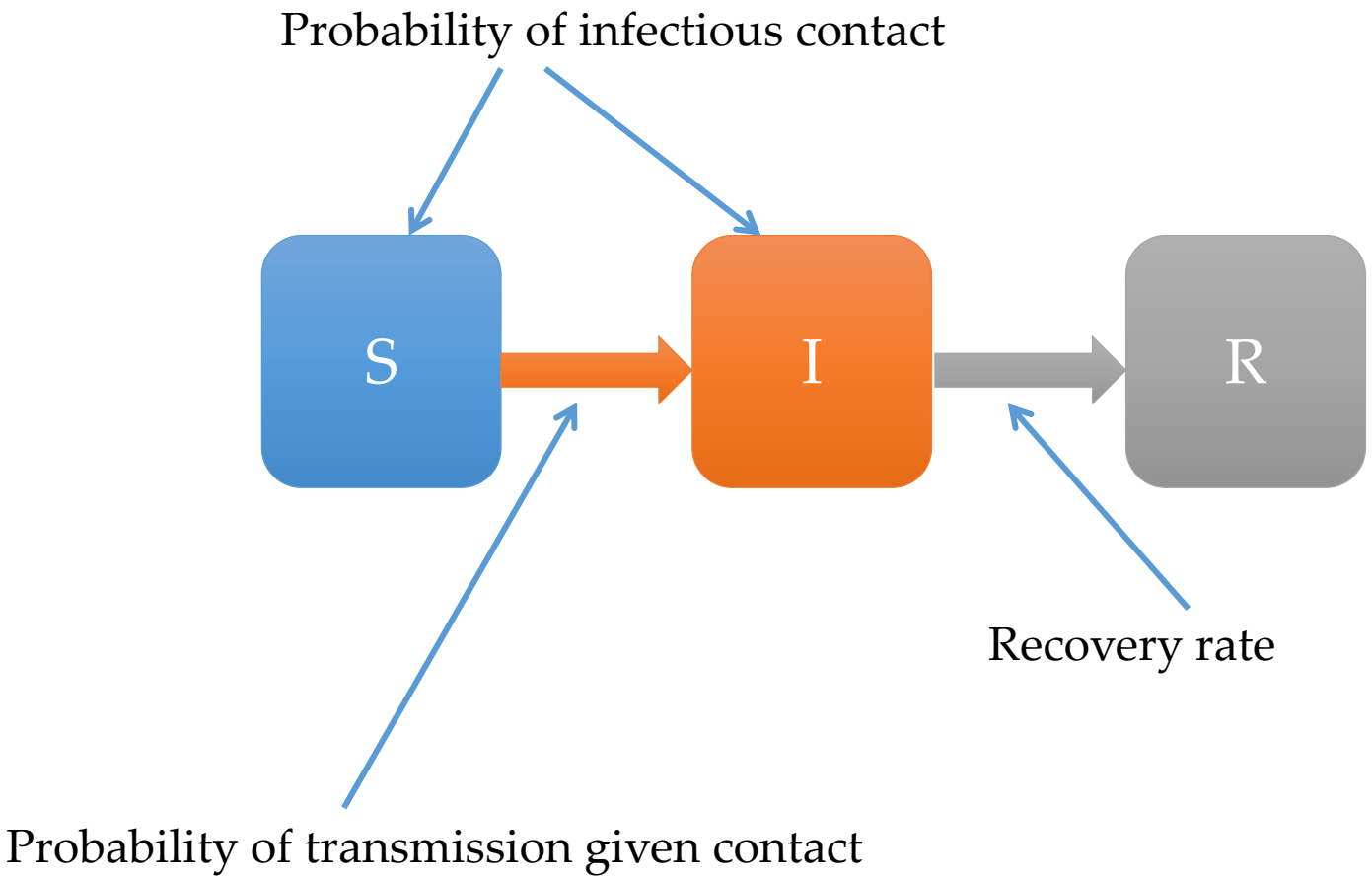
Number of people at time t+1 = Number of people at time t… plus or minus how many people entering that category in one time step

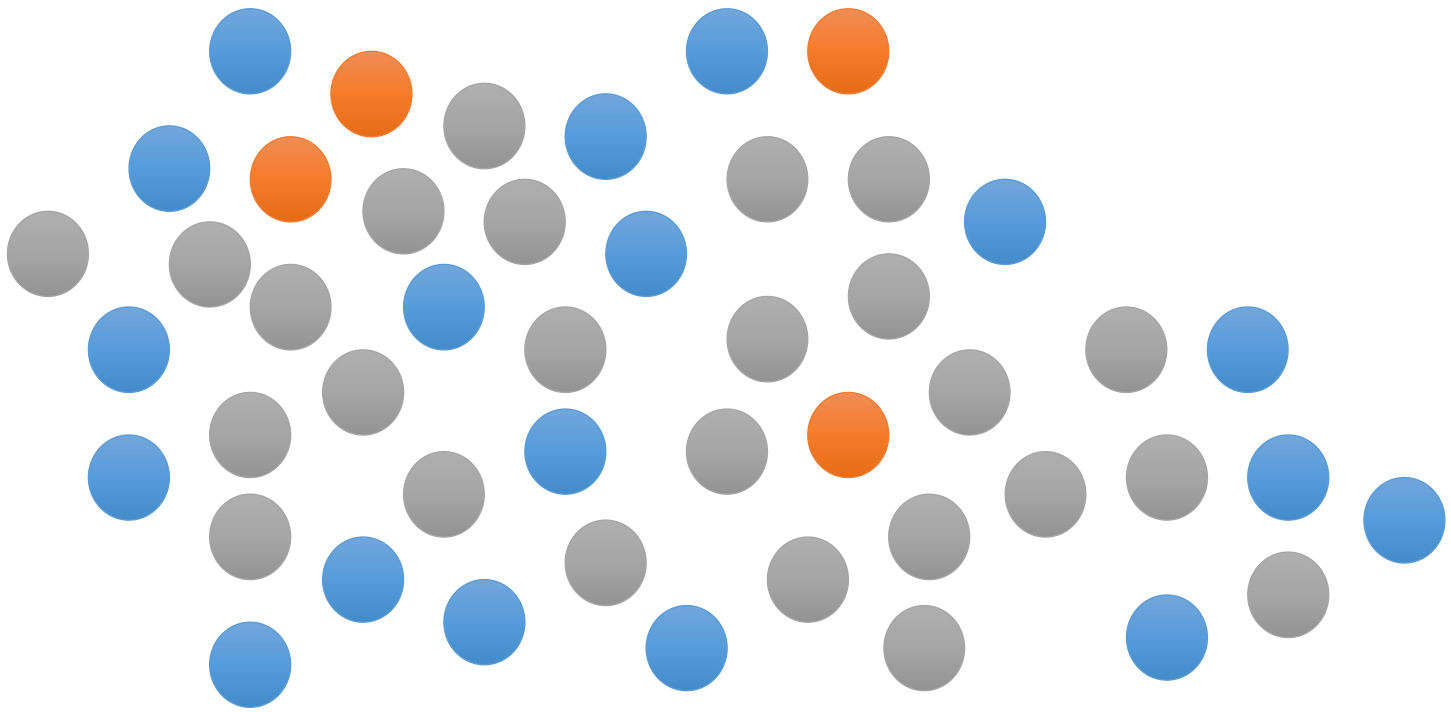
Move to continuous Ordinary Differential Equation (ODE) framework:

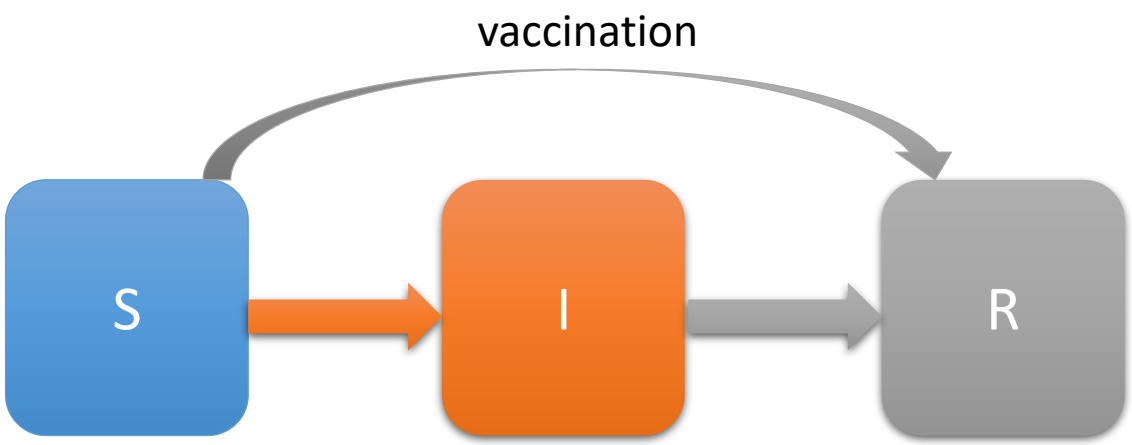


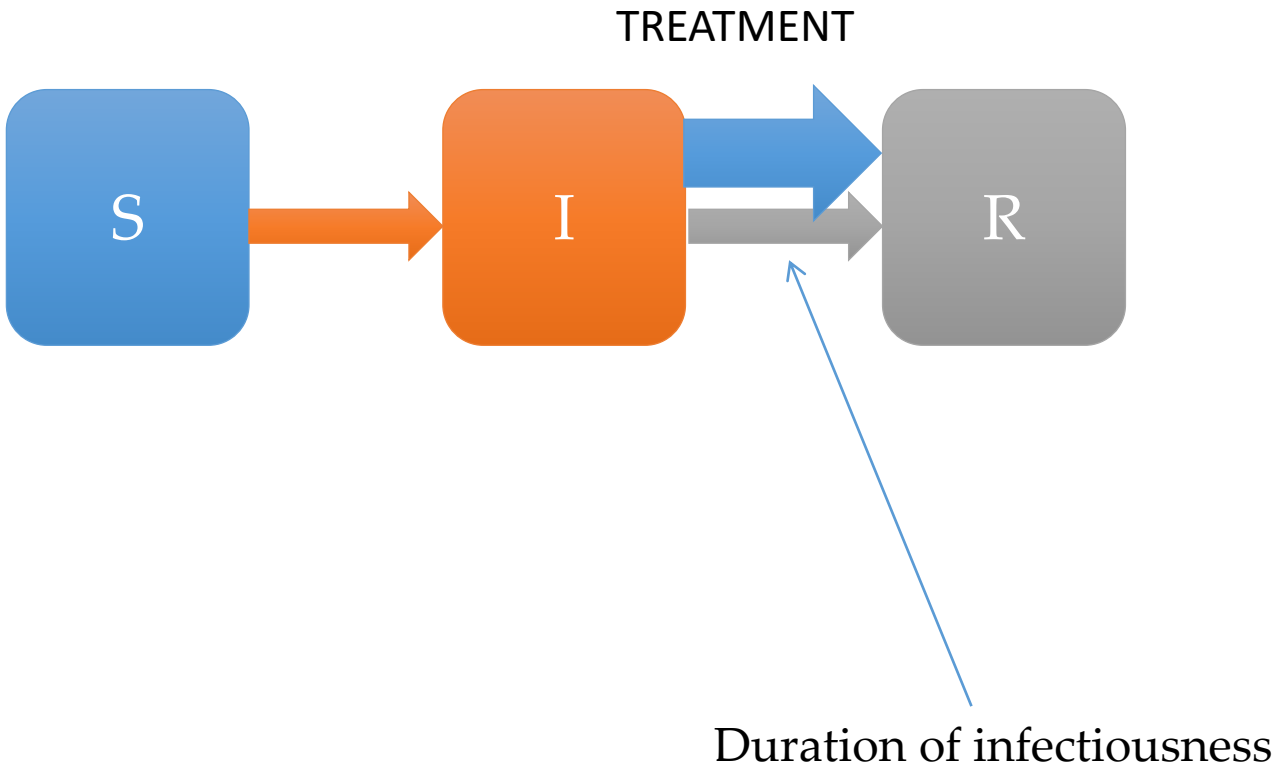

$$
\begin{aligned}
\frac{dS}{dt} &= -\beta S I, \\
\frac{dI}{dt} &= \beta S I - \gamma I, \\
\frac{dR}{dt} &= \gamma I.
\end{aligned}
$$

# Interventions: how can we reduce transmission?

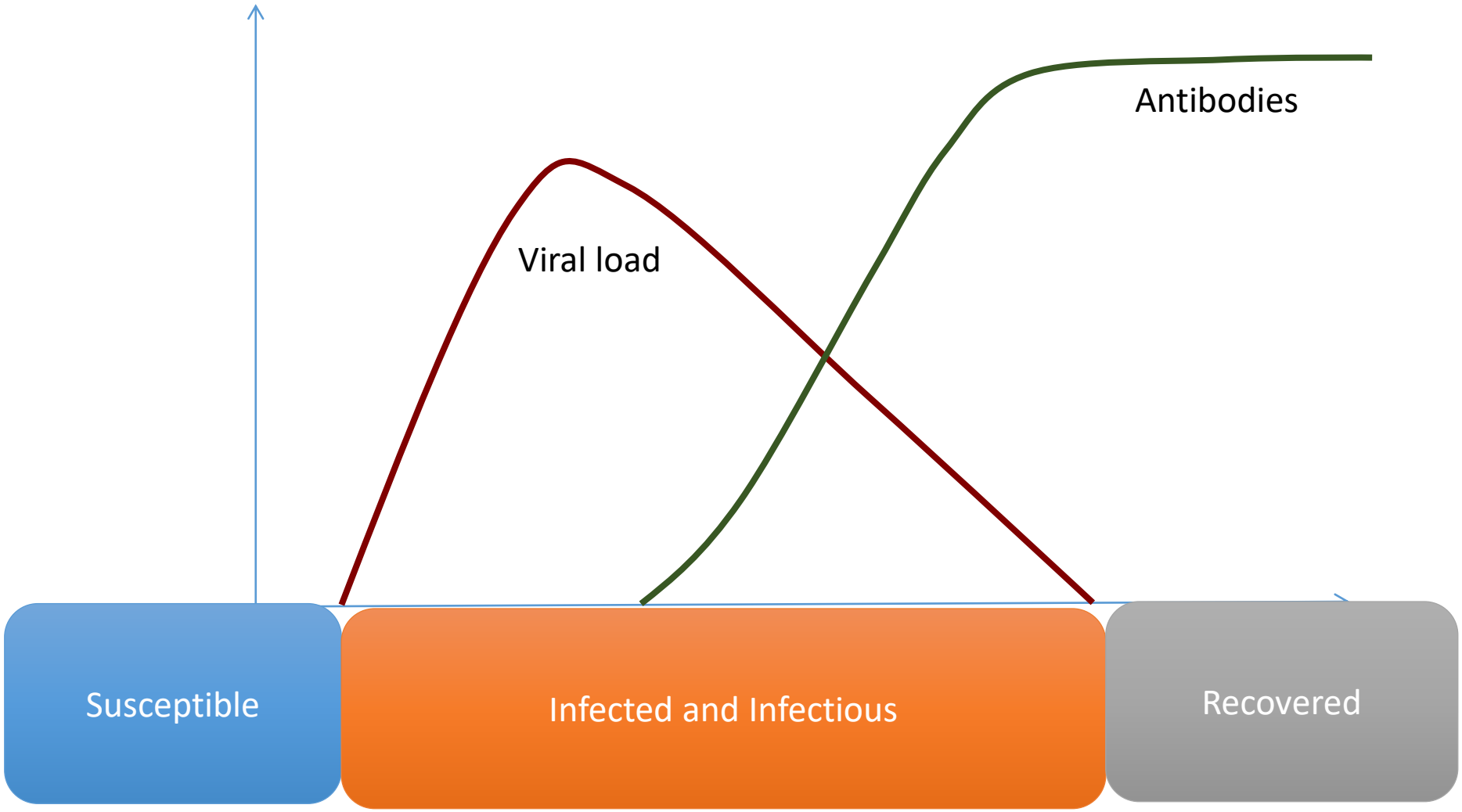


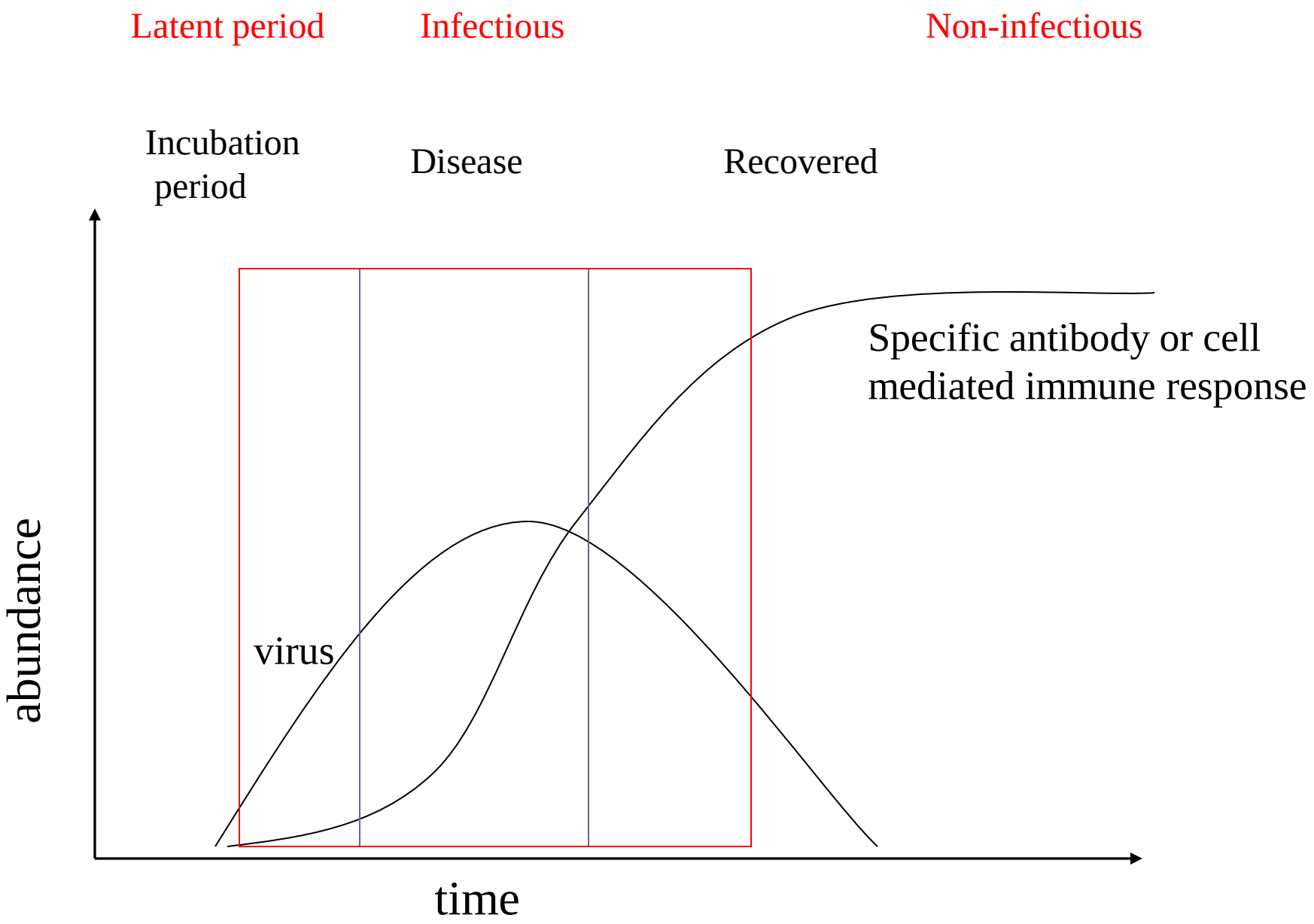



vaccination
S
I
R

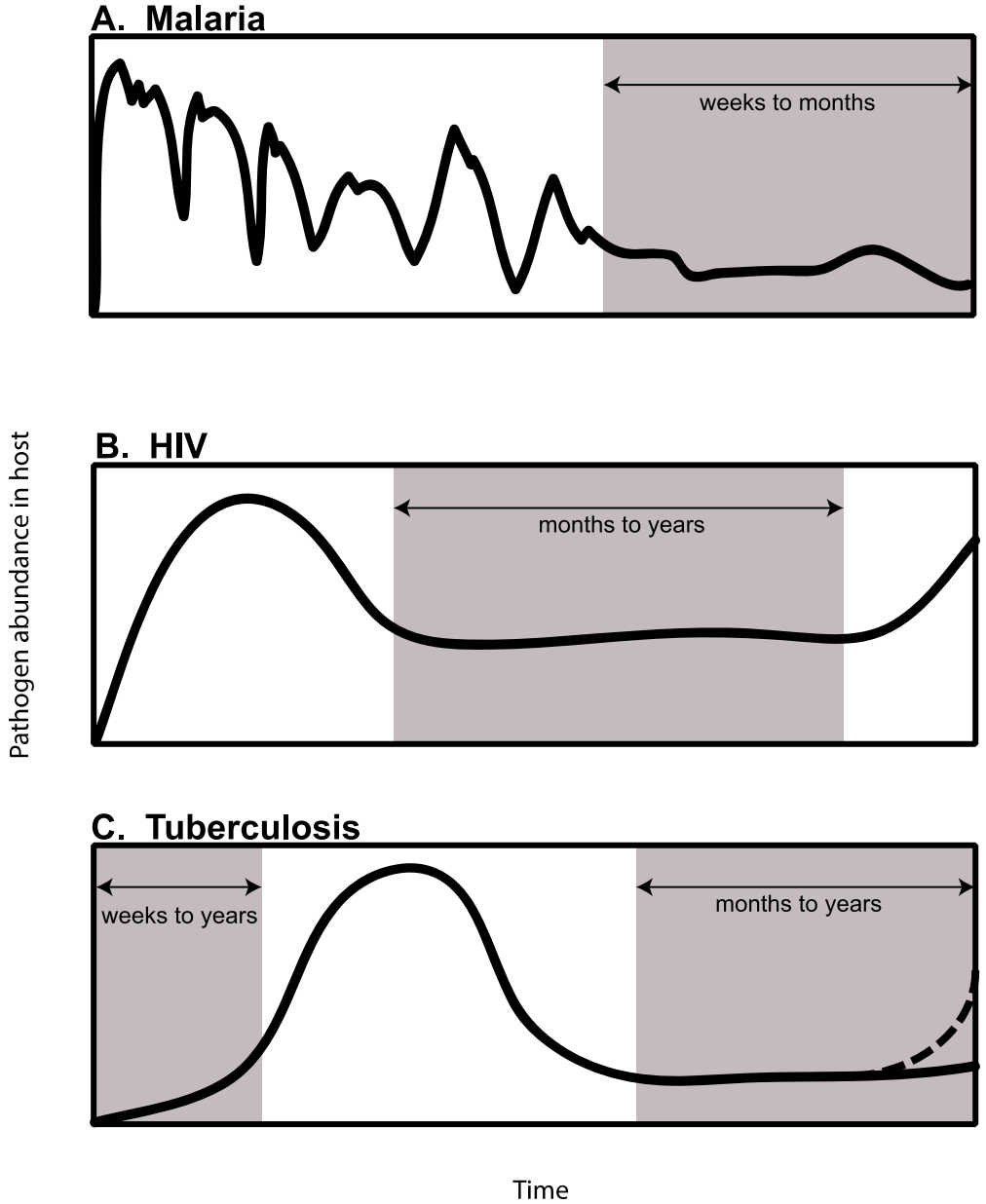

TREATMENT
S
I
R
Duration of infectiousness

# What compartments are needed in our model?




Latent period
Infectious
Non-infectious
Incubation period
Disease
Recovered
Specific antibody or cell mediated immune response
virus
abundance
time

# Dynamics of infection underlie model structure




Childs et al (2015) Epidemics

# Time Lines for chickenpox

Time of infection

Dynamics of infectiousness

latent period

infectious period

Noninfectious

(dead, recovered)

Dynamics of disease

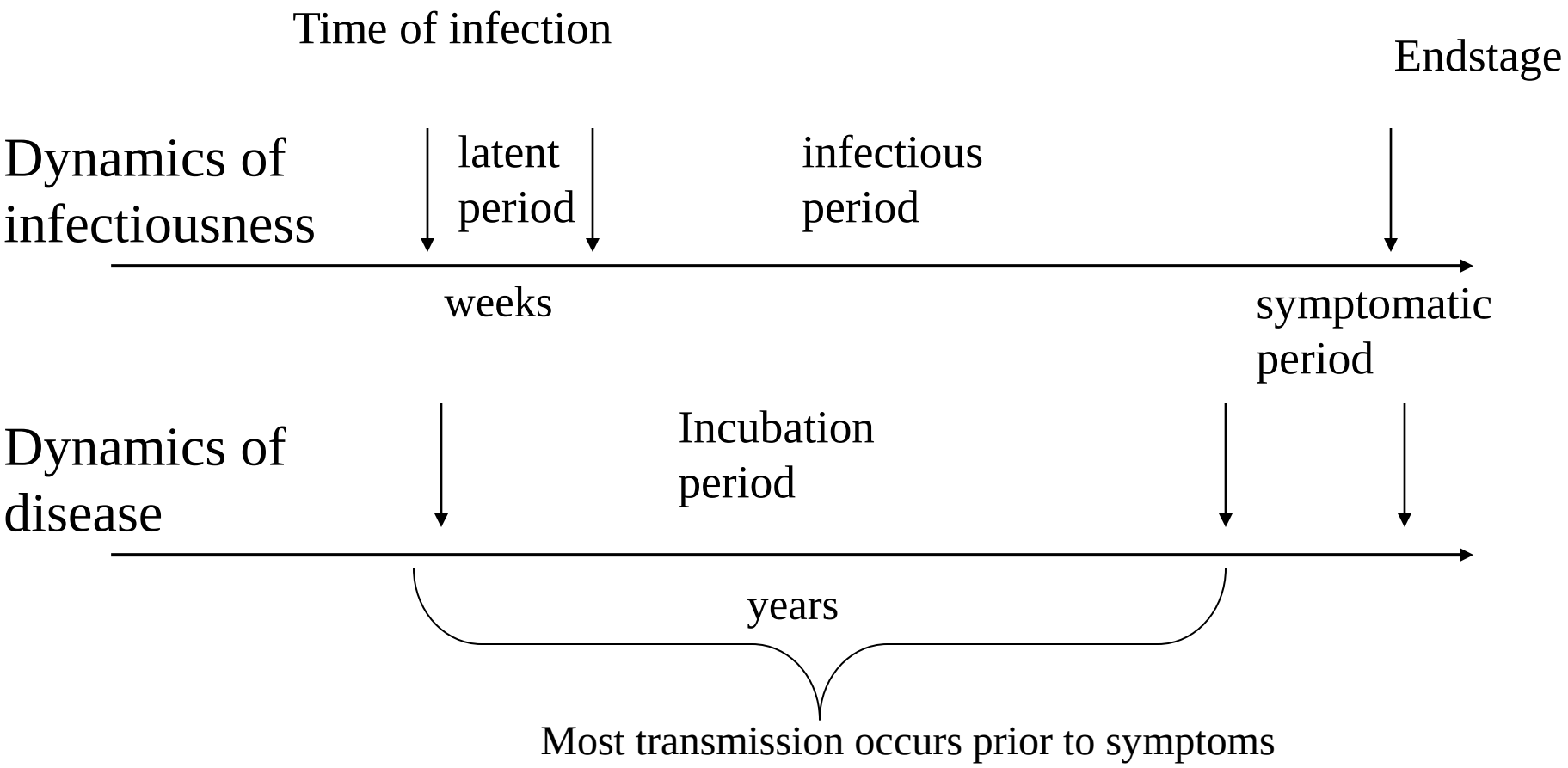
Incubation period

symptomatic period

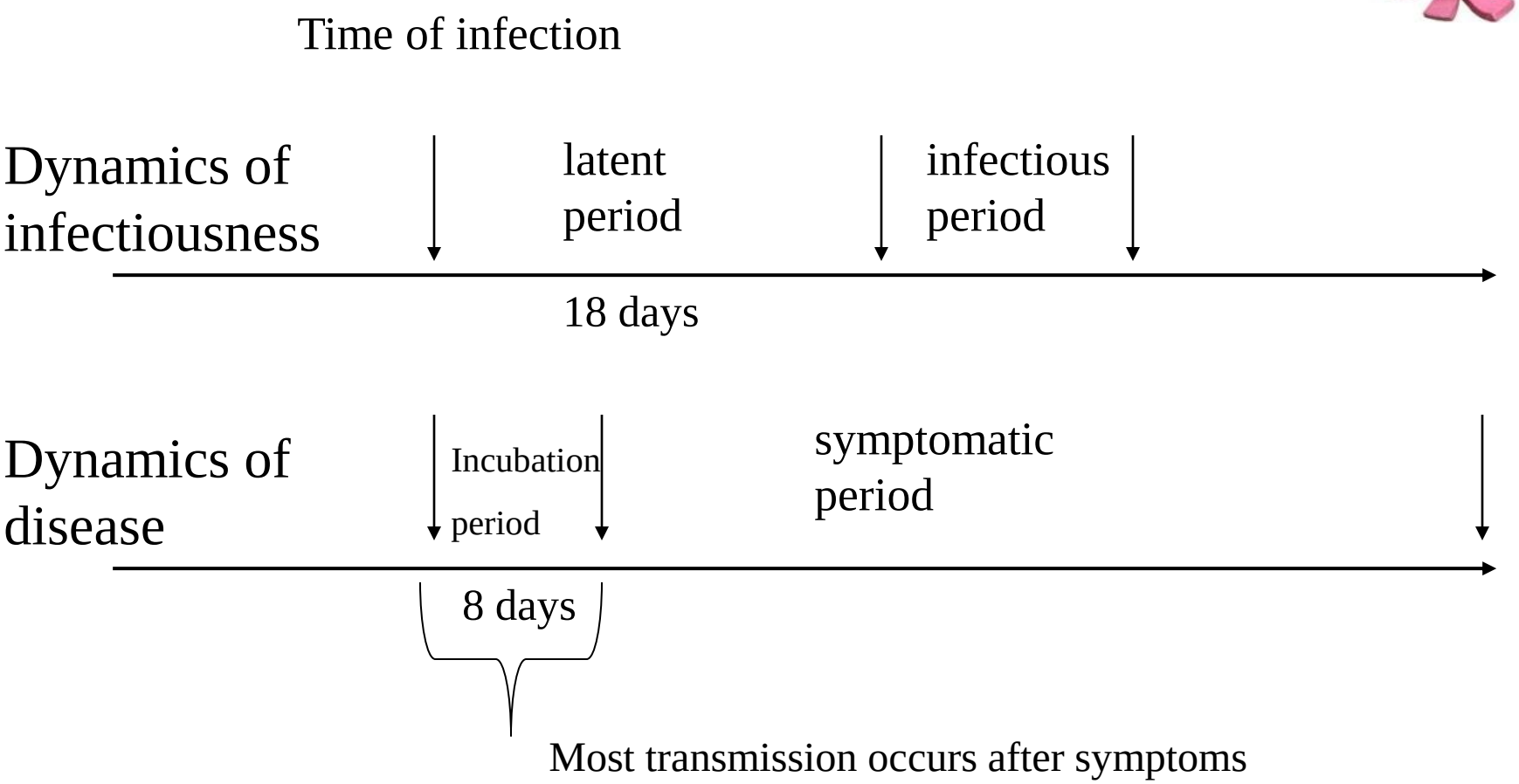
Nondiseased

Most transmission occurs prior to symptoms

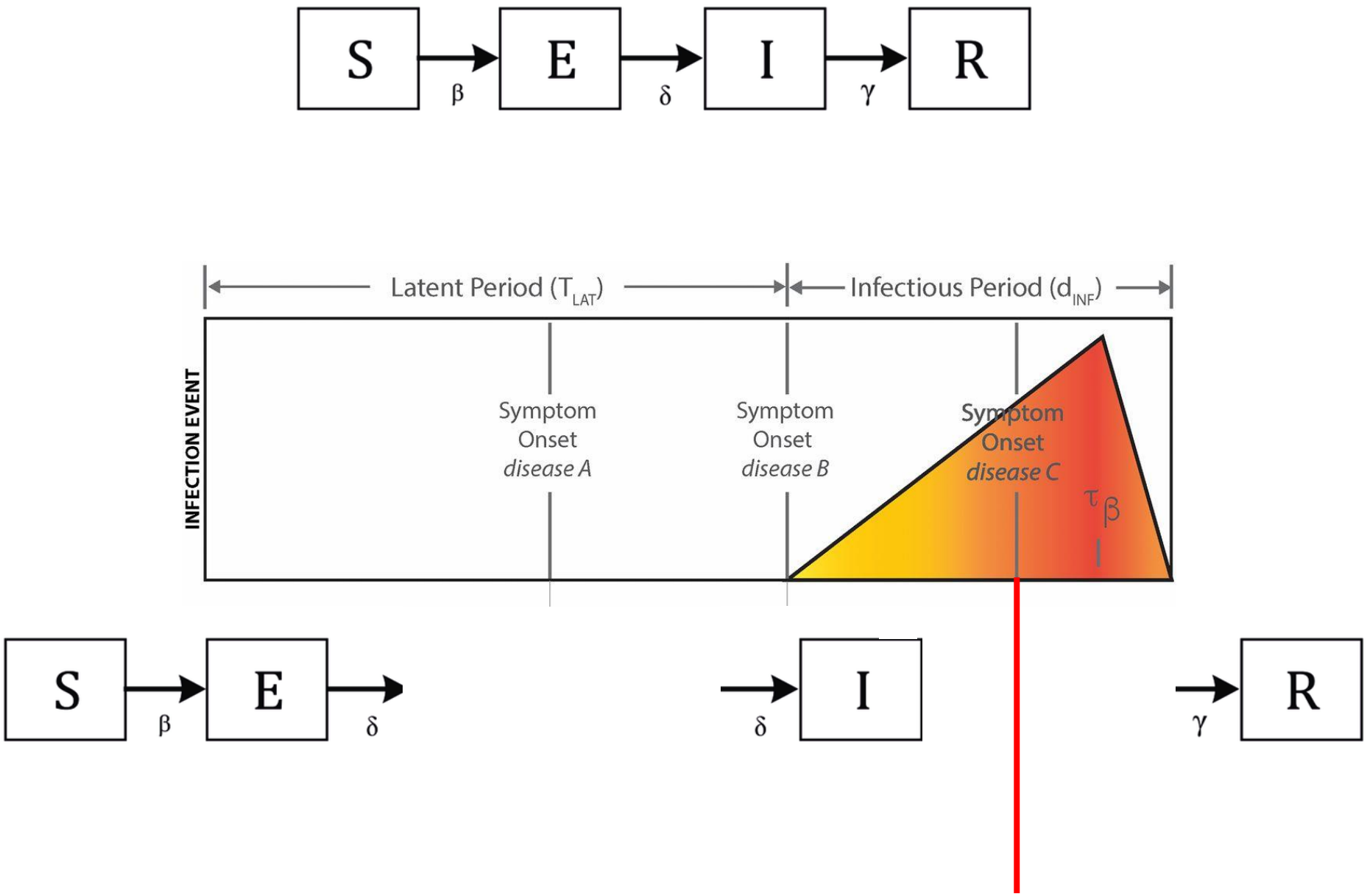
# Time Lines for HIV



# Time Lines for Pertussis



# How would you include a latent period?




Peak et al (2017) PNAS

# Headaches: discrete and ode formulation

SET UP PARAMETERS

```r
## Load deSolve so we can use the ode() command
library(deSolve)

## Set your time steps, initial values, parameters
times <- seq(0, 5000, by = 1)
yinit <- c(no_headache = 0.95, headache = 0.05)
parameters <- c(incidence = 0.02, recovery = 0.01)
```

SOLVE

```r
## Create an ODE model -- the solver needs your model written as a function
## that takes in a vector of times, initial values, and parameters
## (in that order) and returns a list with derivatives of your compartments
## relative to time.
headache_model <- function(times, yinit, parameters) {
    with(as.list(c(yinit, parameters)), {

        ## Define your no headache compartment
        dno_headache <- recovery*headache - incidence*no_headache

        ## Define your headache compartment
        dheadache <- incidence*no_headache - recovery*headache

        ## Save your compartments into a new variable, as a list
        comparts <- list(c(dno_headache, dheadache))

        ## Don't forget you need to return your compartments
        return(comparts)
    })
}
```

# Optional slides on supplemental code

# R code: discrete population model

```
#simple discrete time step model of a population with births and deaths
#the model is run for 1000 timesteps (see the "for" loop)
#when birth rate and death rate are equal, the population is at equilibrium
#we round because there are no "half" people

birth_rate = 0.1
death_rate = 0.1
population_t_current = 10000
population_matrix = NULL

for(t in 1:1000){

population_t_next = population_t_current + round(birth_rate*population_t_current) - round(death_rate*population_t_current)

population_matrix = rbind(population_matrix,population_t_next)

population_t_current = population_t_next

}
```

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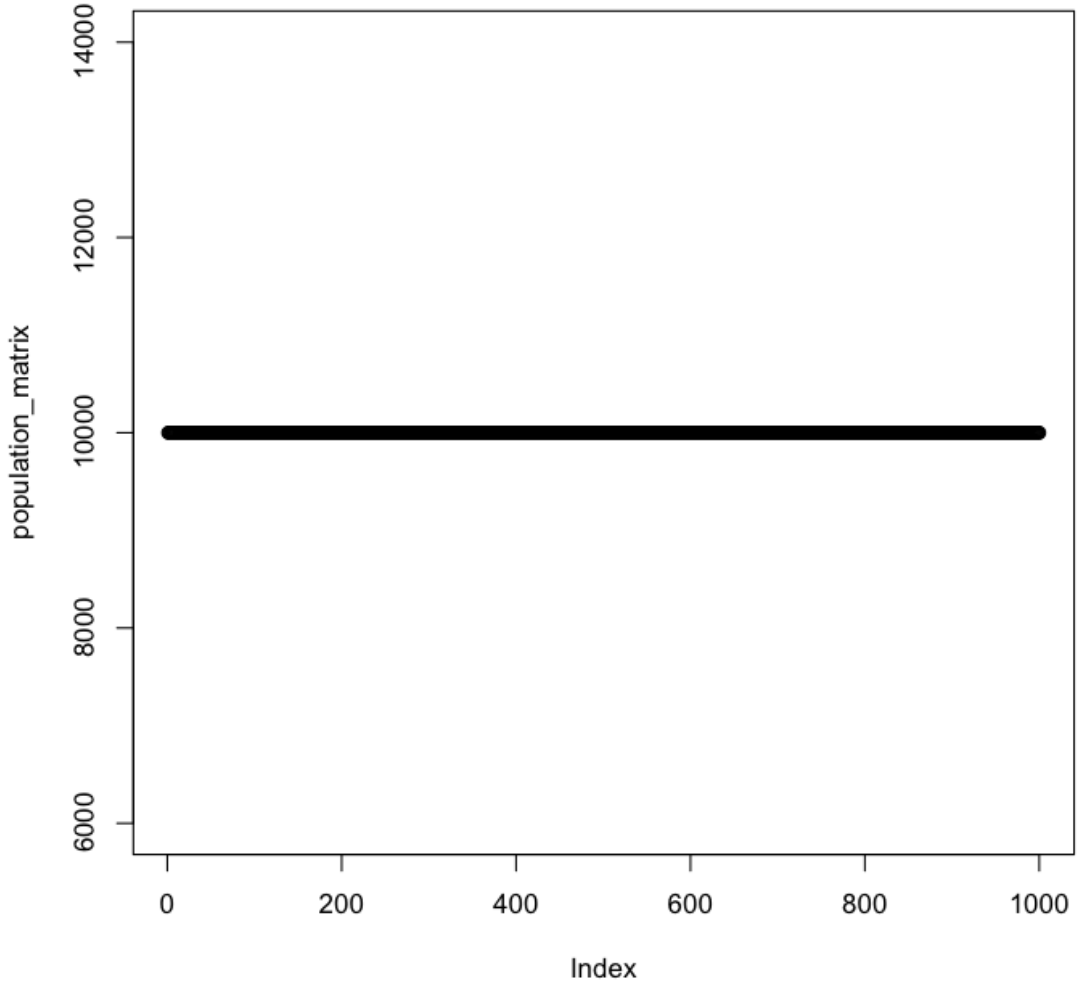
population_matrix = rbind(population_matrix,population_t_next)

population_t_current = population_t_next

}
```

# R code: discrete population model

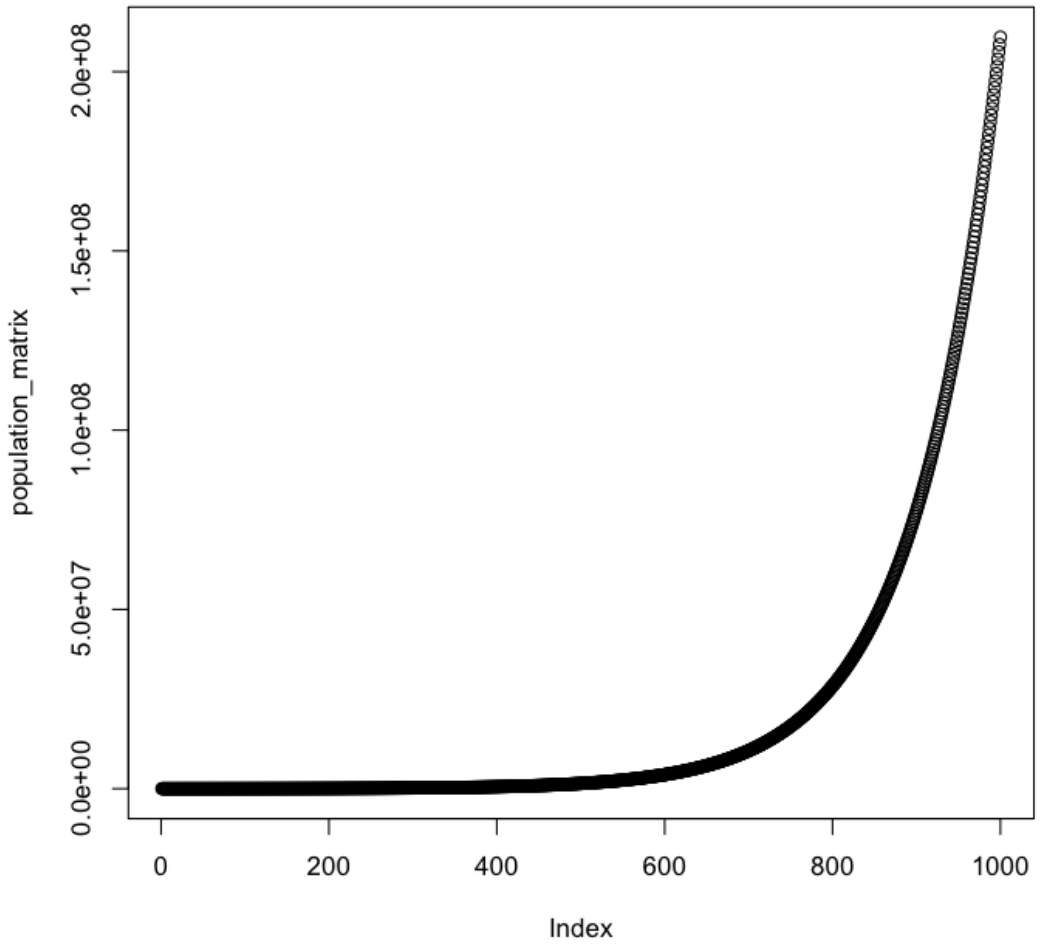
```
plot(population_matrix)
```



# R code: discrete population model

Try births > deaths
and births < deaths

```
plot(population_matrix)
```



# Headaches: discrete and ode formulation

```r
## Headache example: discrete model of a non-infectious process

## Let's set some initial values and parameters
N_t <- 500      # Number of people without a headache at time zero
P_t <- 0        # Number of people with a headache at time zero
incidence <- 0.05  # Probability of going from {No Headache} to {Headache}
recovery <- 0.9    # Probability of going from {Headache} to {No Headache}

## Again, we make a data container
dat <- NULL

## Make a sequence of time steps
timesteps <- 1:100  ## Or, equivalently, seq(1, 100, 1)

## Loop through our sequence of time steps
for (t in timesteps){

    ## Calculate the number of unaffected at time t + 1
    N_t1 <- N_t - round(incidence*N_t) + round(recovery*P_t)

    ## Calculate the number of affected at time t + 1
    P_t1 <- P_t + round(incidence*N_t) - round(recovery*P_t)

    ## Bind these numbers as a new row (rbind) in our data container
    dat <- rbind(dat, c(N_t1, P_t1))

    ## Update the unaffected and affect for the next time step
    N_t <- N_t1
    P_t <- P_t1
}

## Plot it
matplot(dat, xlab="time", ylab="number of people", type="l", lty = 1)
legend("topright", col = 1:2, legend = c("no headache","headache"), lwd=1)
```

SET UP PARAMETERS

LOOP

PLOT

Do the calculation

Put it into the data matrix

Update the values