
Module I: Morbiliviruses
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Lecture outline

- Microparasite (morbilivirus) Dynamics
    - Motivation: PDV outbreak in northern Europe
    - Pathogen fitness & Basic Reproductive Ratio, R_0
    - The anatomy of an epidemic (epizootic)
    - Vaccination & Herd Immunity
- Frequency- & Density-Dependent Transmission
- Within-host dynamics
- Polymicrobial Herd Immunity

Catastrophic seal mortality in North Sea, 1988

Harbor seal (*Phoca vitulina*)

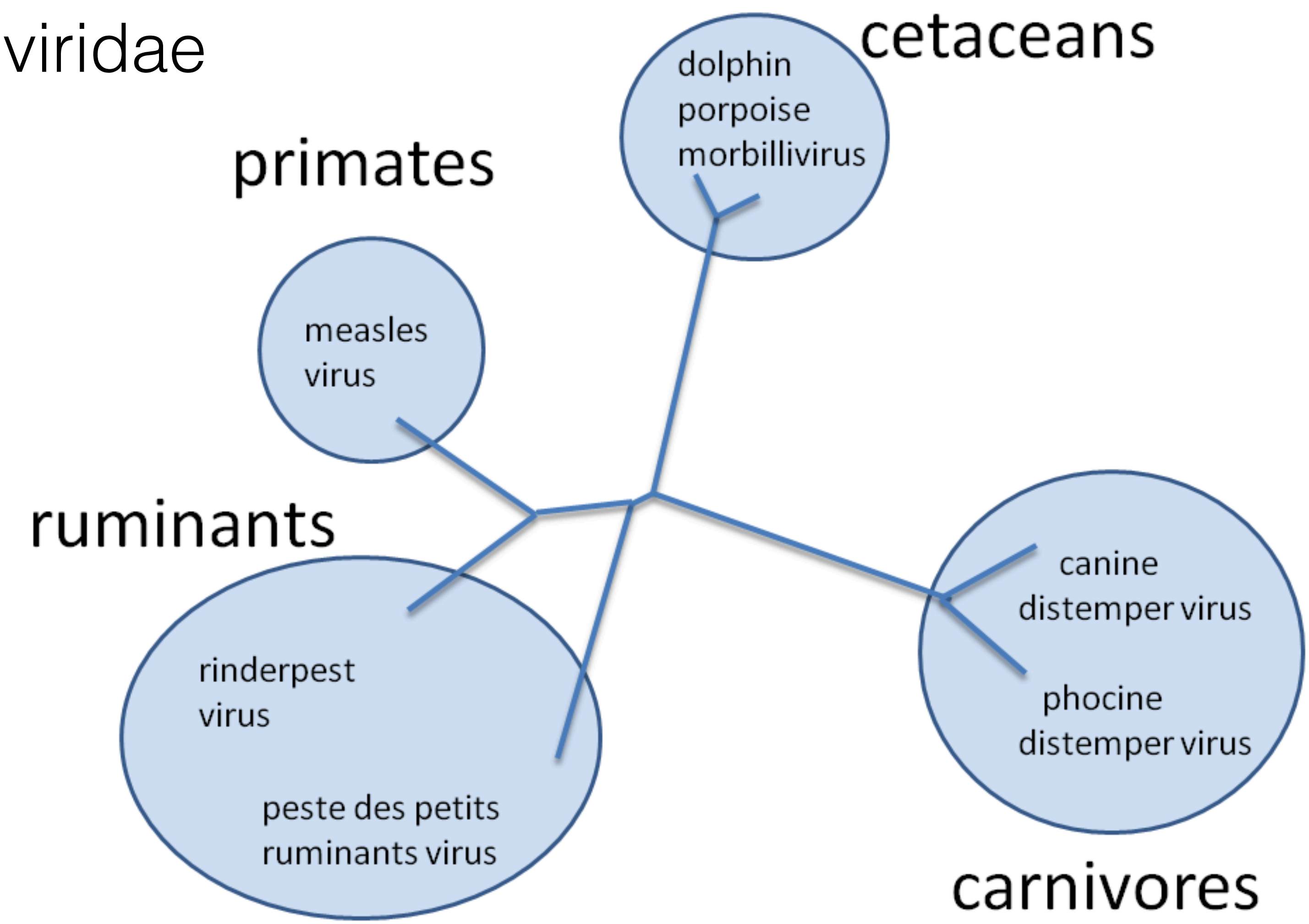
- April 1988: First record in Denmark
- Started in Wadden sea
- Spread through Baltic & North sea
- Reached UK by late summer
- Subsided by winter

Phocine distemper virus (PDV)

- Caused by a morbillivirus …

Morbiliviruses

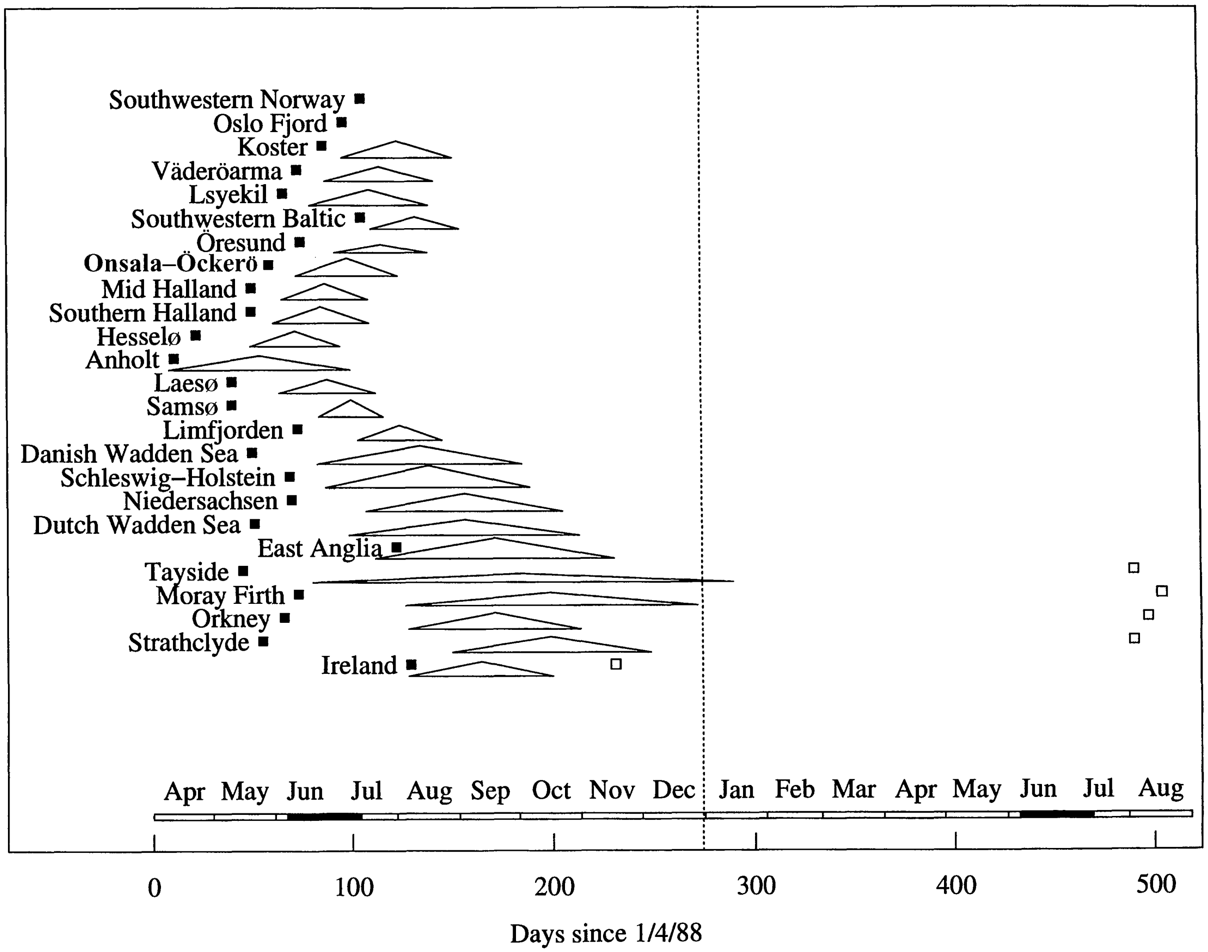
Single-stranded RNA viruses
Family: paramyxoviridae



Phocine distemper virus (PDV)

- Caused by a morbillivirus …
- Spread through respiratory aerosol
- Harbor seals develop severe pneumonia
- Seals with damaged lungs cannot dive
- Many starve or die of secondary infections
- Recovered individuals become effectively immune

Spatial wave of spread



Spread through Northern Europe

- Thousands of dead seals washed ashore ~60% of each colony lost
- Seals haul out during summer months to breed
    - Aggregations may help trigger outbreaks
- Seals move around a lot

Where did PDV come from?

Origin: Most likely Harp Seals

~30% harp seals seropositive in Greenland

Harp seals had carried virus even before 1988

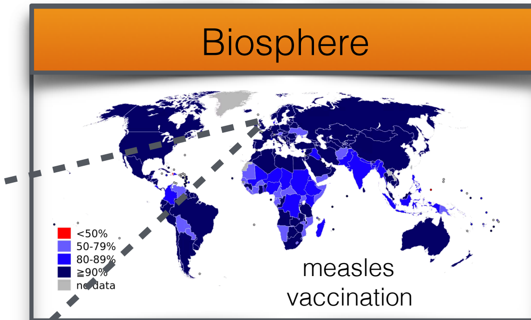
Virus has little effect on harp seals

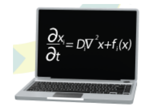
Harp seal (*Phoca groenlandica*)

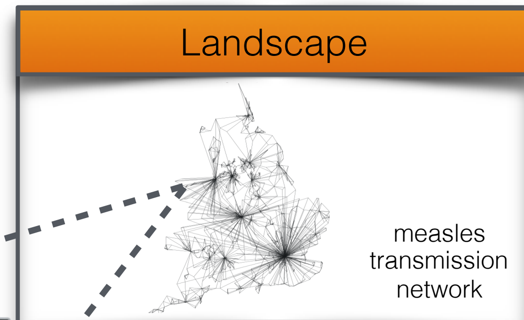
Harp seals migrated from Arctic regions to Danish waters during 1988 in response to exploitation of Atlantic fisheries

Interdisciplinary Disease Ecology Across Scales

- How does pathogen ‘abundance’ vary in space?
- Why are there risk hotspots?

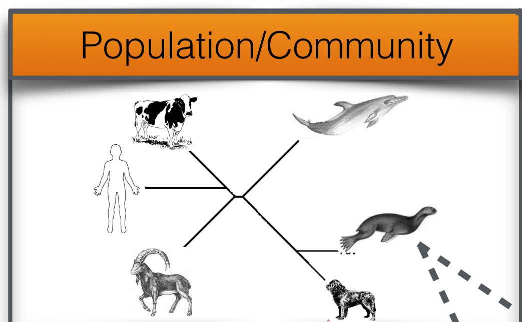


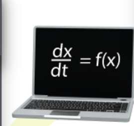




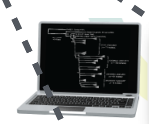
- How does diversity of hosts and/or pathogen affect emergence, evolution and control of pathogens?

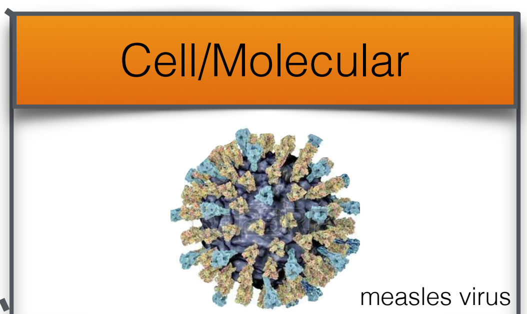
- What are impacts of anthropogenic factors (climate, land-use, hunting, vaccination) on pathogen population biology?





- Why are there epidemics?
- What determines pathogen invasion and establishment?
- Why are recurrent epidemics seasonal?



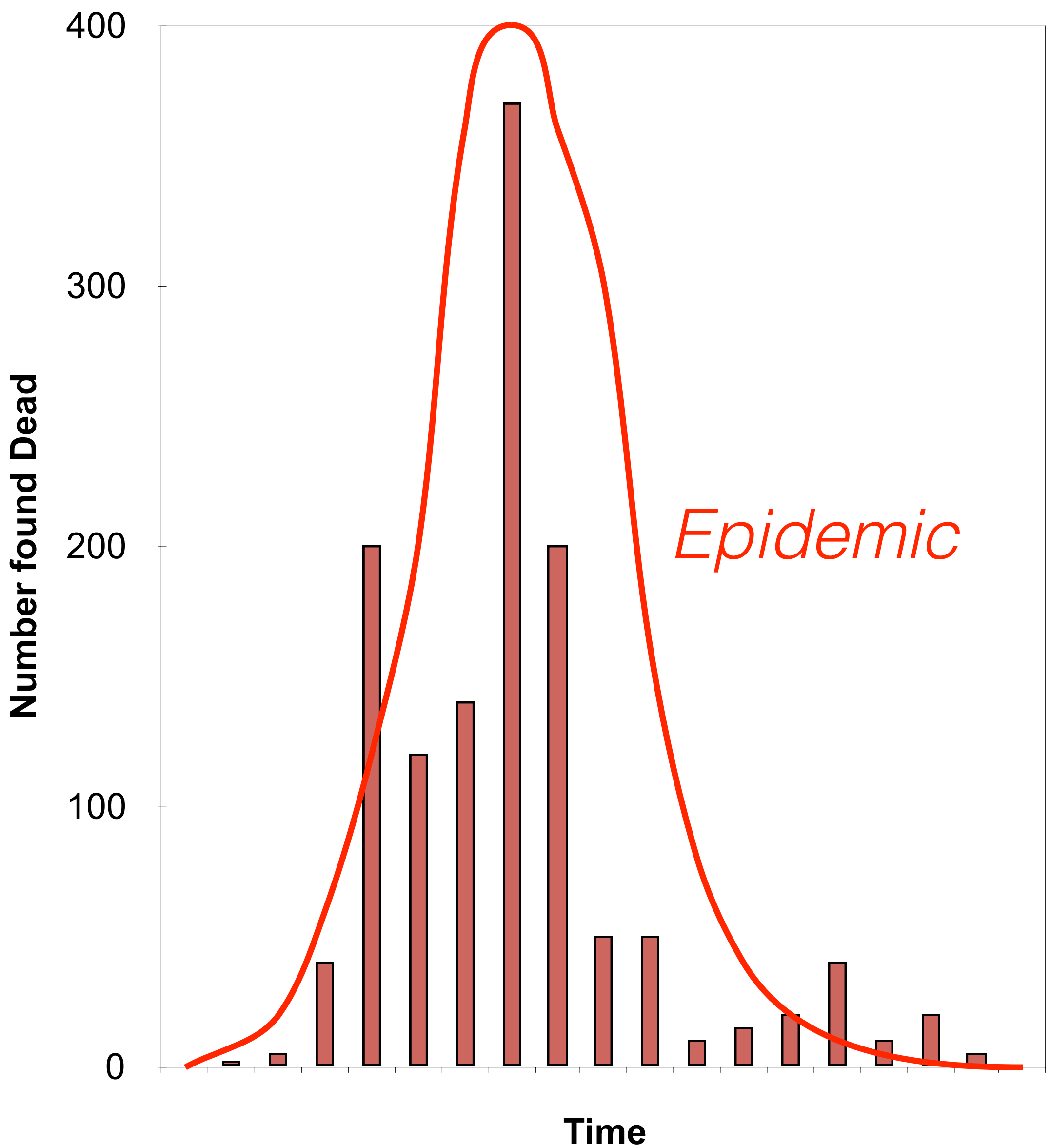


- How do pathogens from different species to infect novel hosts?
- What are pathogenesis, virulence and immunological impacts in hosts?

IDEAS

- Gain knowledge of infectious diseases that spans traditional disciplinary boundaries, e.g. cell biology, ecology, epidemiology, genetics, immunology, molecular biology, geography
- Successful conducting independent research addressing cross-scale questions in infectious disease biology with a view to solving problems relevant to population health
- Develop advanced computational skills that can be applied to formulating and implementing research that spans levels of organization

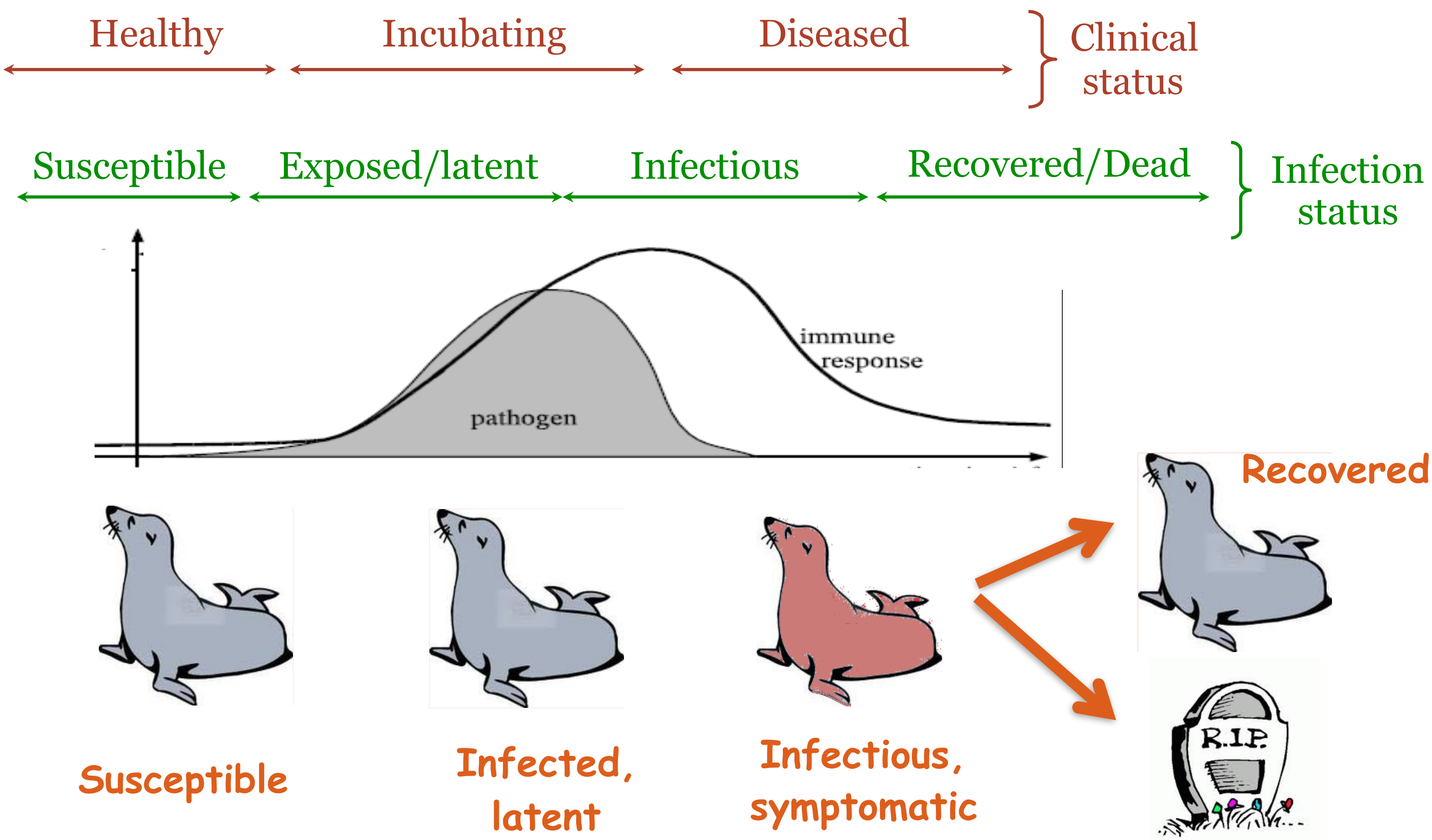
Seals & Phocine Distemper Virus



Counts of Dead Seals in The Wash

- Why are there epidemics?
- What determines pathogen invasion and establishment?

Categorising individuals

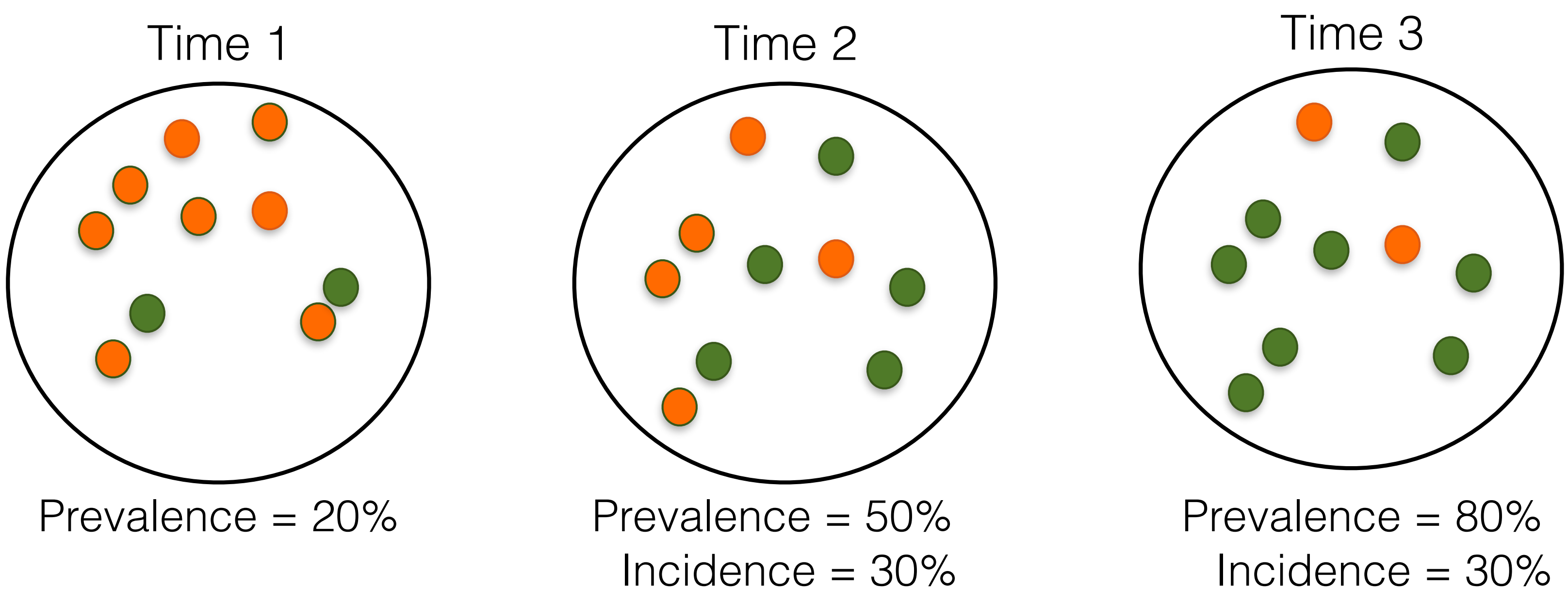


Host susceptibility

- Susceptible - an individual who will acquire infections if exposed to a pathogen
- Infectious – harboring a pathogen, able to transmit, and experiencing negative effects of disease
- Recovered/Immune - resistant to infection following exposure to previous infection

Quantifying infections at population level

- Epidemiologists/epizootiologists: measure and monitor disease changes over time and space
- **Prevalence** – proportion of hosts infected or expressing disease (# Infected / total N)
- **Incidence** – number/fraction of new cases per unit time



Basic reproductive number (R_0)

- Parasite establishment will be most strongly influenced by R_0 – The Basic Reproductive Number

- Equivalent to parasite's fitness or 'birth rate' early in an epidemic

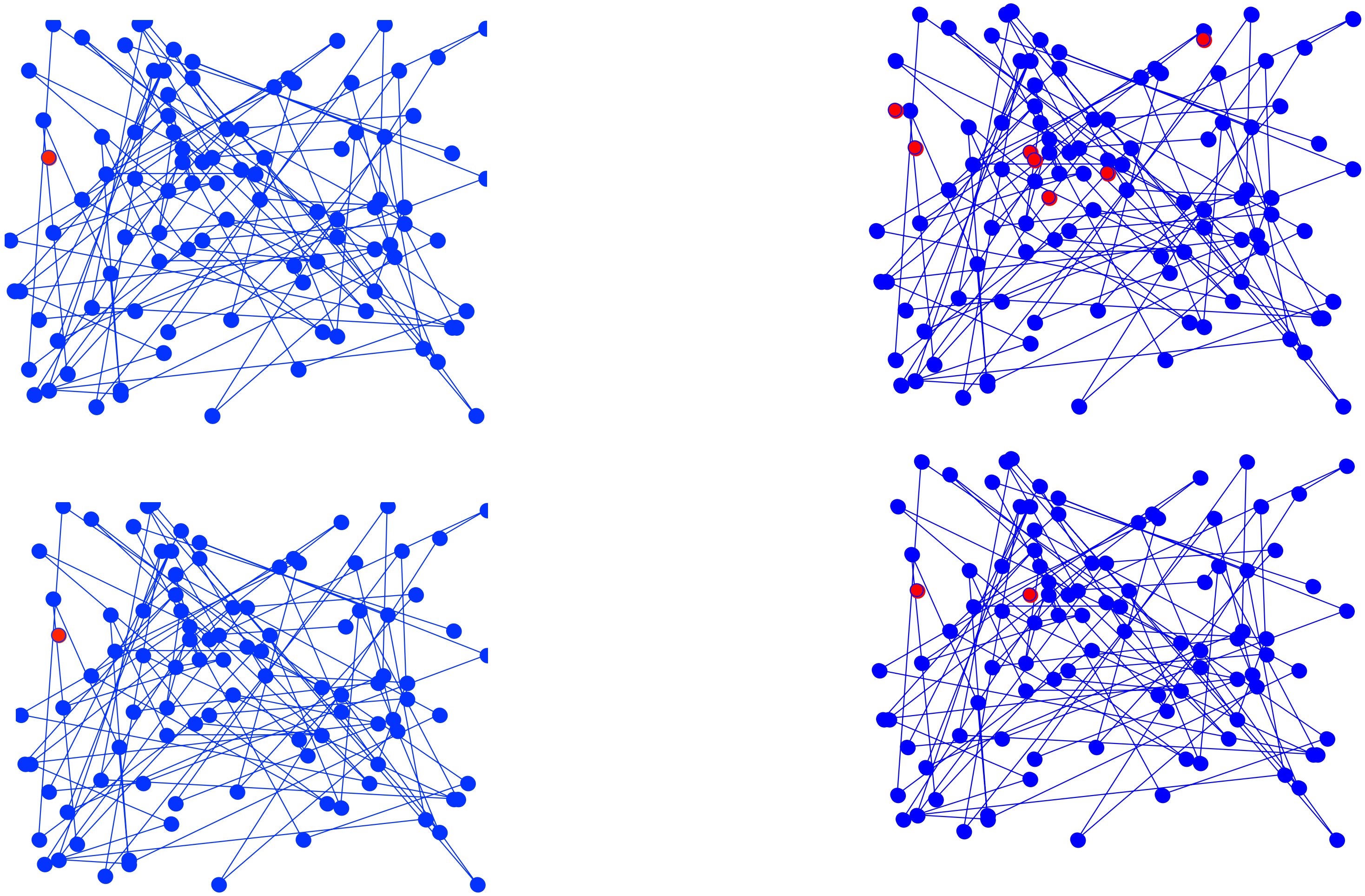
Pathogen Invasion

Now

Next generation

Pathogen A

Pathogen B



Which pathogen is ‘fitter’?

Can use # secondary infections when everyone susceptible as a measure

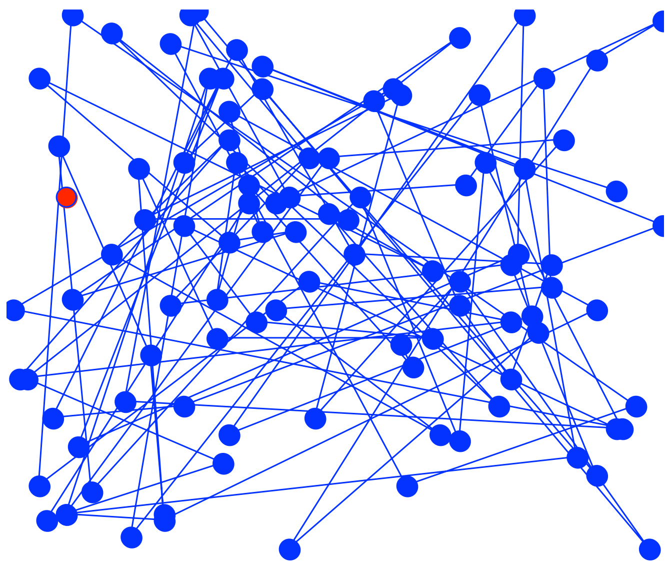
Basic reproductive number (R_0)

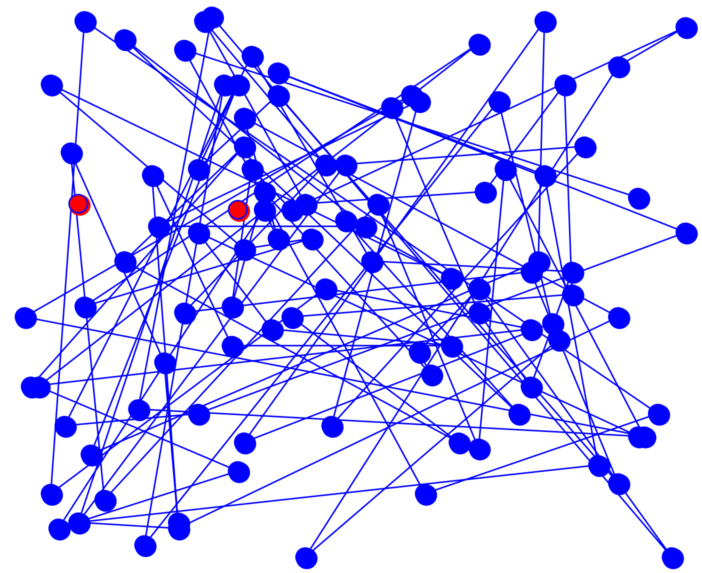
- Parasite establishment will be most strongly influenced by R_0 – The Basic Reproductive Number

- Equivalent to parasite's fitness or 'birth rate' early in an epidemic

- Definition: number of secondary cases generated by a typical primary case when entire population is susceptible

Basic reproductive number



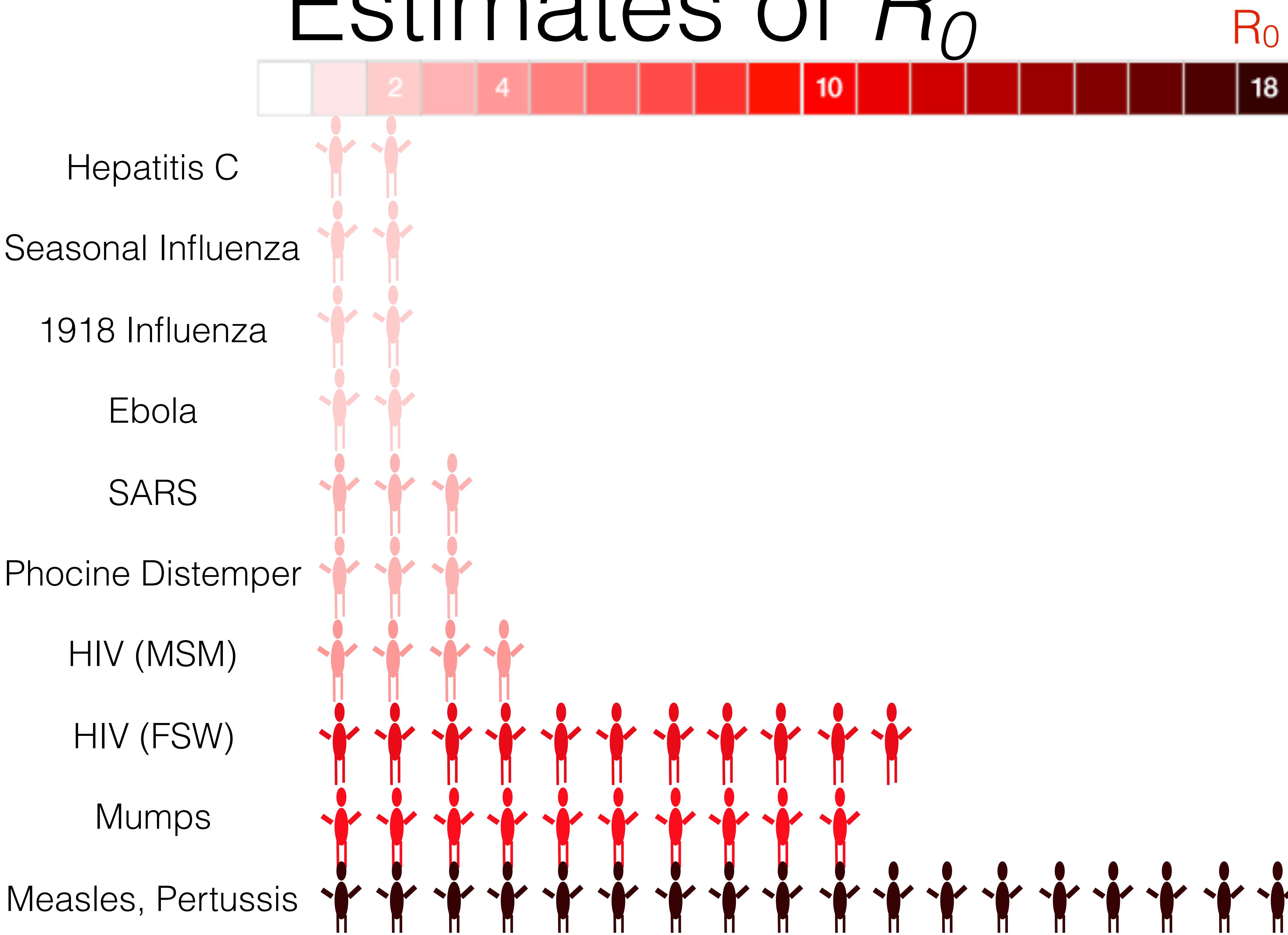


- When $R_0 > 1$ – Pathogen invades
- When $R_0 < 1$ – Pathogen cannot invade
- When $R_0 = 1$ – Pathogen just replaces itself

R_0 is key to understanding disease invasion

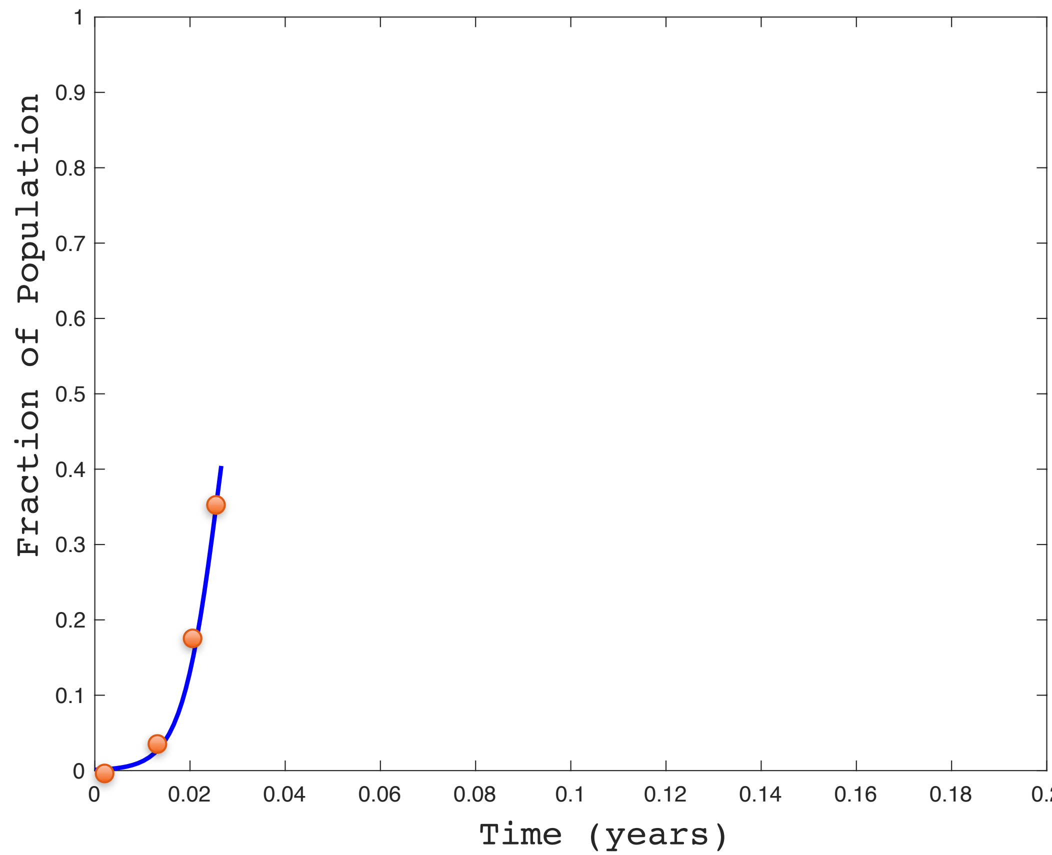
 # secondary infections from single infected host in a susceptible population

Estimates of R_0



The Anatomy of a simple Epidemic

Initially, exponential growth of infecteds at rate given by R_0



The Anatomy of a simple Epidemic

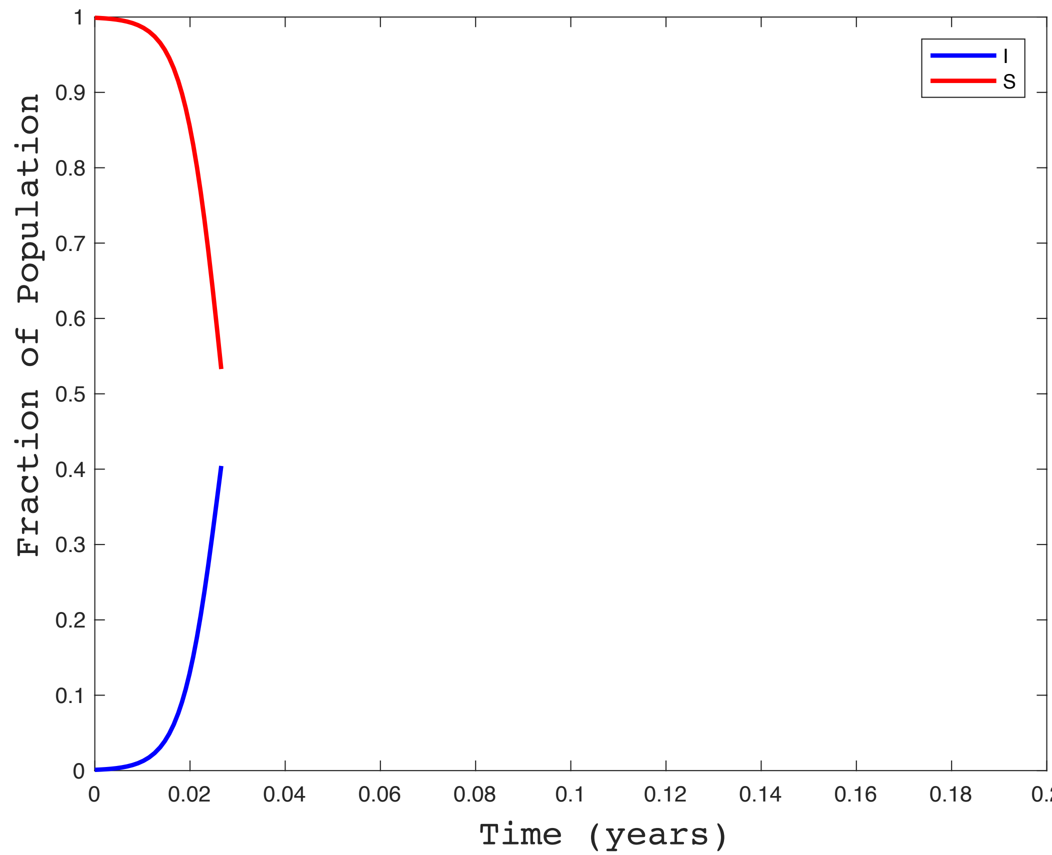
BUT …

Chain of transmission eventually depletes pool of susceptibles

So, need to define effective value of R_0 taking into account susceptibles

R_e scales with proportion of susceptibles in population (s=S/N):

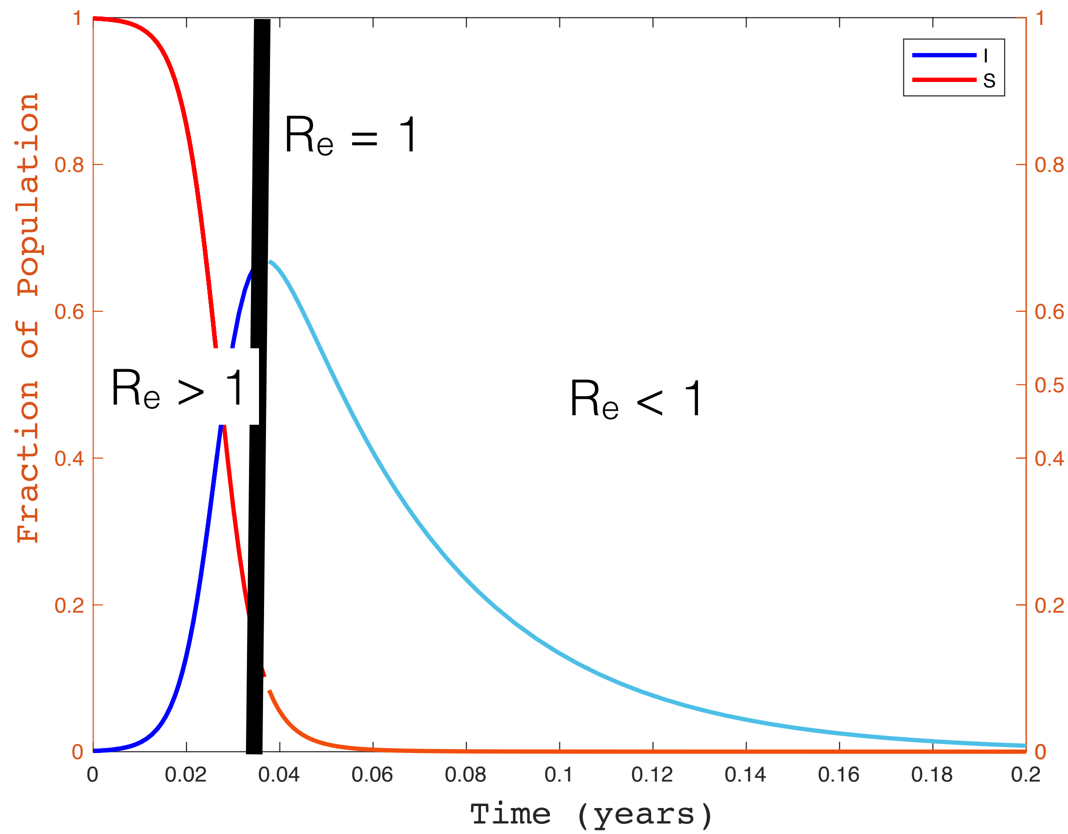
$$R_e = R_0 s$$



The Anatomy of a simple Epidemic

When $R_e<1$, each infectious individual infects fewer than one new person, breaking transmission chain

Number/fraction of infecteds falls and epidemic eventually dies out



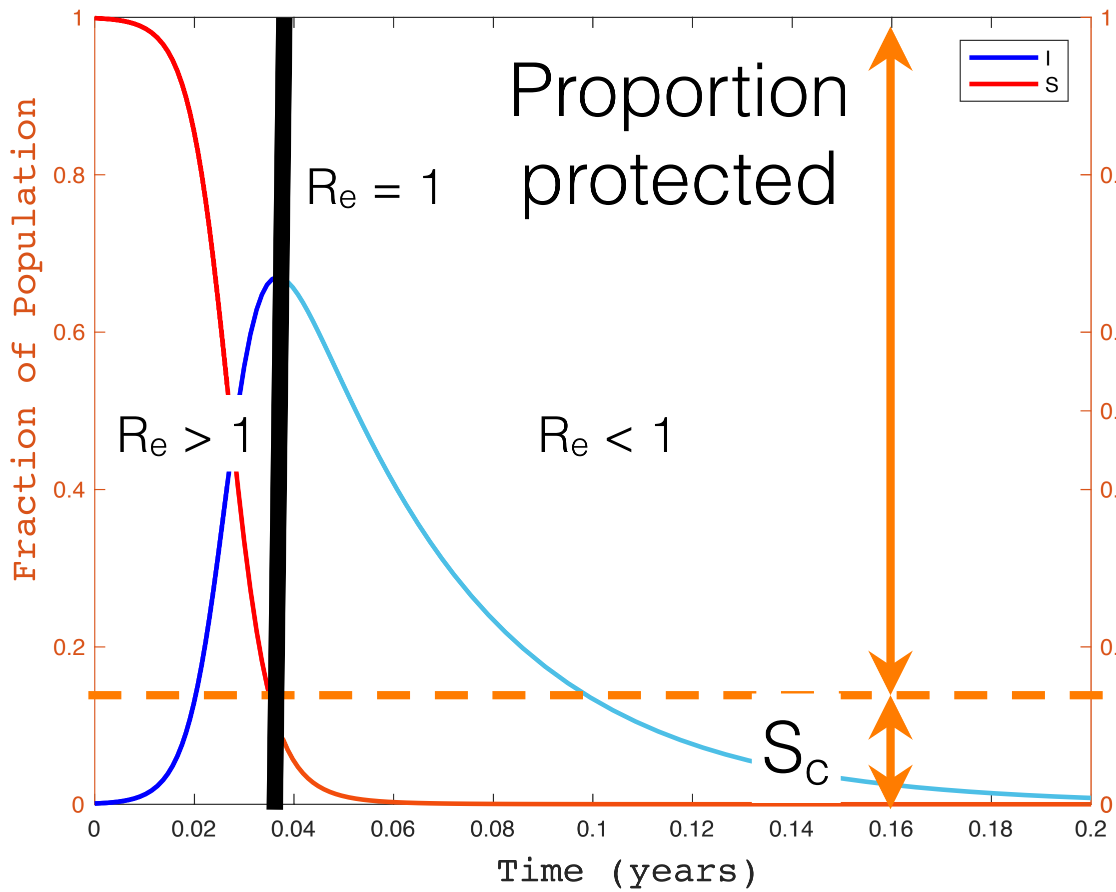
Vaccination

- “vacca” = Latin for cow

- *A priori* Goal
  - Protect individual from infection
    - Individual immunity

Control implications

If, somehow, we reduce proportion of susceptibles below a critical level, s_c, then $R_e<1$ and infection cannot 'invade' population



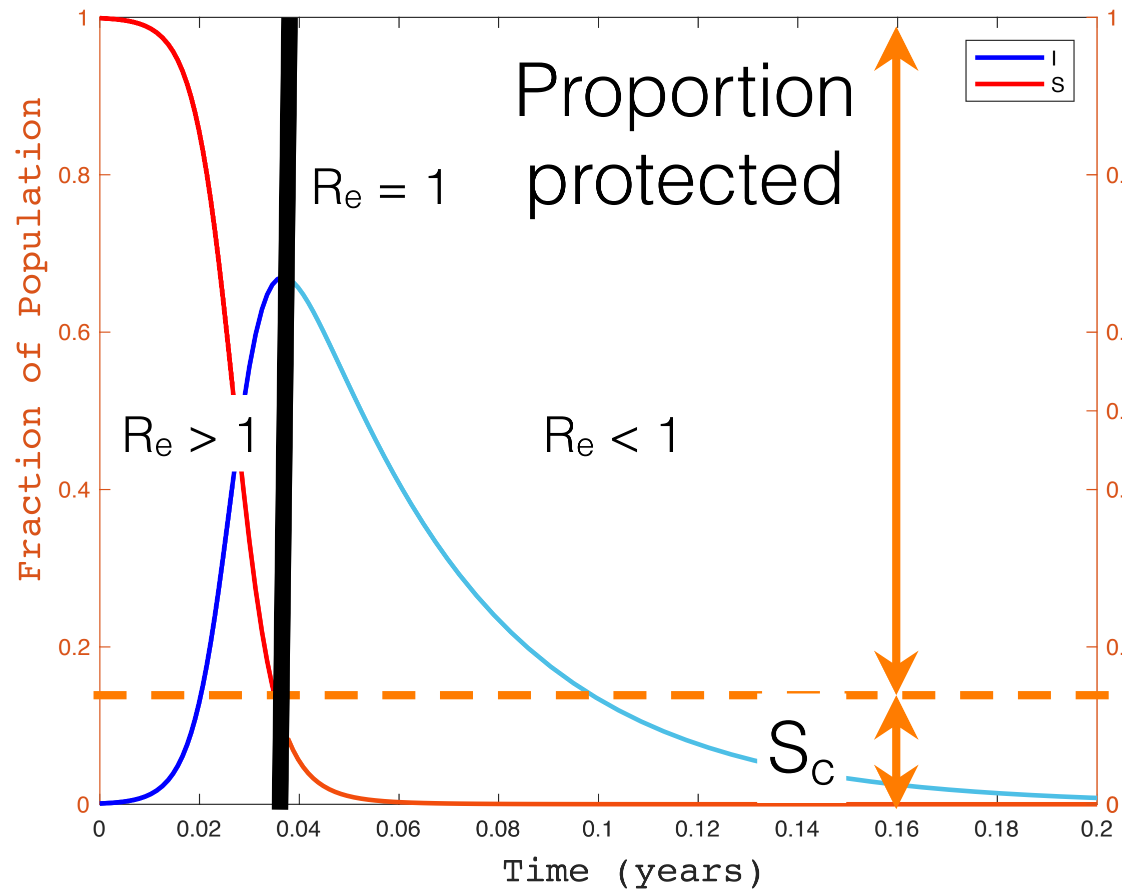
Control implications

Recall: $R_e = R_0 s$

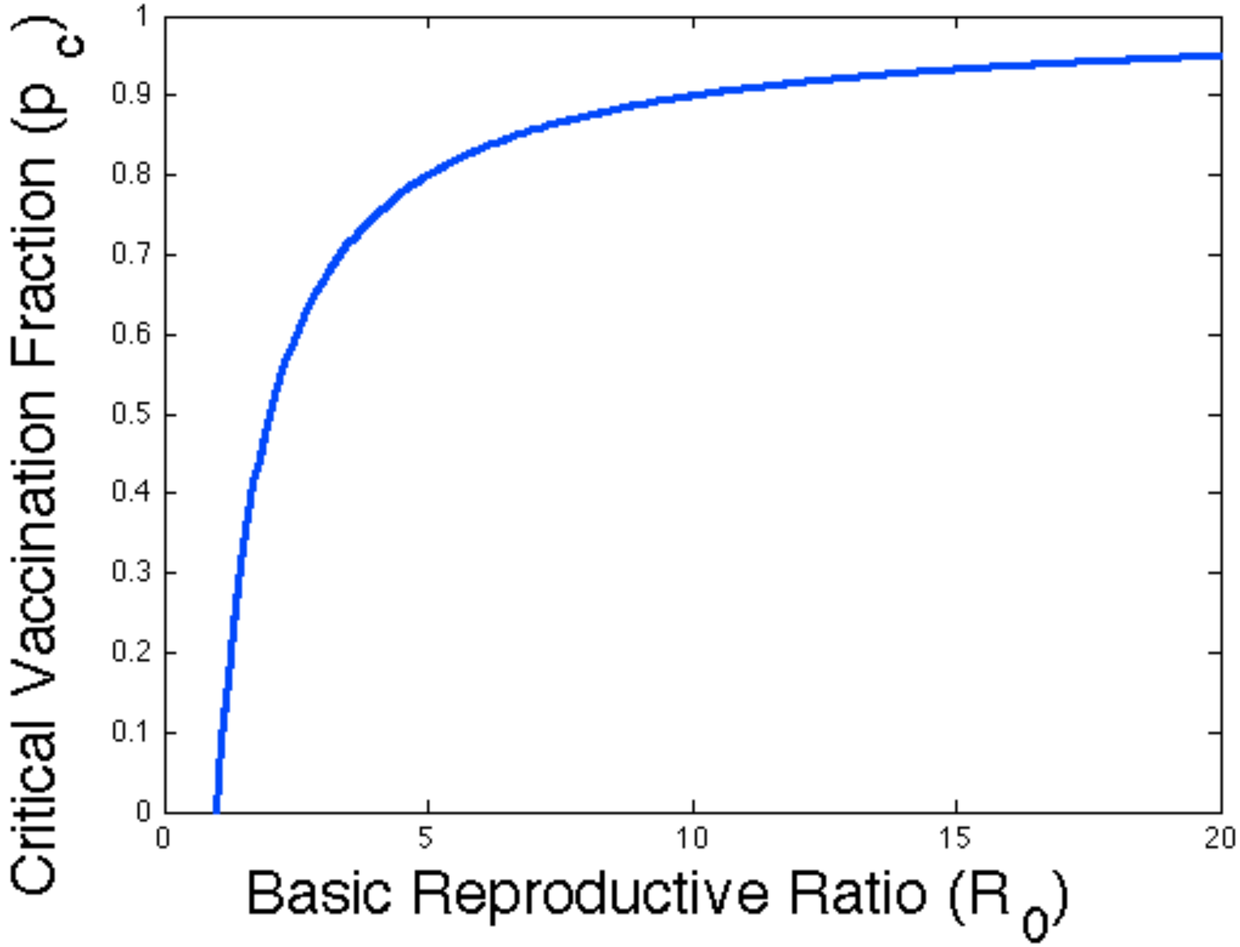
So, $s_c = 1/R_0$ represents $R_e = 1$ and will achieve our goal

Thus, critical proportion we need to vaccinate in order to eradicate an infection of this type is

$p_c = 1 - s_c = 1 - 1/R_0$

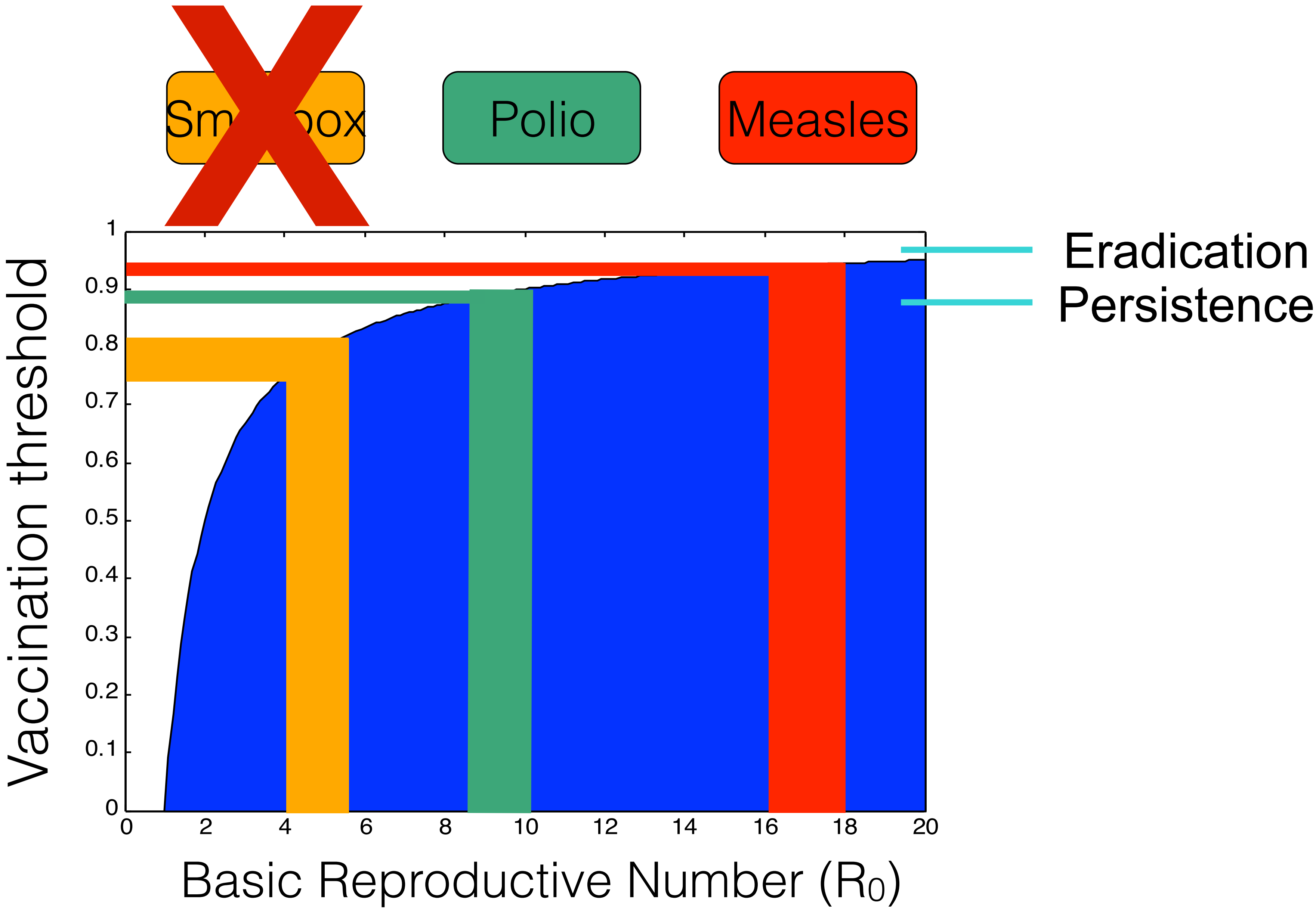


Eradication Criterion



$$p_c = 1 - \frac{1}{R_0}$$

Eradication Criterion



Vaccination

- *A priori* Goal:
  - Protect individual from infection
    - Individual immunity

- Unexpected bonus:
  - Protect population from an epidemic
    - “Herd immunity”

Herd immunity:

Protection of individual from infection via others in population gaining immunity

If neighbors have been vaccinated, probability of acquiring disease is lower

Don't need to vaccinate everyone to eradicate an infectious disease

Extent of vaccination effort determined by simple quantity, R_0

Recap

- Motivation: PDV outbreak in northern Europe
- Pathogen fitness & Basic Reproductive Ratio, R_0
- The anatomy of an epidemic
- Vaccination & Herd Immunity
- Control requires sustained vaccination

- Next:
  - Formulating a (mathematical) model for a morbillivirus
  - Density-dependent transmission
  - Invasion thresholds & extinction dynamics

Mathematical/computational models in disease ecology

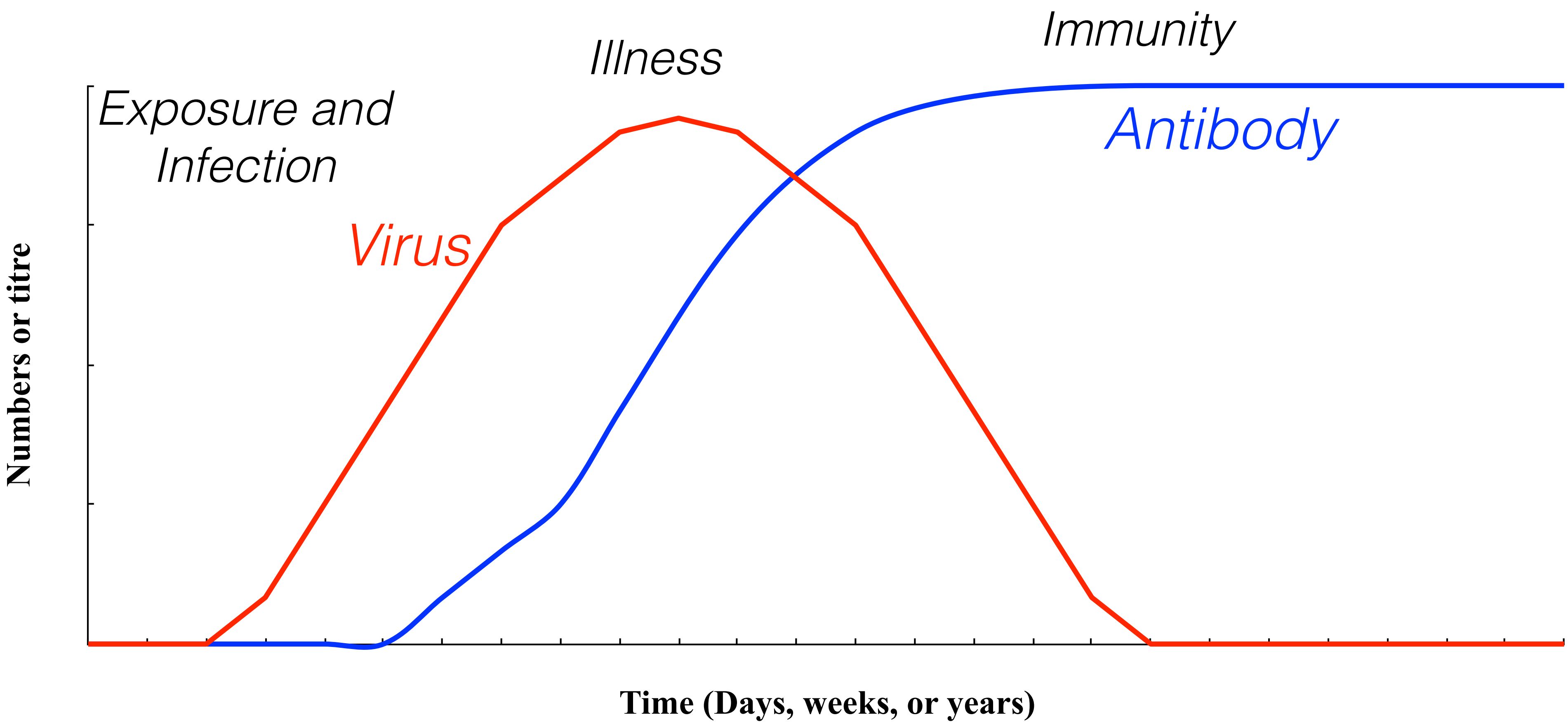
- **Integrate across scales:** translate how processes important at individual level (eg, transmission, recovery, death) influence population-level phenomena (eg, outbreaks, host population crashes)

Model ingredients:

- Assumptions: simplify world
- Variables: host infection status that change
- Parameters: measurable quantities that affect outcomes
- Predictions/results: Dynamics and equilibria

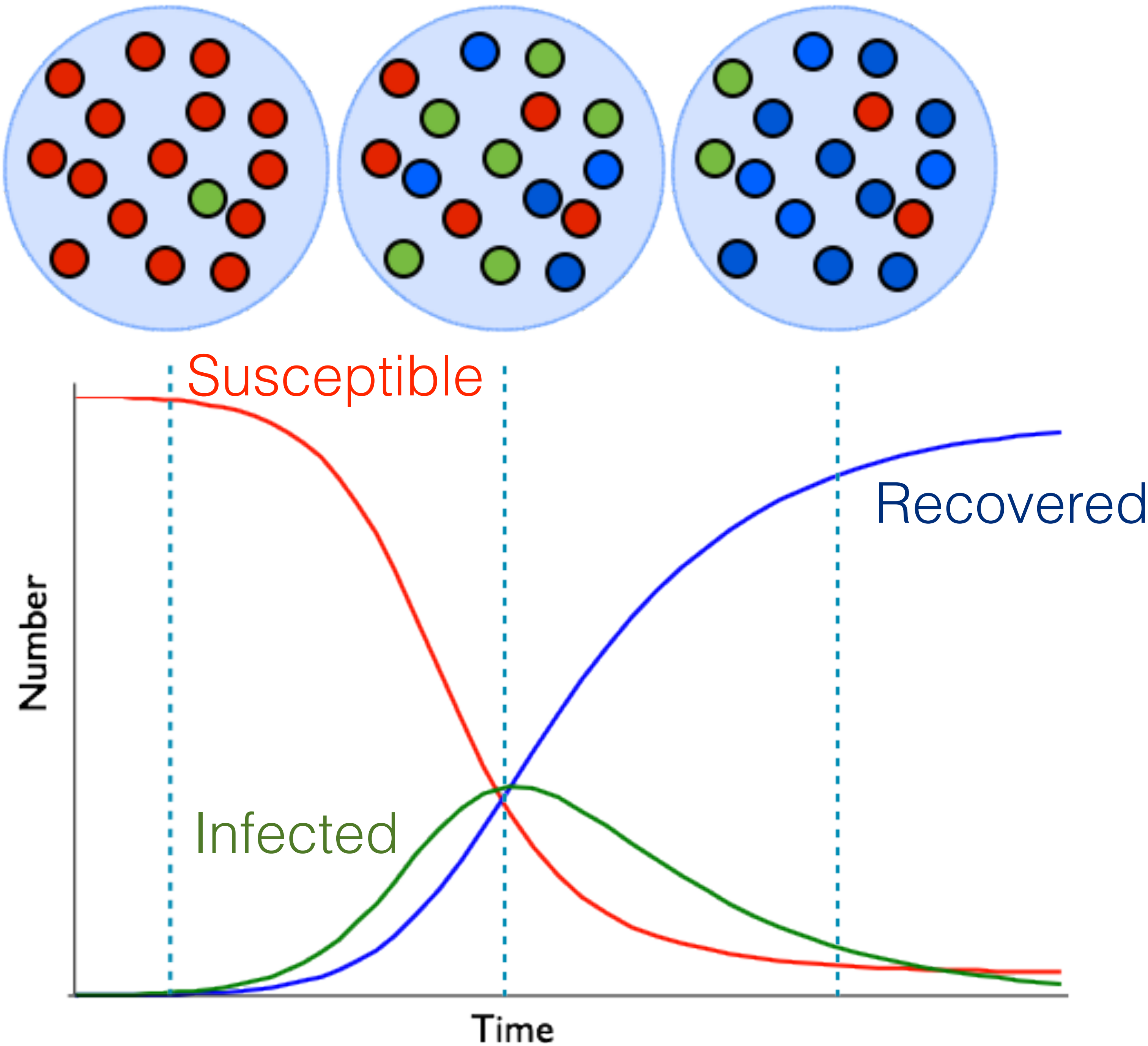
- Overall goal: Keep model as simple as possible, but no simpler

At individual level....

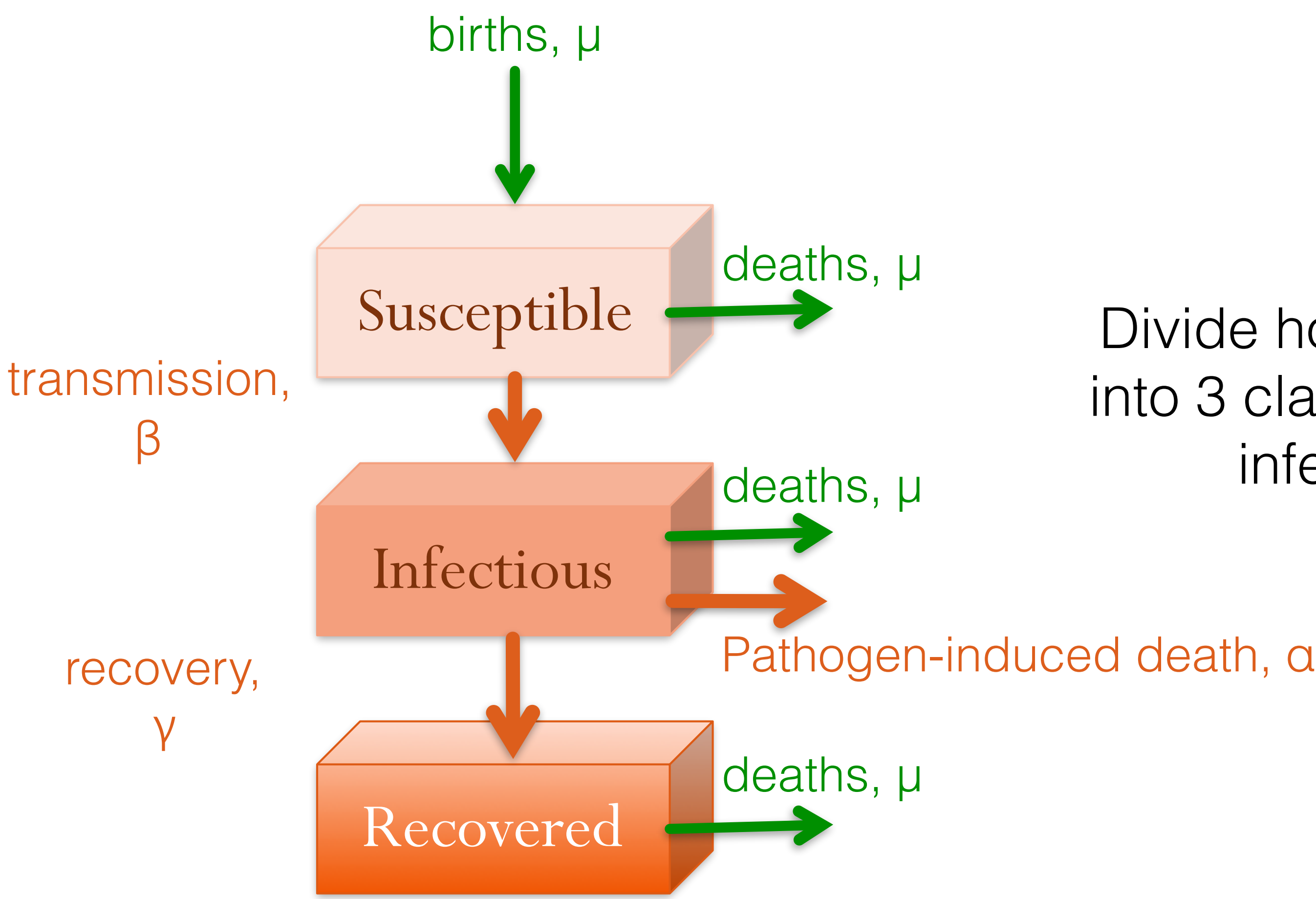


Susceptible	Infectious	Recovered
S	I	R
Years	Days	Many years

At population level….



3 host categories (for microparasite)



Divide host population (N) into 3 classes according to infection status

Important: $N = S + I + R$