Introduction to Infectious Disease Epidemiology

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Computational Biology, SDS 348
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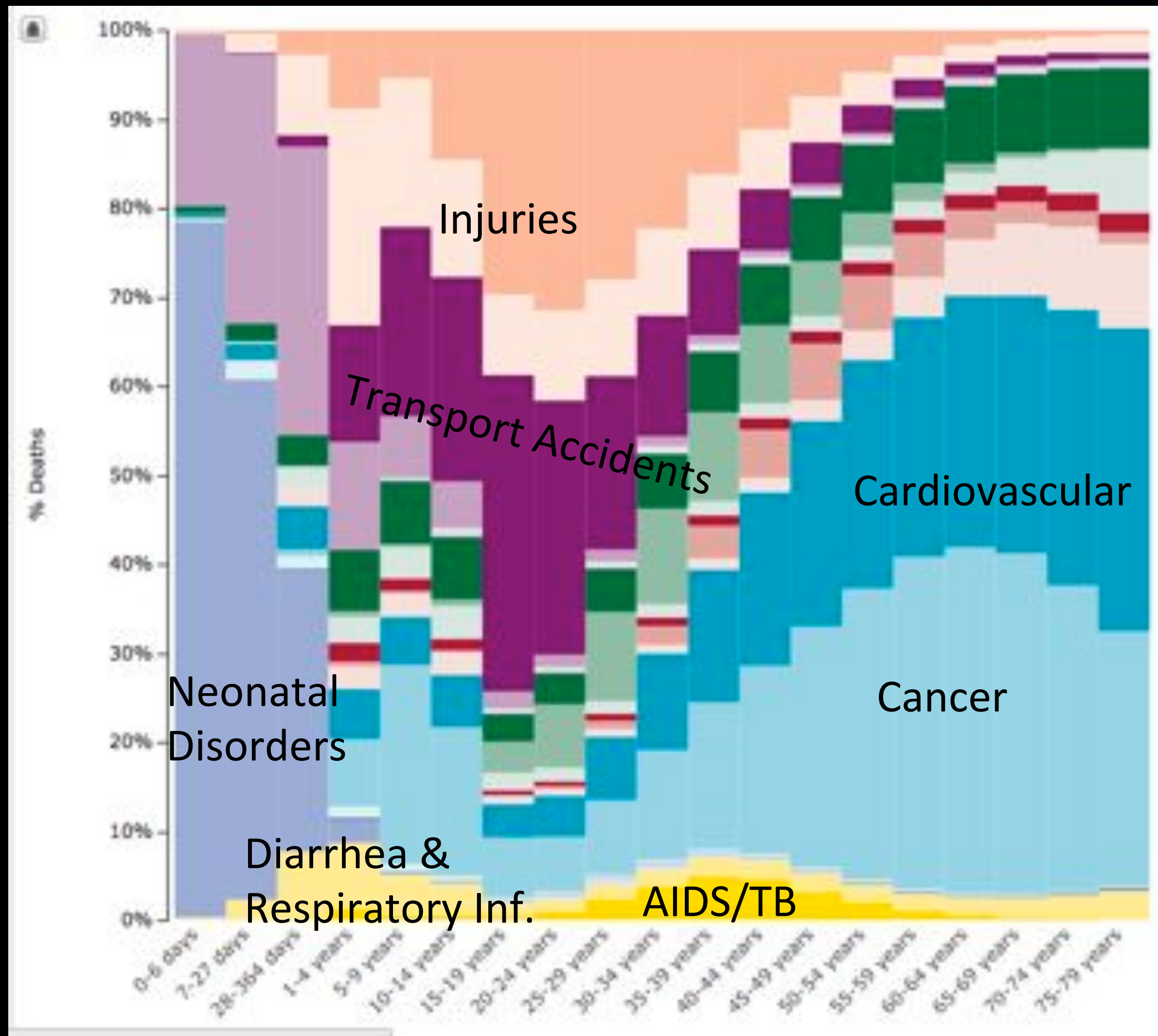
USA Burden of Mortality

% of Deaths

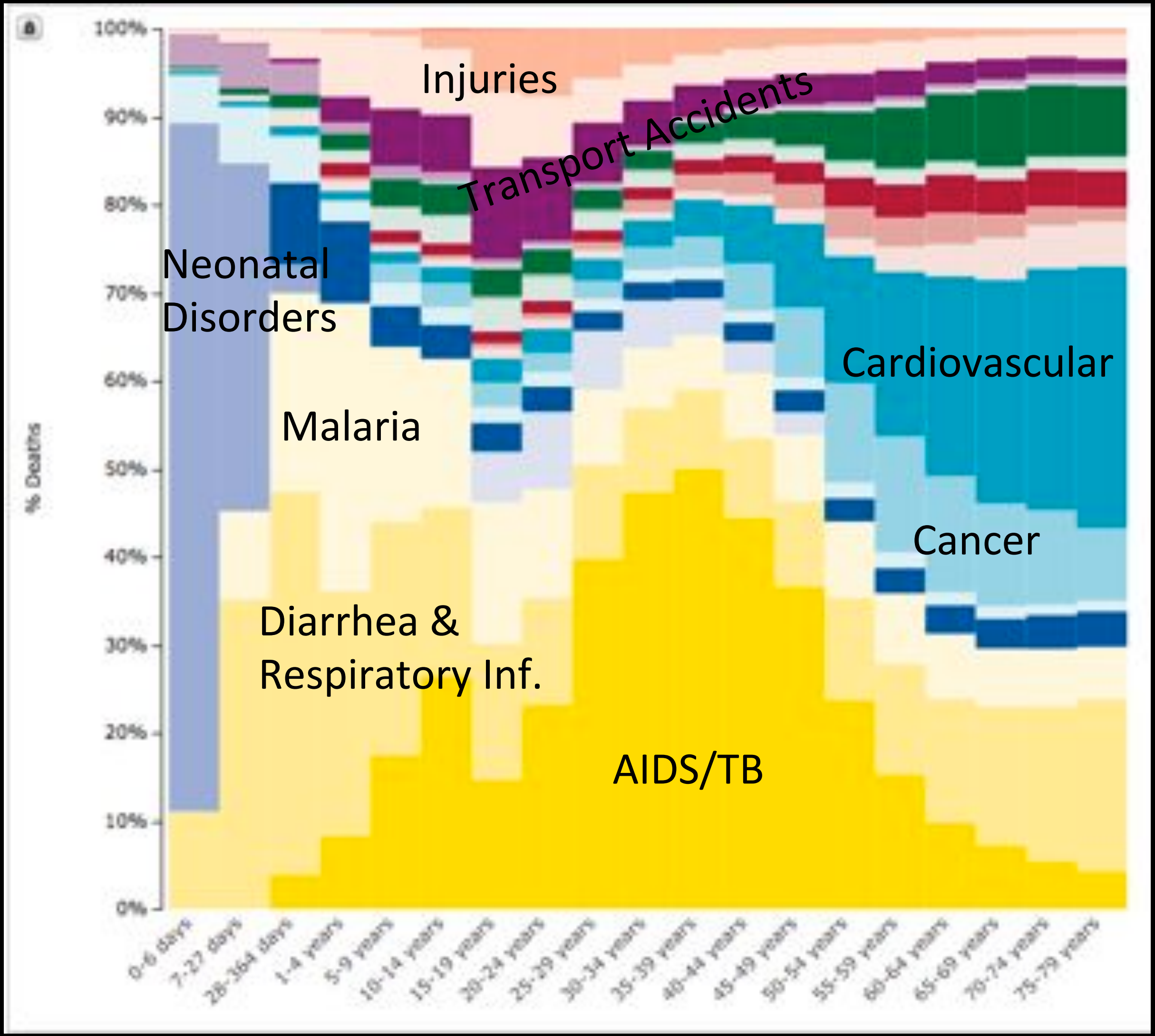


Age Group

Lozano et al.
(2012) *Lancet*

Sub-Saharan African Burden of Mortality

% of Deaths

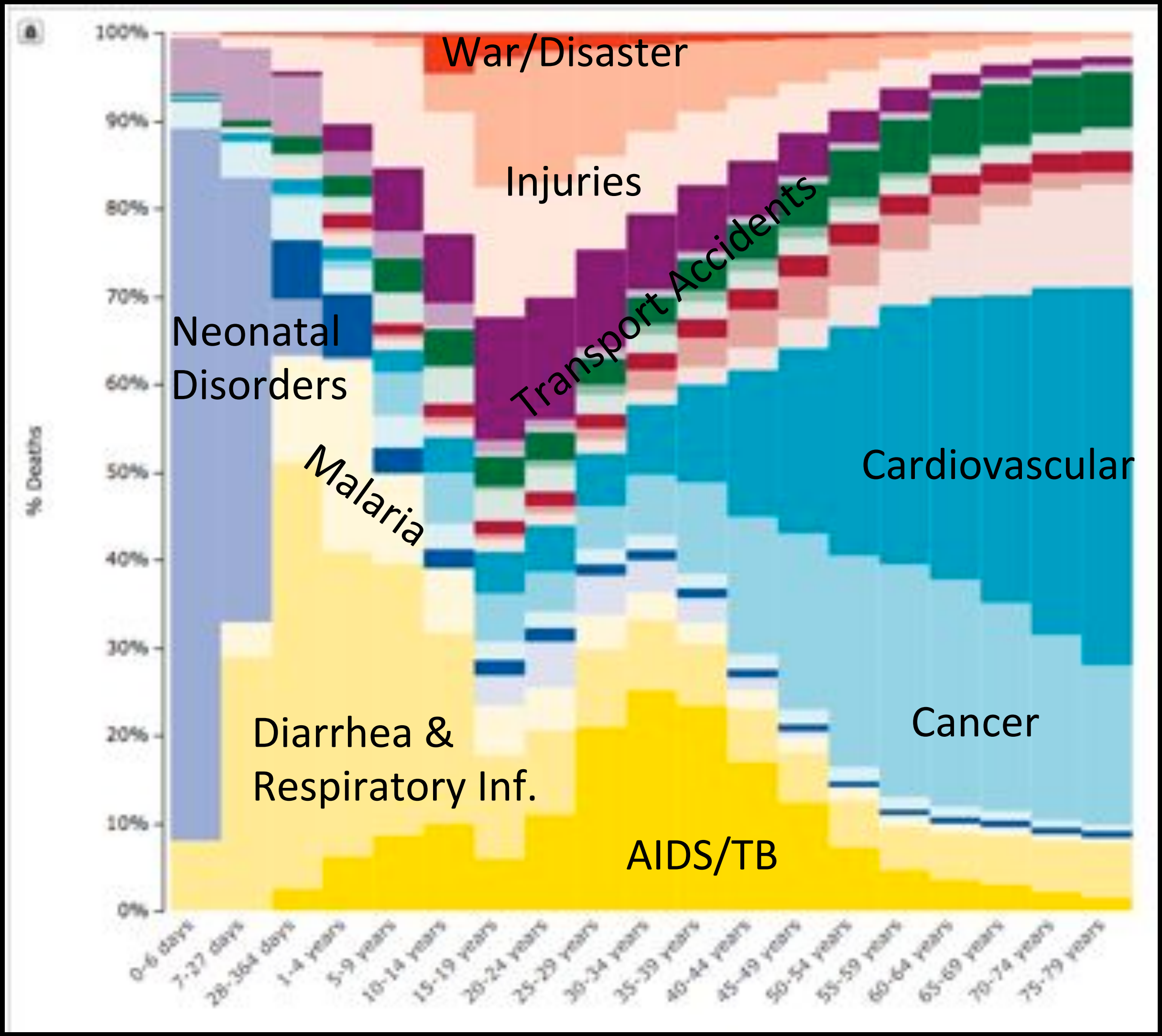


Age Group

Lozano et al. (2012) *Lancet*

Global Burden of Mortality

% of Deaths



Age Group

Lozano et al. (2012) *Lancet*

Outline

- Background and Definitions
- The Basic & Effective Reproduction Numbers
- SIR Models
- Transmission-Virulence Tradeoff
- Vector-Borne Diseases
- Zoonotic Diseases & HIV Emergence
- Treatment as Prevention and HIV Control
- Designing Ebola Vaccine Trials

Defining Epidemiology

"The study of the
distribution and determinants of
health related states and events
in populations,
and
the application of this study to
control health problems."

John M Last
Dictionary of Epidemiology

Infectious Disease Definitions

Pathogen: Microorganism that causes disease.
(virus, bacteria, parasite)

Ebola Virus

Tuberculosis Bacteria

HIV

Infectious Disease Definitions

Pathogen: Microorganism that causes disease. (virus, bacteria, parasite)

Infection: Invasion and multiplication of pathogen inside another organism.

Disease: Change from the normal physiological status of an organism that negatively affects its survival or reproduction.

R_0: The Basic Reproductive Number

Average # of secondary infections
an infected host produces in
a susceptible population.

R_0 = how many people each person infects before they recover/die

R_0: The Basic Reproductive Number

Average # of secondary infections
an infected host produces in
a susceptible population.

R_0 = (infectious contact rate) × (duration of infectiousness)

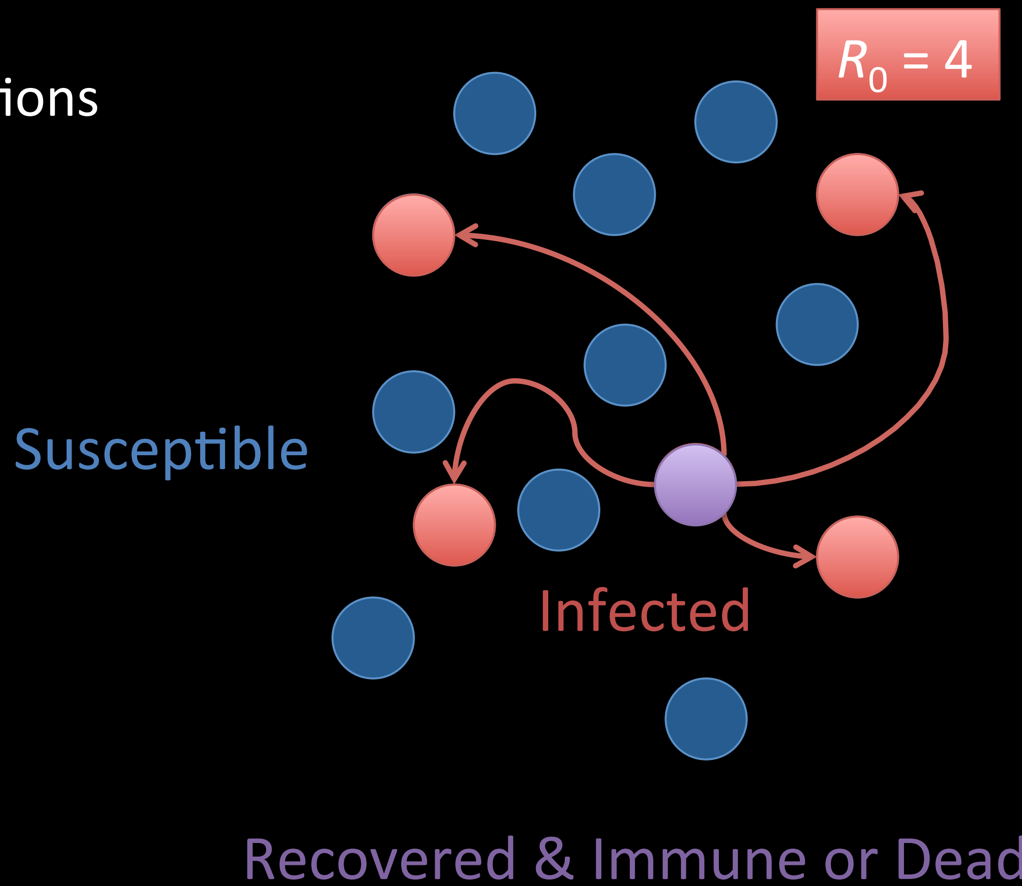
R_0 = (sneezing on someone rate)
× (probability being sneezed on leads to infection)
× (3 days sneezing)

R_0: The Basic Reproductive Number

Average # of secondary infections an infected host produces in a susceptible population.

If $R_0 < 1$, disease dies out

If $R_0 > 1$, disease persists



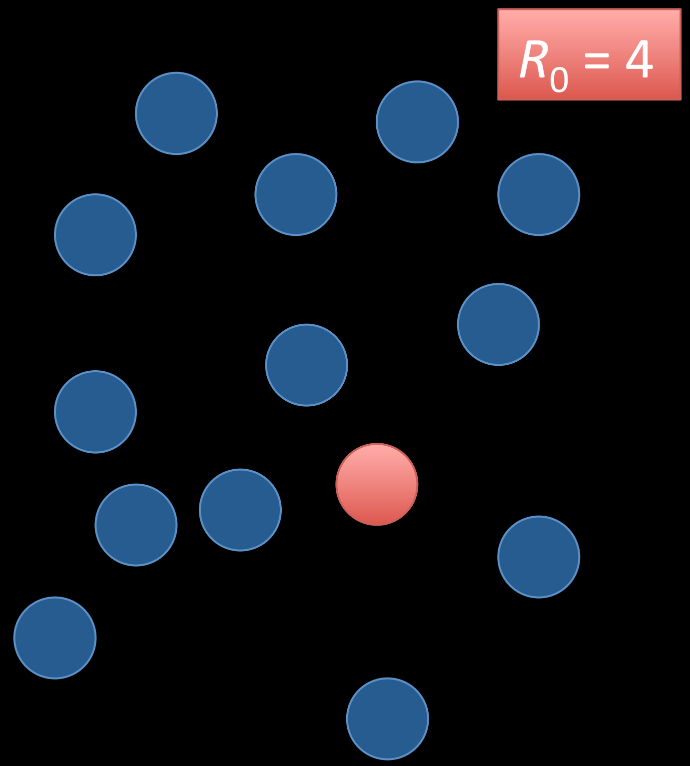
Which spreads faster:

Influenza (R_0 = 1.5) or HIV (R_0 = 5)?

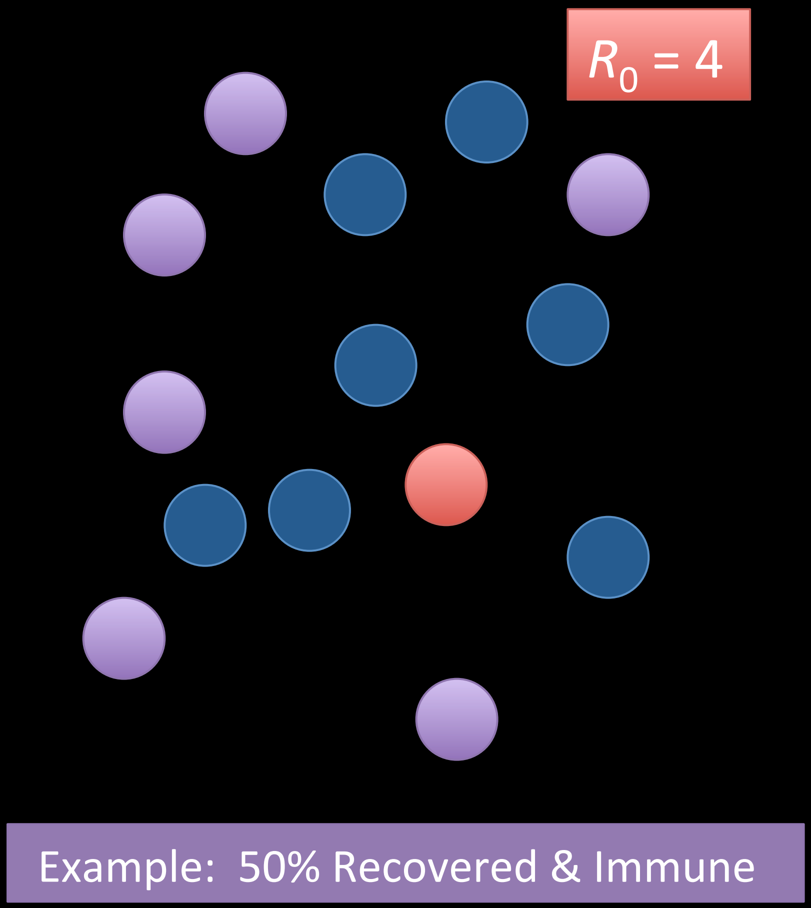
Generation Interval: Average time between infection & infecting someone else.

R_0 & generation interval both determine epidemic growth rate.

R_{eff}: The Effective Reproductive Number

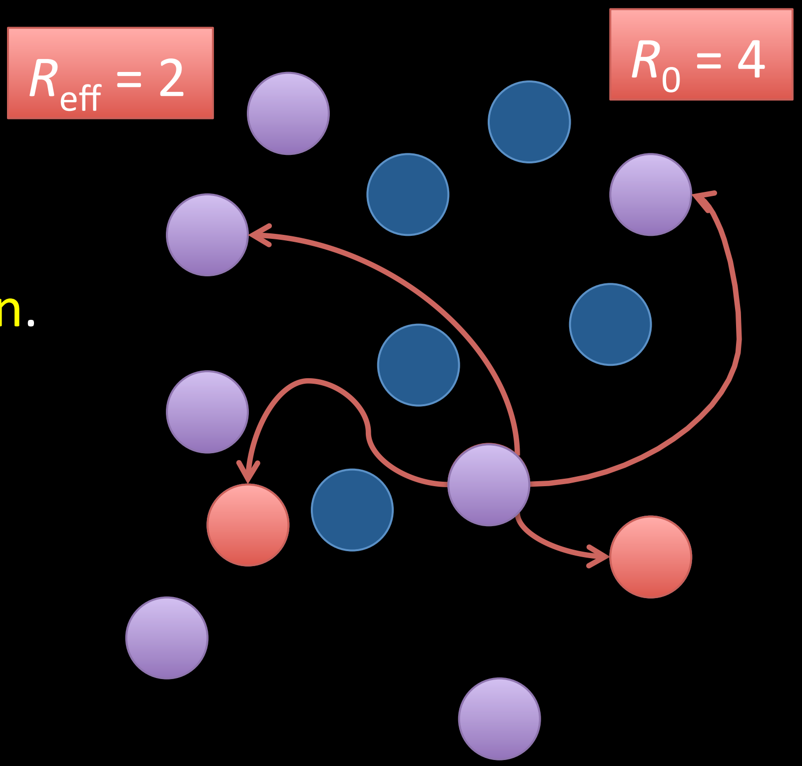


R_{eff}: The Effective Reproductive Number



R_{eff}: The Effective Reproductive Number

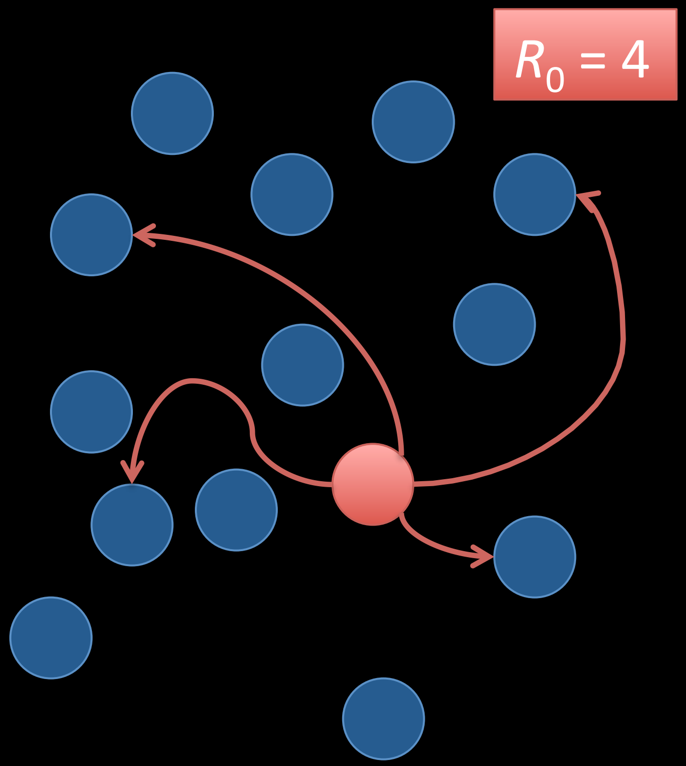
- The average # of secondary infections that an infected host produces in an only partially susceptible population.



Example: 50% Recovered & Immune

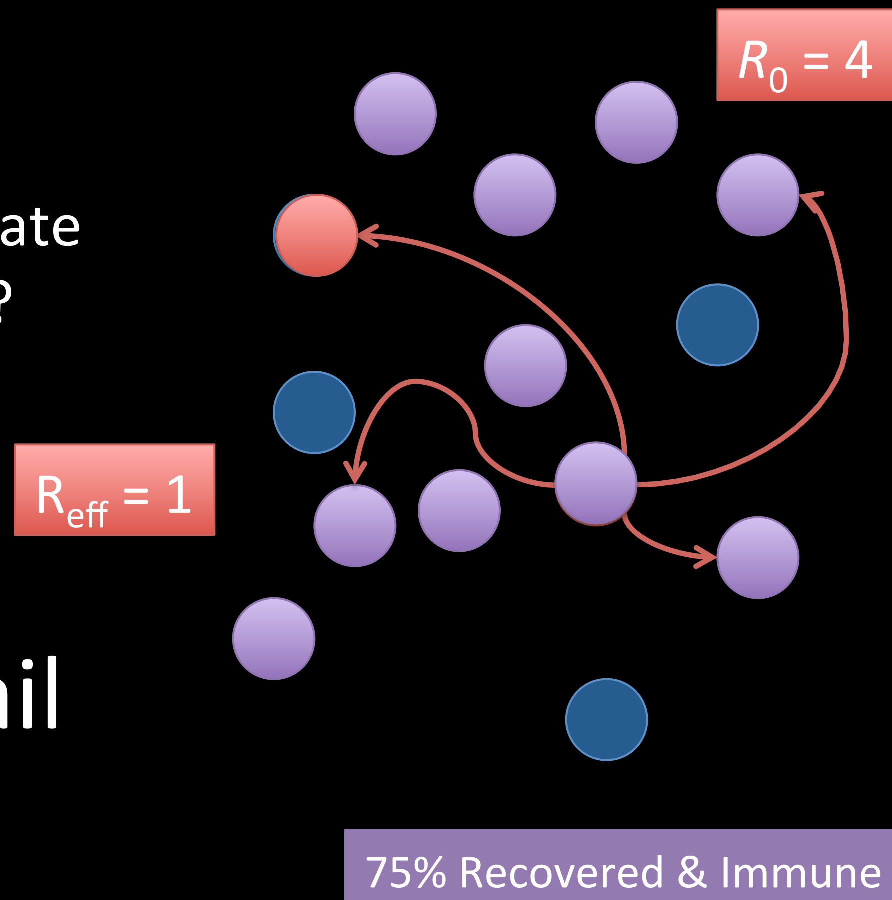
Proportion to Vaccinate

- So what % of the population must be vaccinated to eliminate transmission in a population?



Proportion to Vaccinate

- So what % of the population must be vaccinated to eliminate transmission in a population?



3/4 infections fail

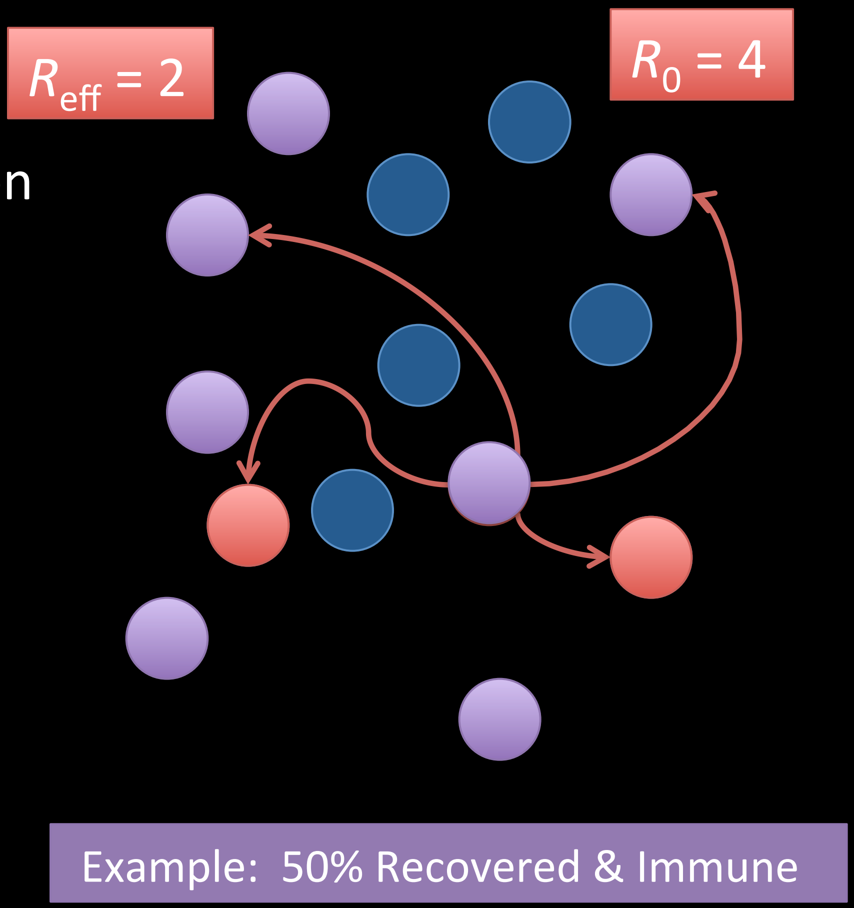
Herd Immunity

Diseases can be eliminated without vaccinating everyone!

Other Interventions Also Affect R_{eff}

If half of the population is immune,

by how much must we cut the infection rate to eliminate the disease?

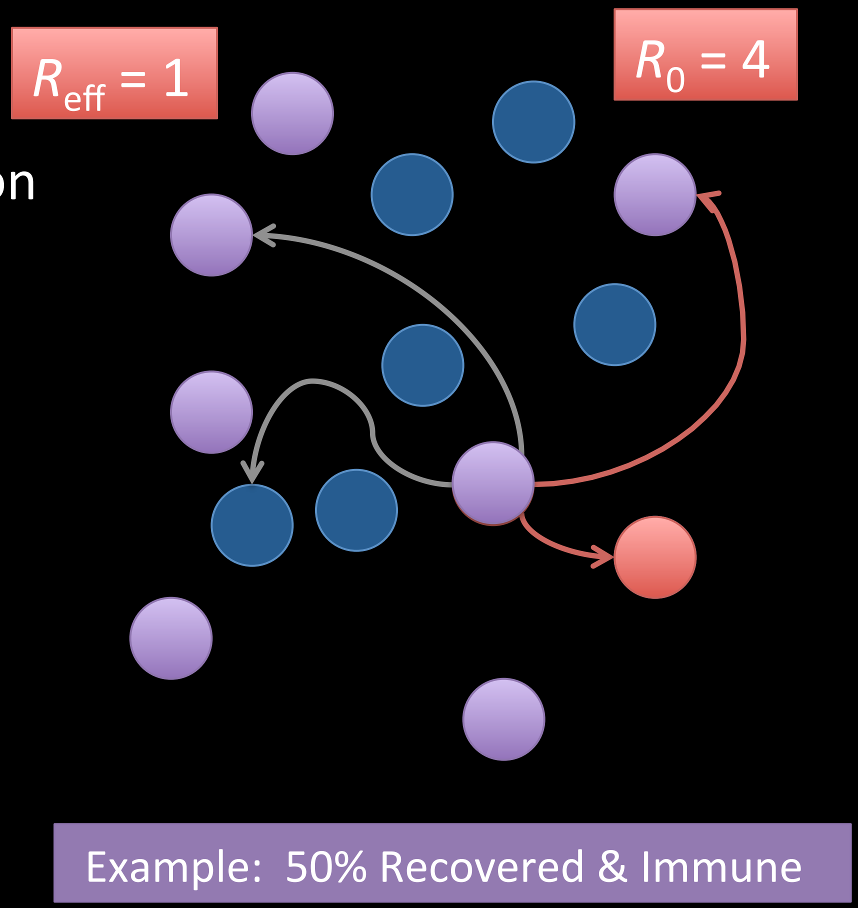


Other Interventions Also Affect R_{eff}

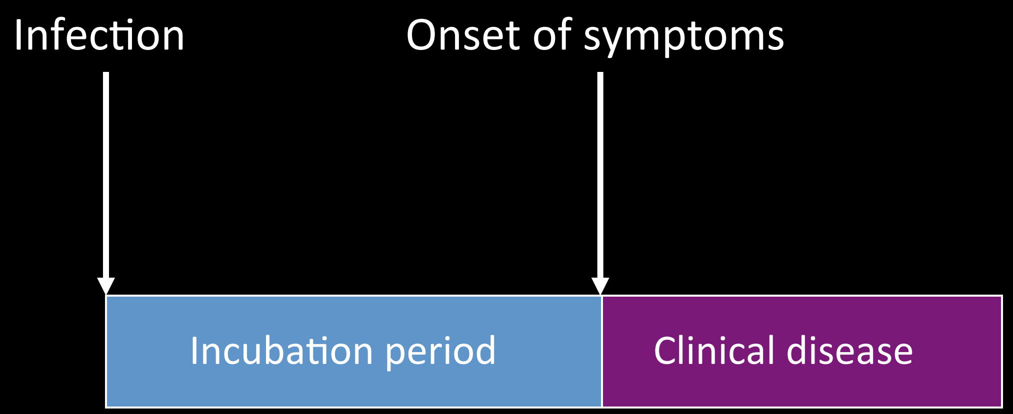
If half of the population is immune,

by how much must we cut the infection rate to eliminate the disease?

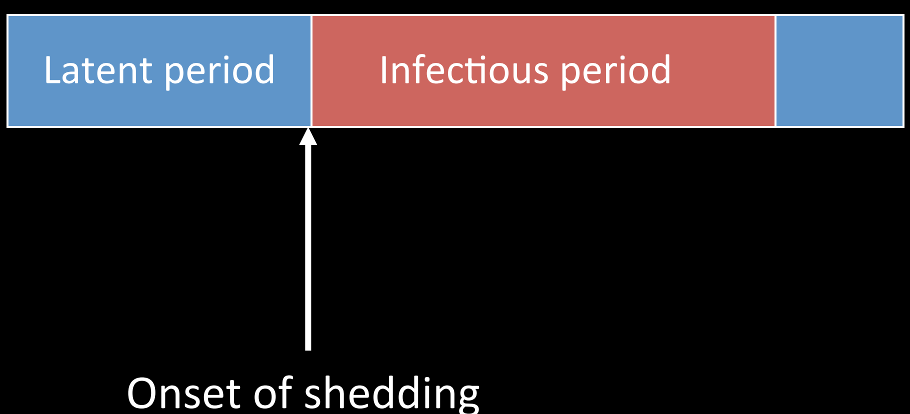
Cut transmission by more than 50%



Natural History of Infection

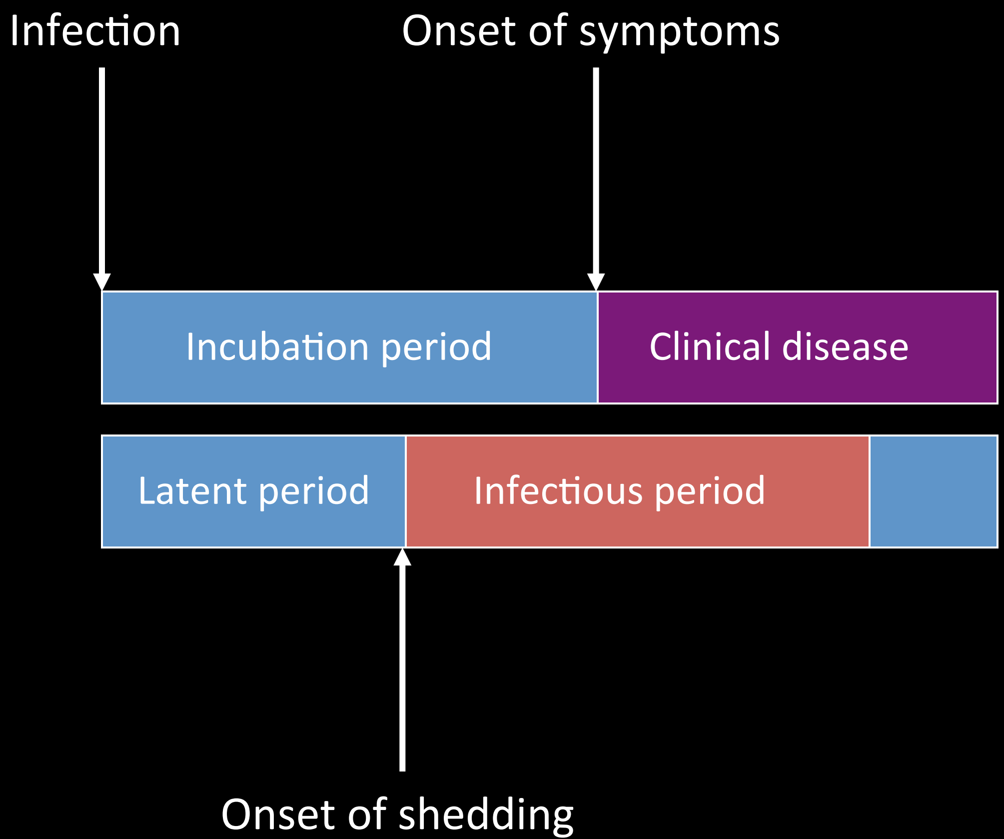


Natural History of Infection



Natural History of Infection

Childhood vaccine-preventable diseases = acute & immunizing



<u>Acute</u>

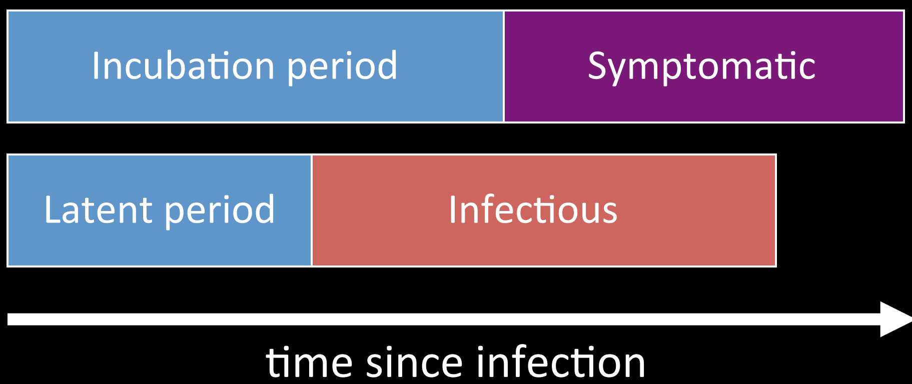
Infection time course
<<<
host lifespan

<u>Immunizing</u>

infection → antibody production

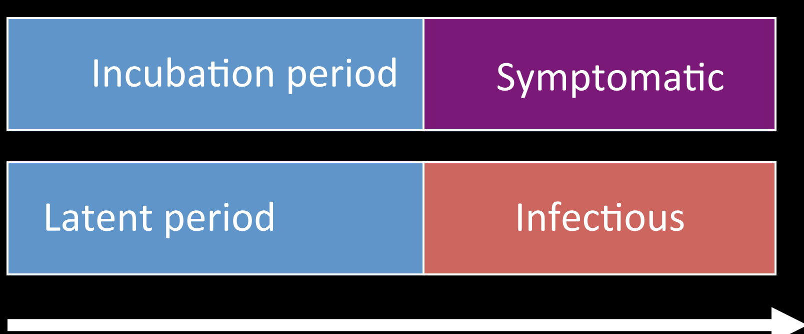
prevents future infection

Timeline of Infection



infectiousness precedes disease
control = difficult.

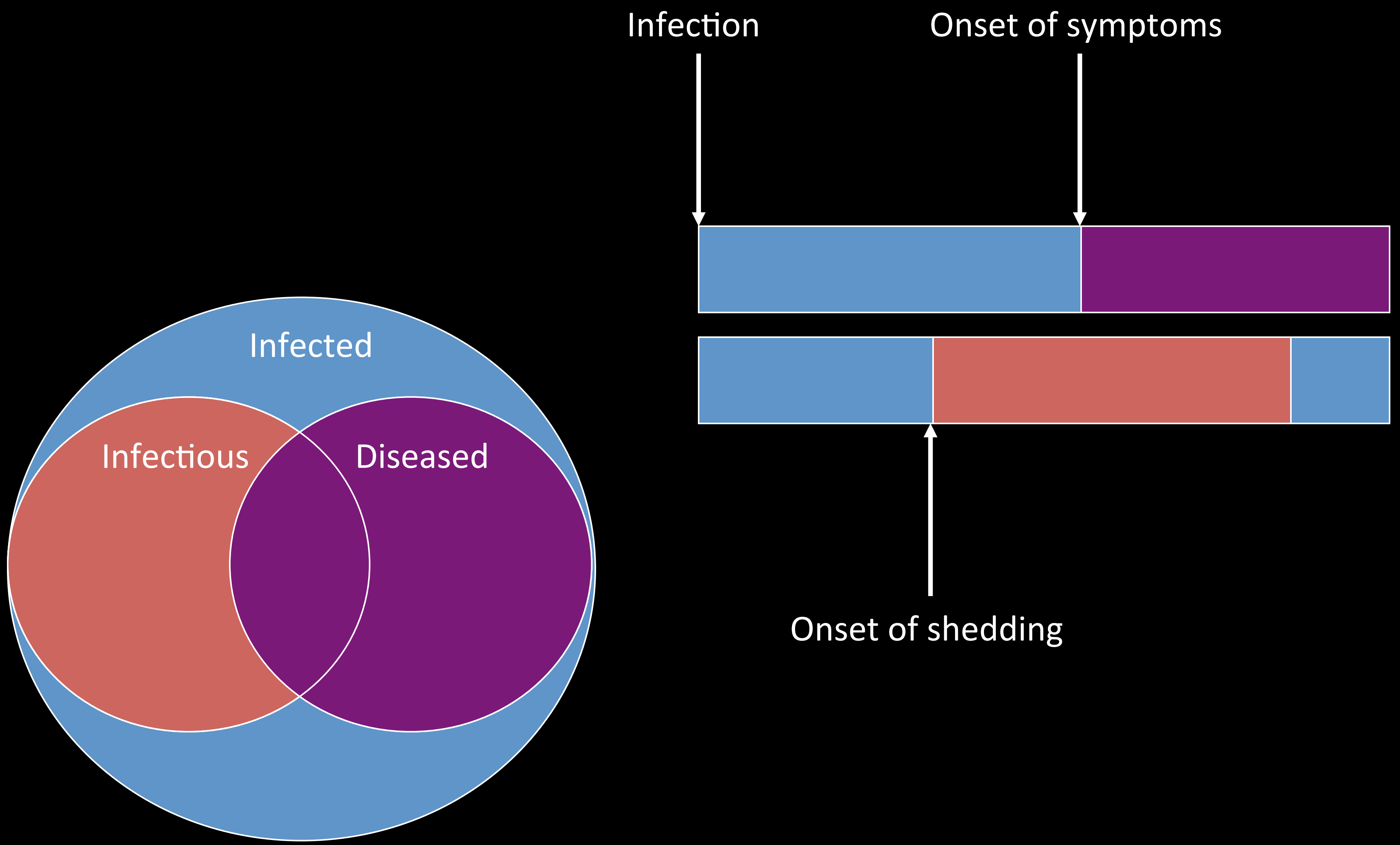
(HIV, influenza)



timing of
symptoms and infectiousness match
control = easier

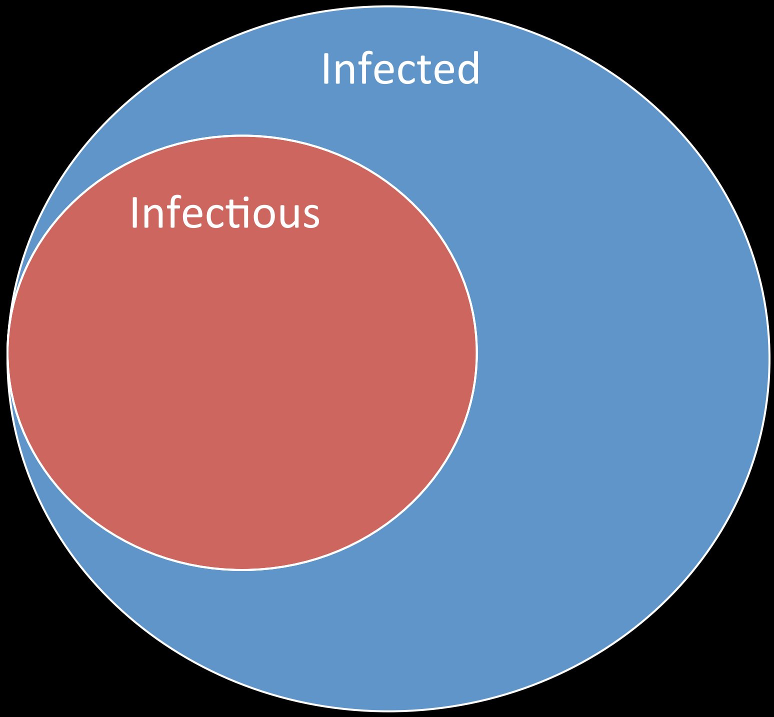
(SARS, Ebola)

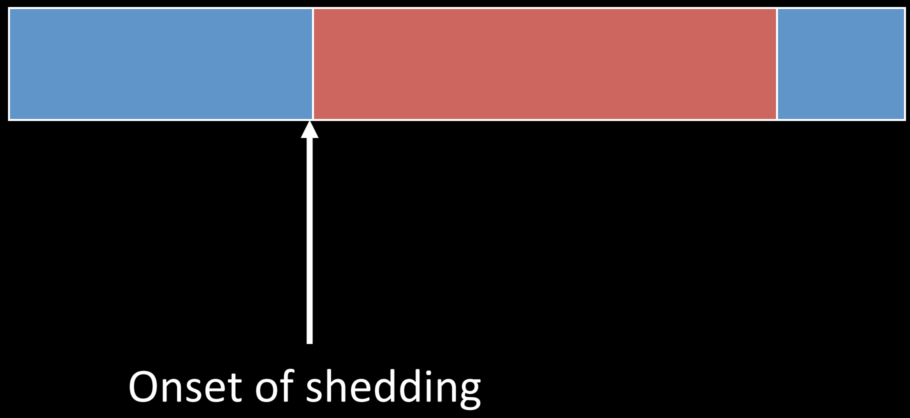
A simple view of the world



A simpler view of the world

Don’t worry about symptoms and disease!

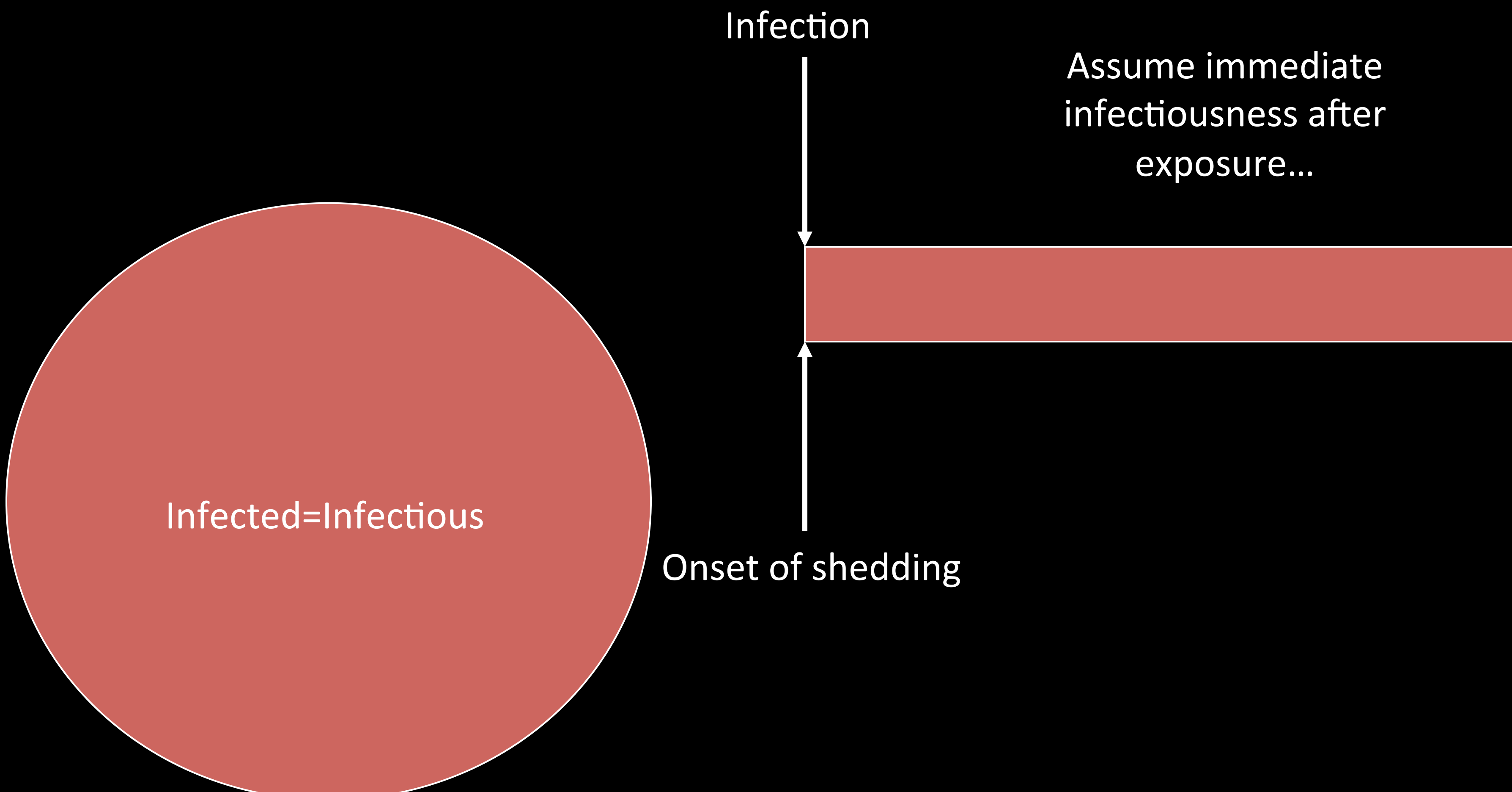




An extremely simple view of the world

Don’t worry about symptoms and disease!

Assume immediate infectiousness after exposure…



An extremely simple view of the world

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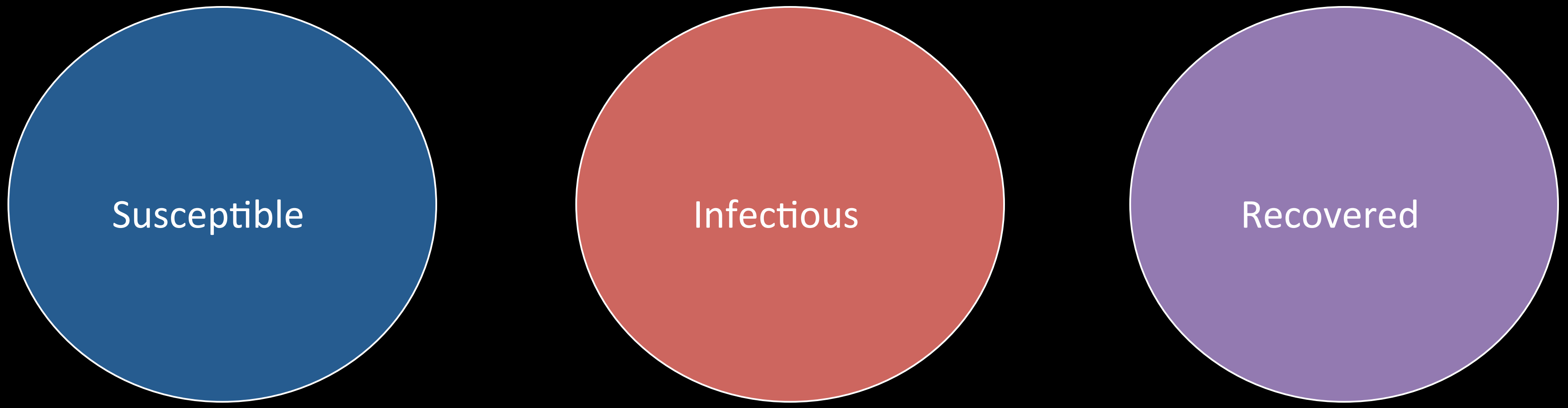

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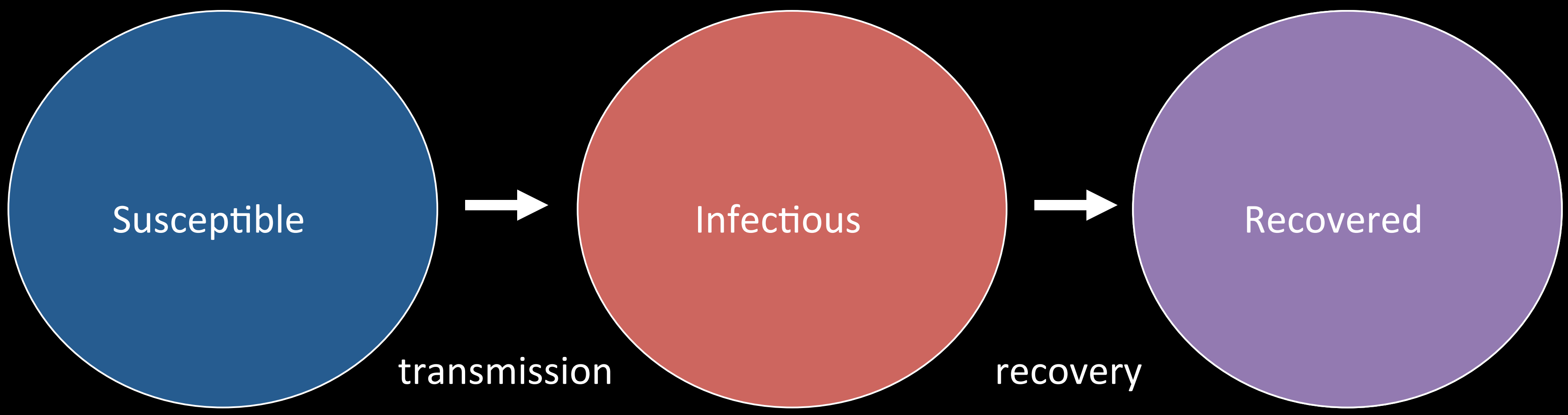
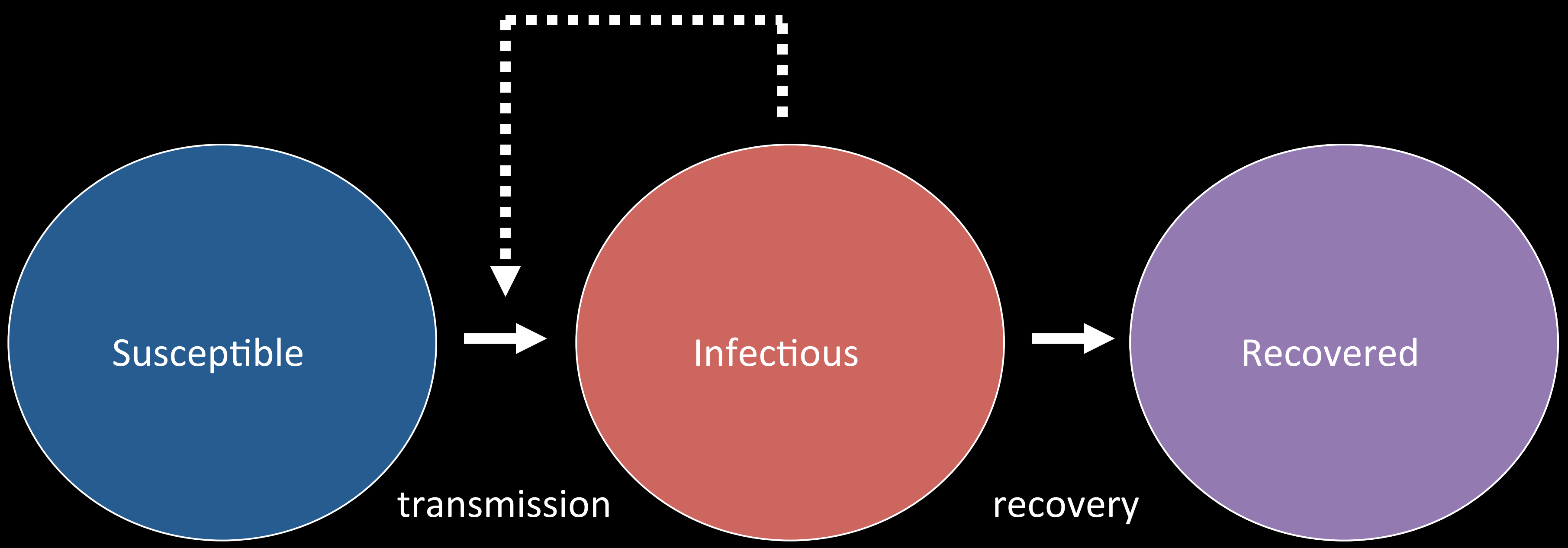
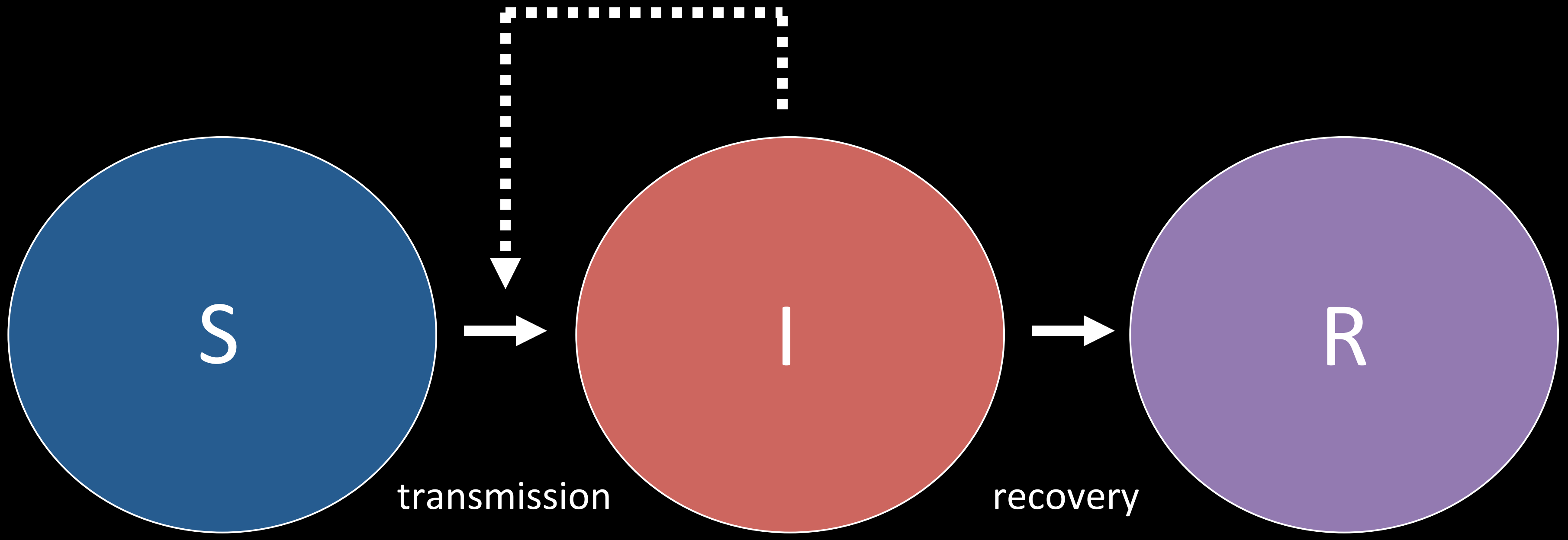


Susceptible-Infected-Recovered Model

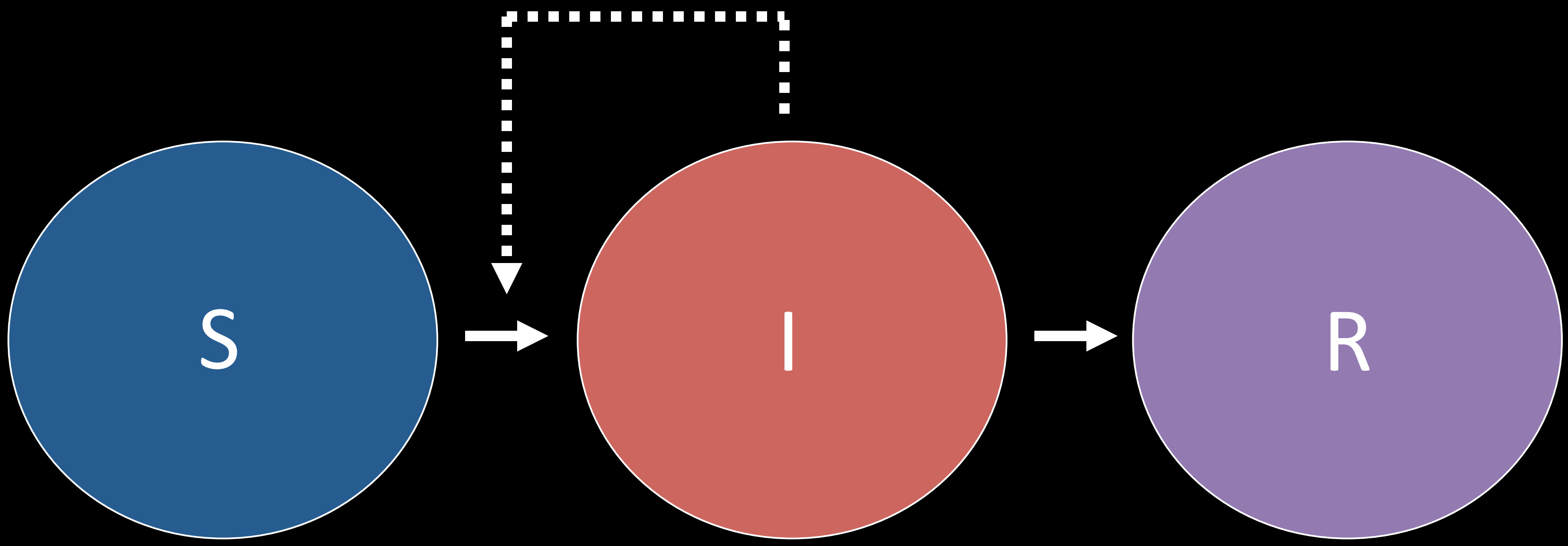


The rate at which susceptible individuals become infected depends on how many infectious people are in the population

SIR Model

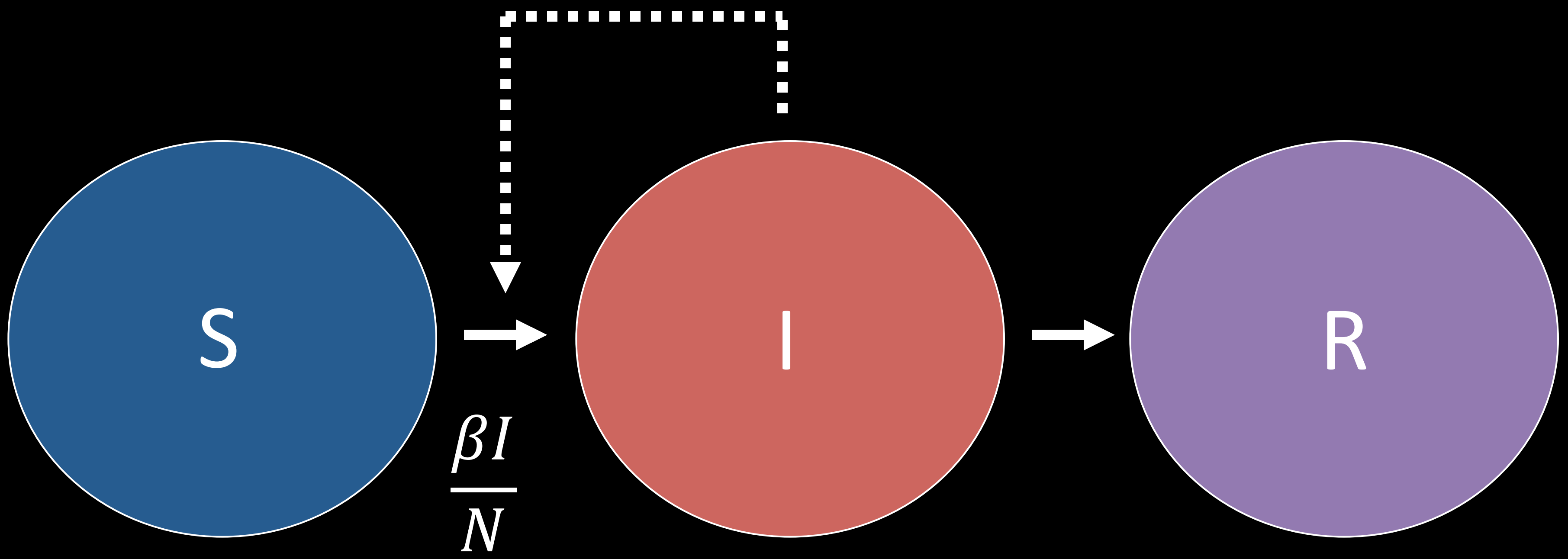


SIR Model



We can use equations to describe the rate at which individuals flow between states

SIR Model

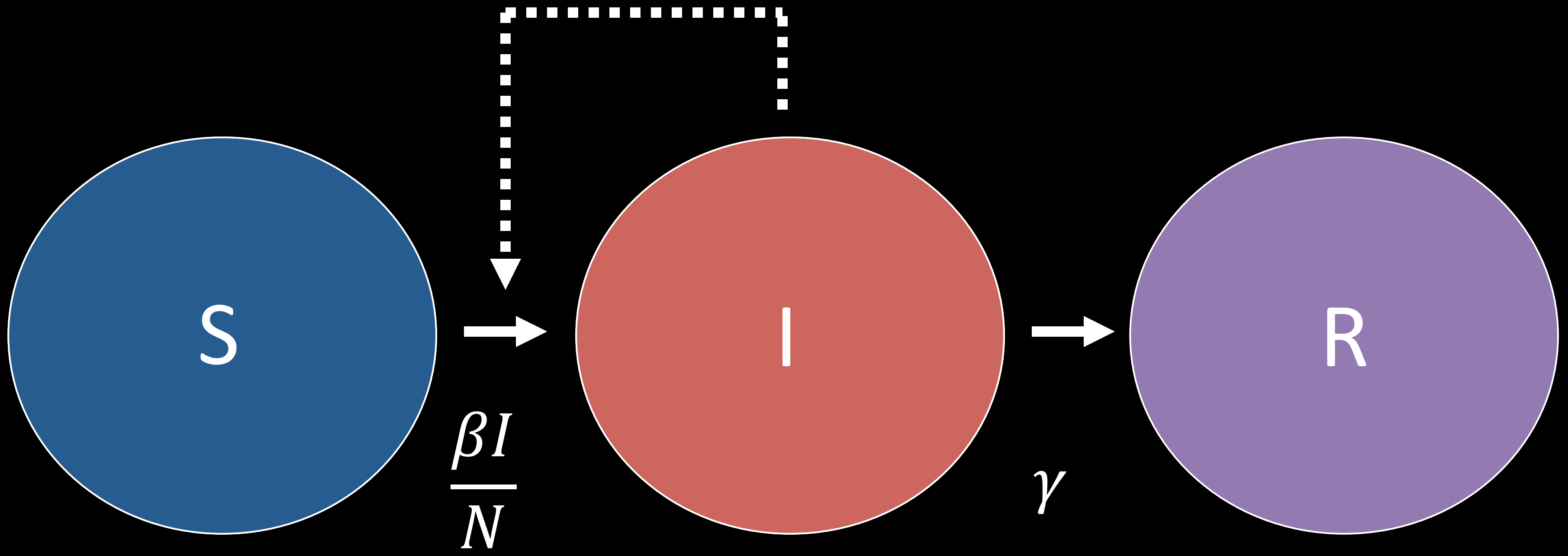


β = infectious contact rate

(for example, sneezing, sex, touch, etc… depending on the pathogen)

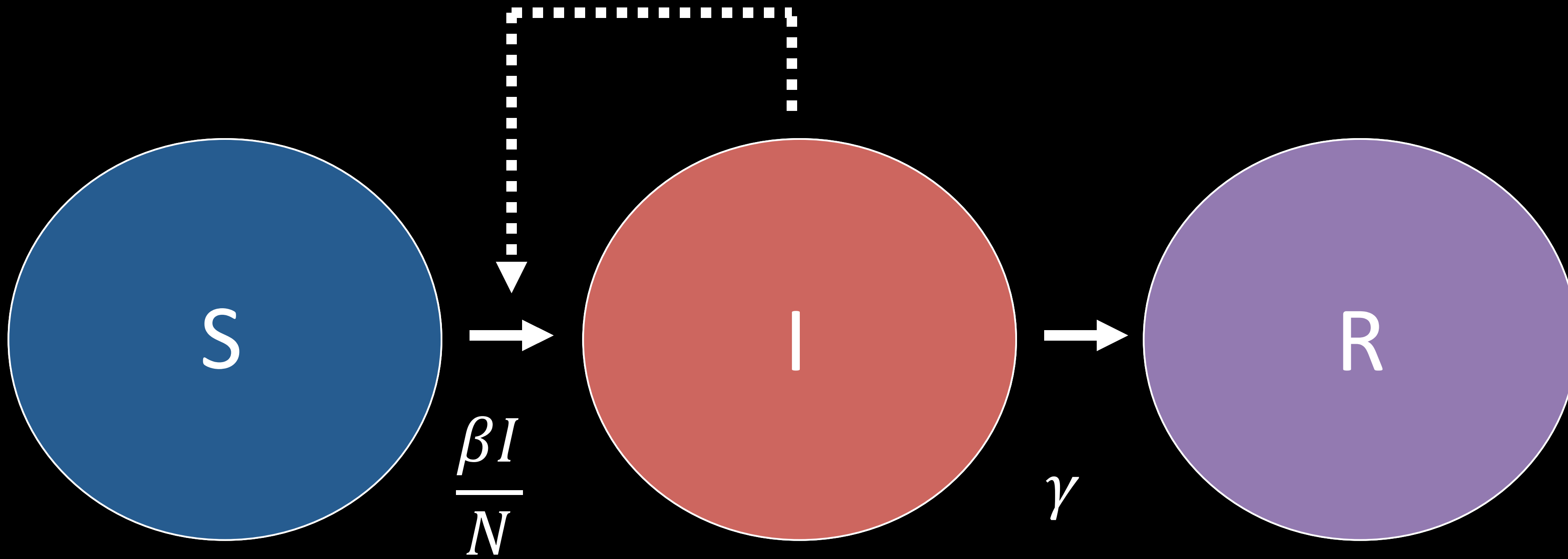
$\frac{I}{N}$ proportion of contacts that are with an infectious individual

SIR Model



Recovery rate tells us how long people stay infectious

SIR Model

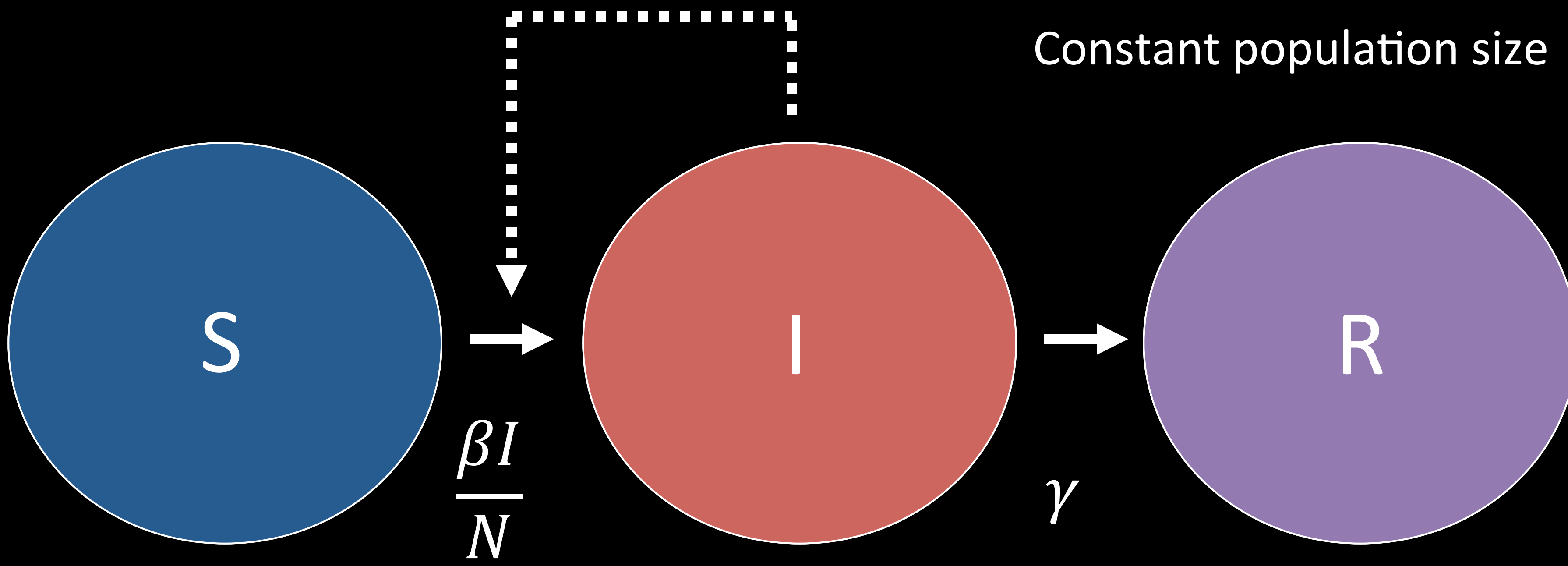


$$\frac{dS}{dt} = -\frac{\beta SI}{N} \qquad \frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I \qquad \frac{dR}{dt} = \gamma I$$

SIR Model

$$N = S + I + R$$

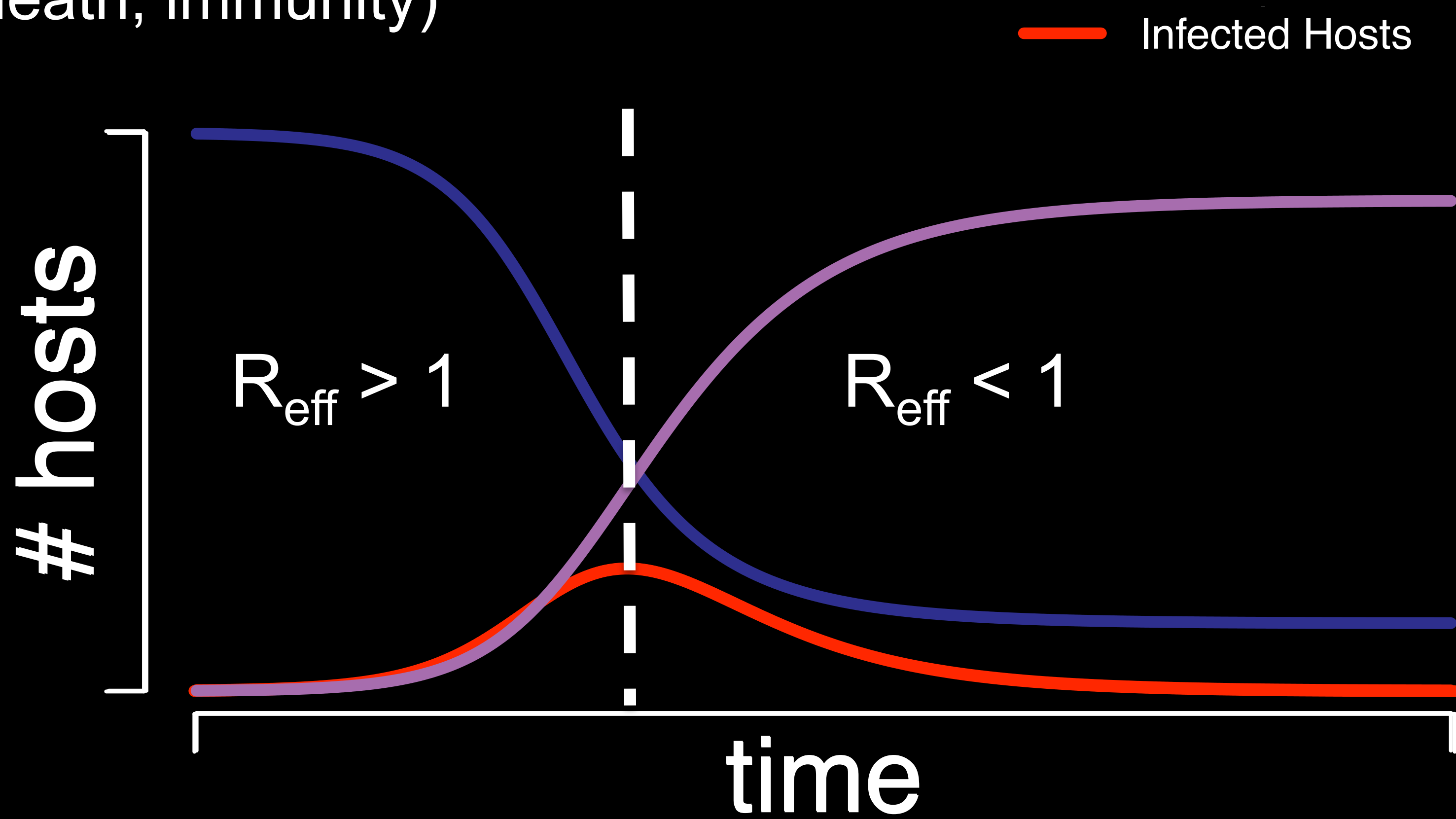
Constant population size



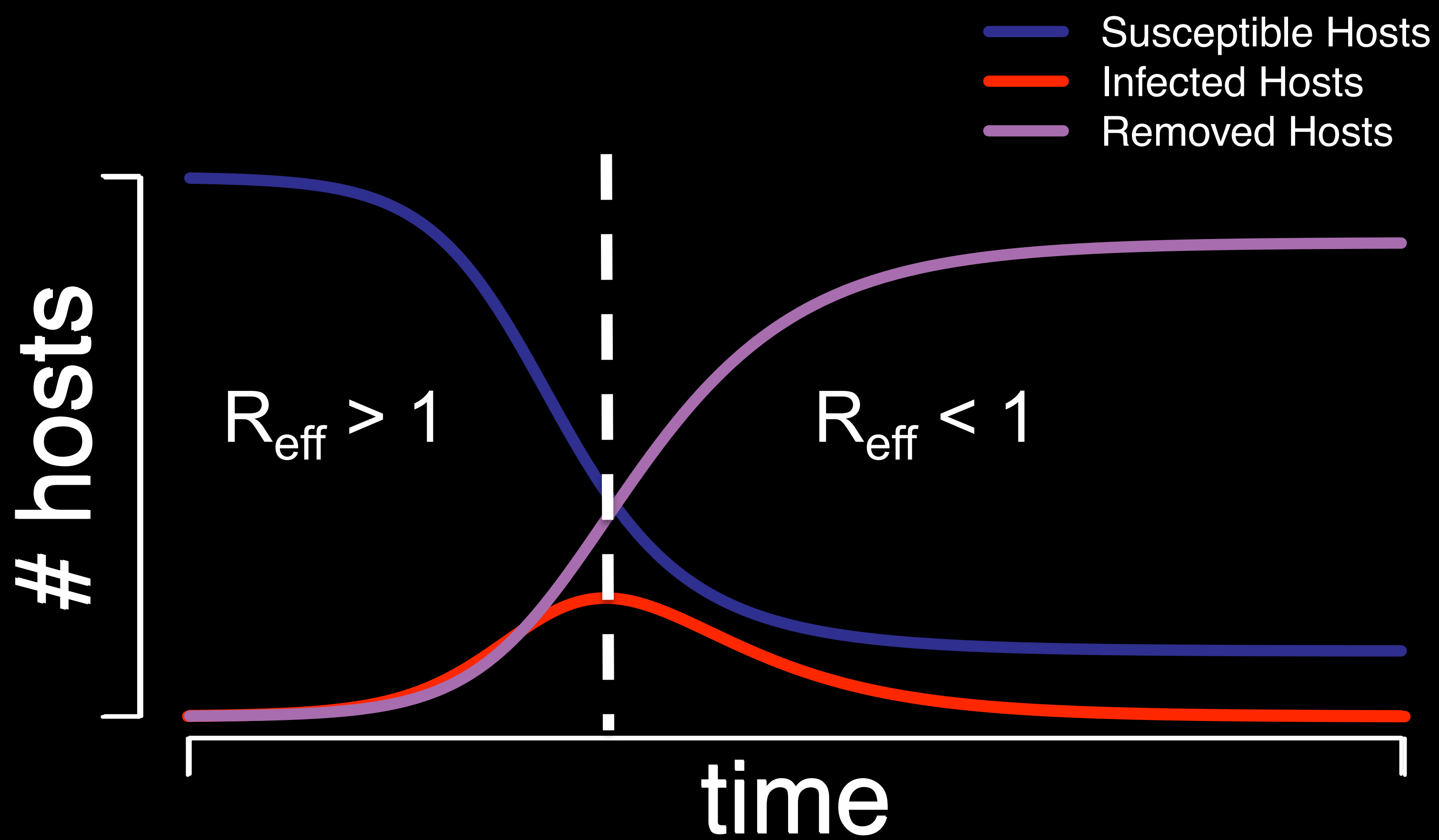
$$\frac{dS}{dt} = -\frac{\beta SI}{N} \qquad \frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I \qquad \frac{dR}{dt} = \gamma I$$

Why do epidemics peak?

Susceptible population declines over course of an outbreak (death, immunity)

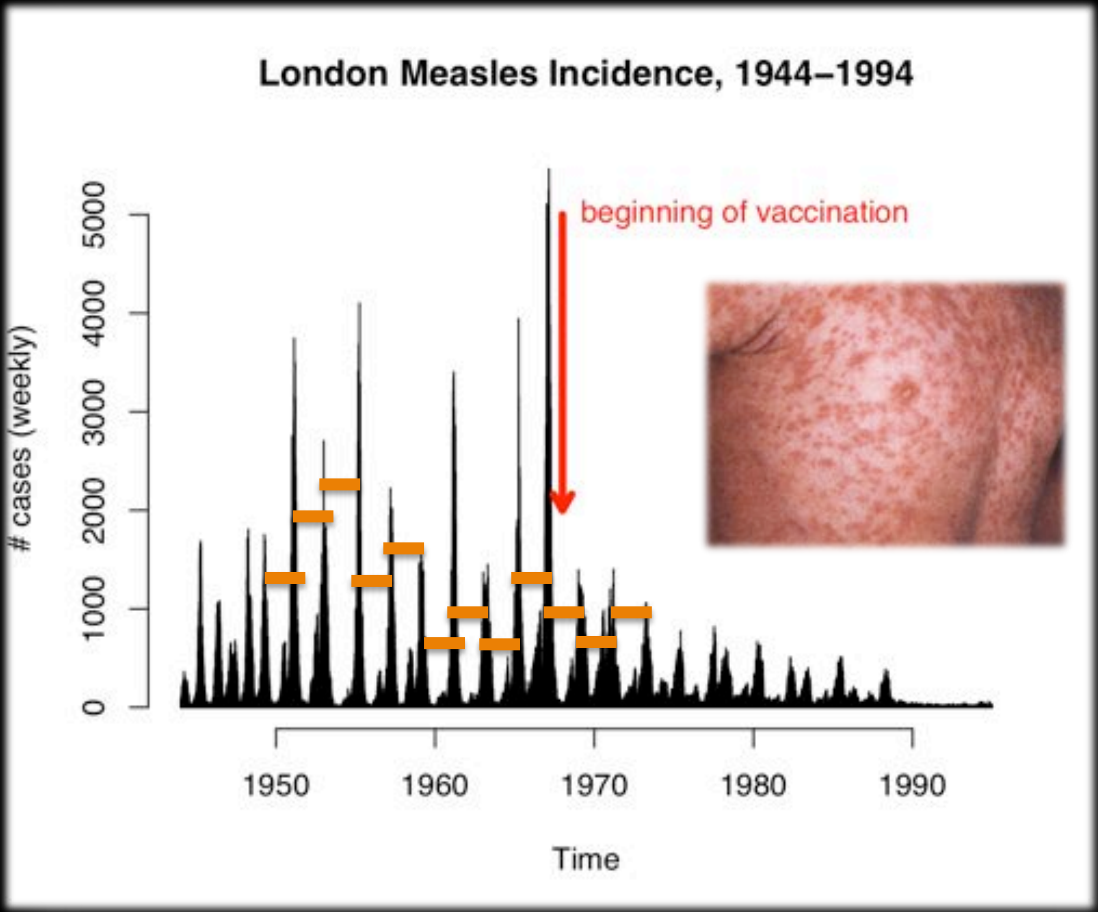


Single Peak Epidemic



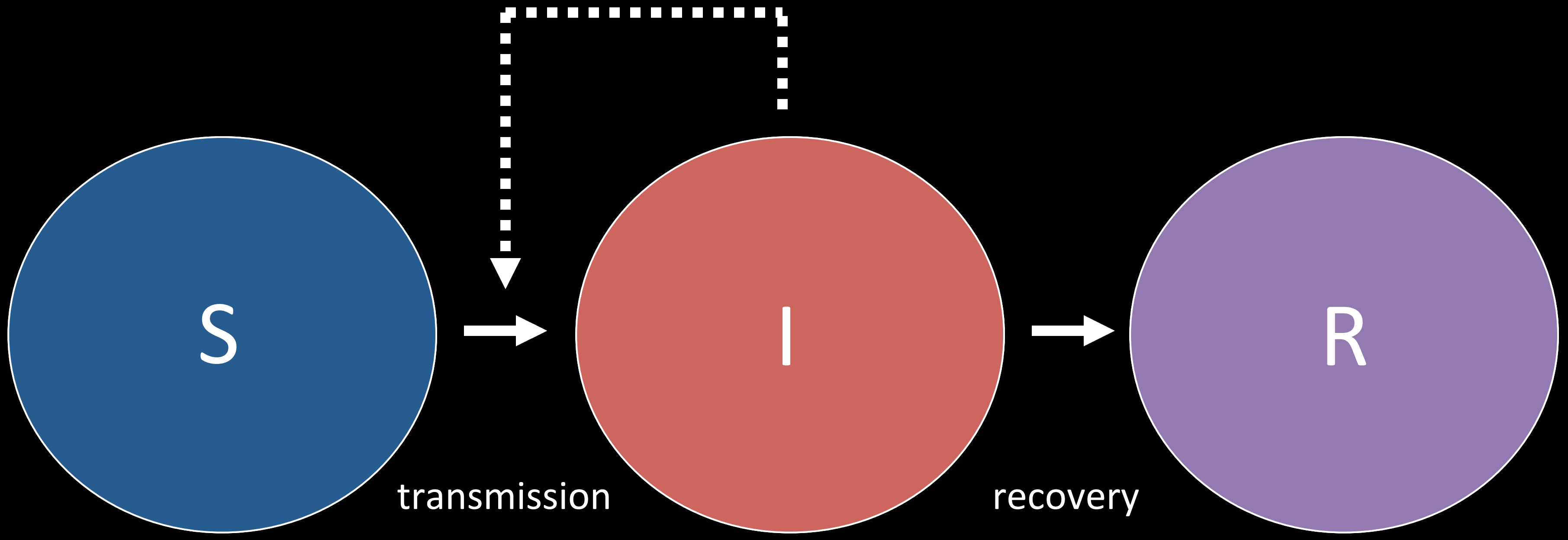
What accounts for epidemic cycles?

2 year cycles! WHY?

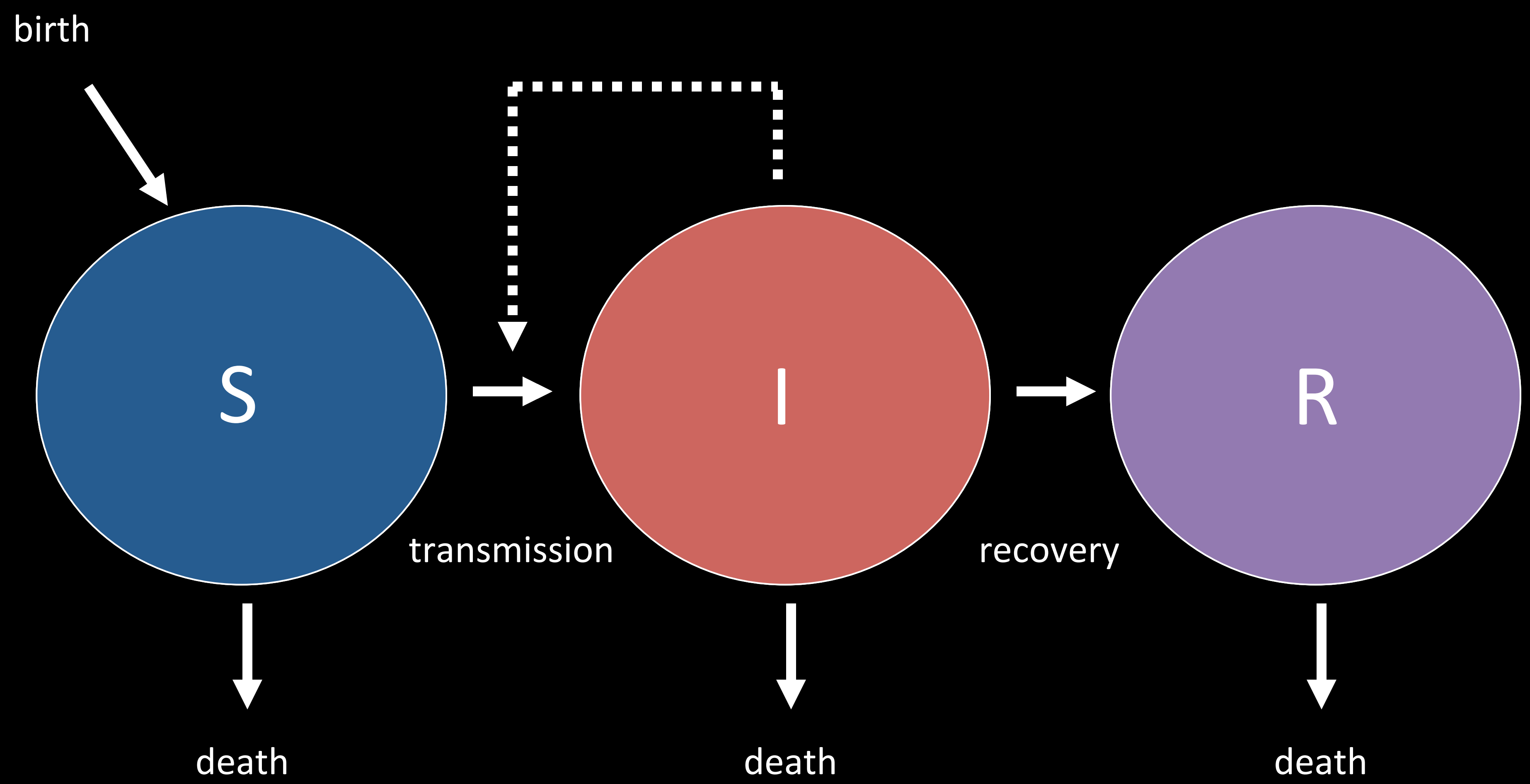


Earn et al. 2000. *Science.*

SIR Model



SIR Model with Birth & Death



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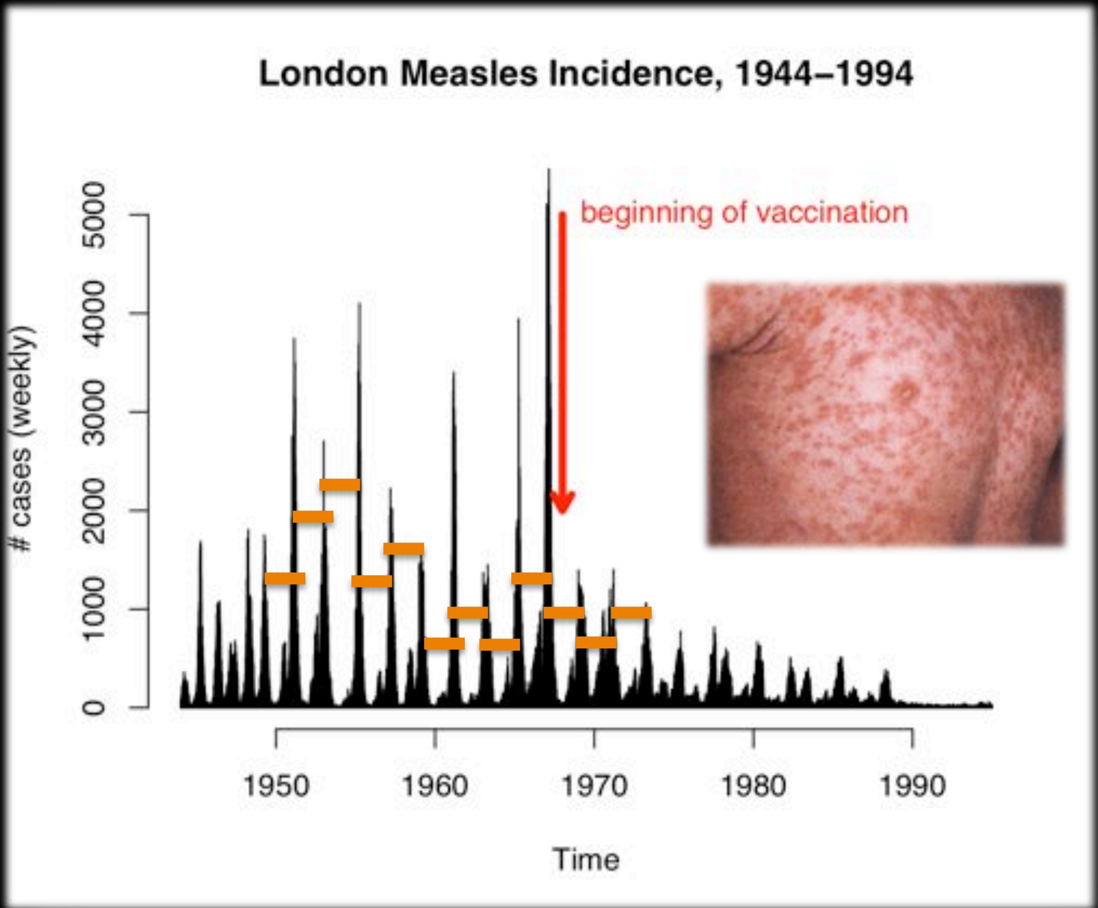
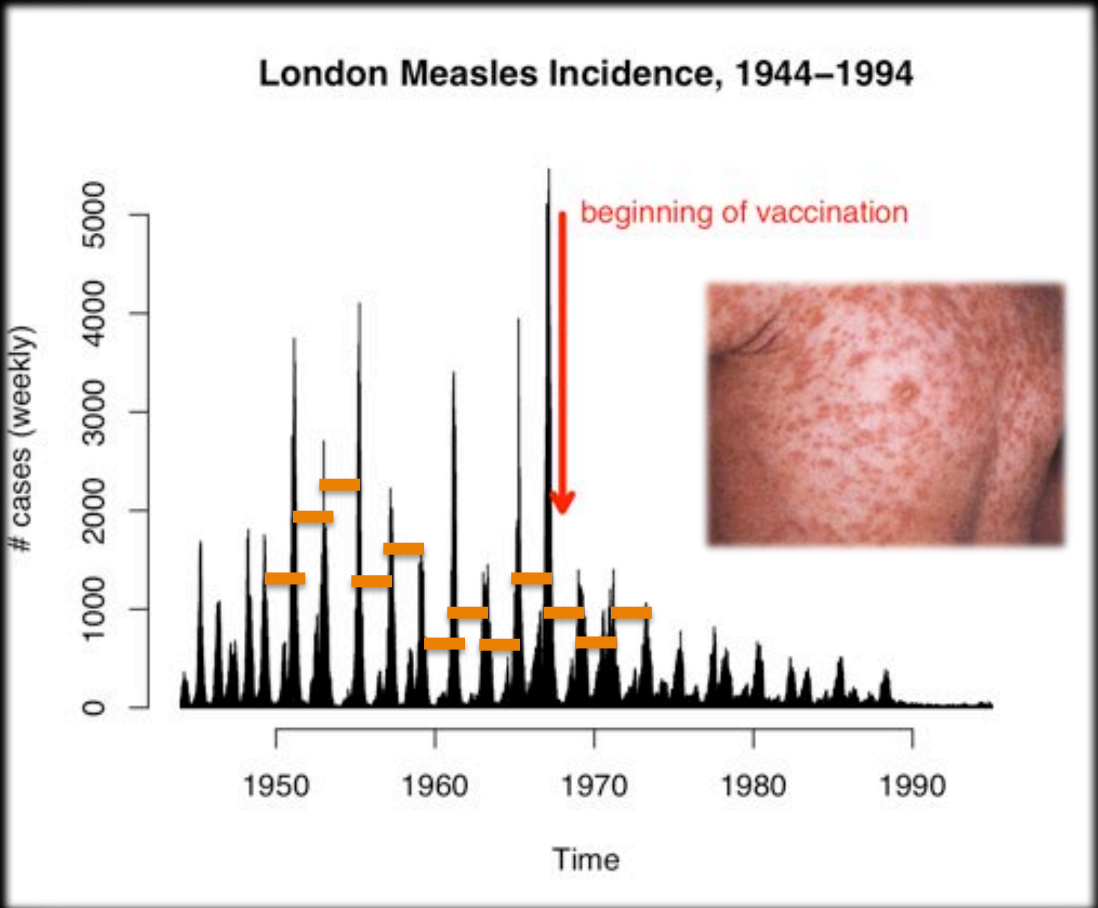


Earn et al. 2000. *Science.*

What accounts for epidemic cycles?

- Susceptibles depleted from an epidemic
- Disease does not completely die out (or is reintroduced).
- Susceptibles replenished through birth or loss of immunity, epidemic occurs.



Earn et al. 2000. *Science.*

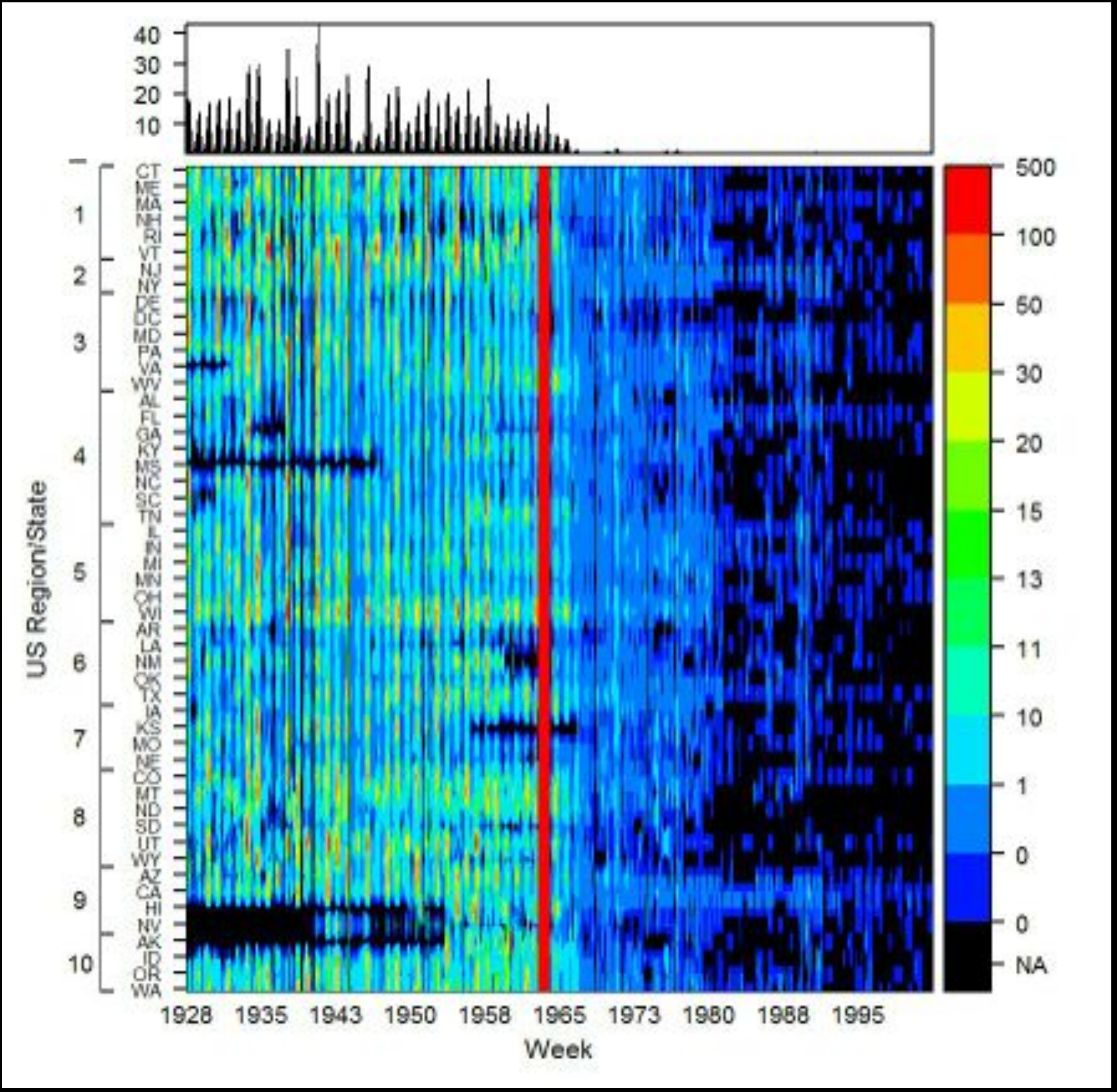
100 years of Infectious Diseases in the US

Project Tycho Video:
https://www.youtube.com/watch?v=Kn9OJy1BPDo

Project Tycho Website:
https://www.tycho.pitt.edu/

Measles Cases in the US

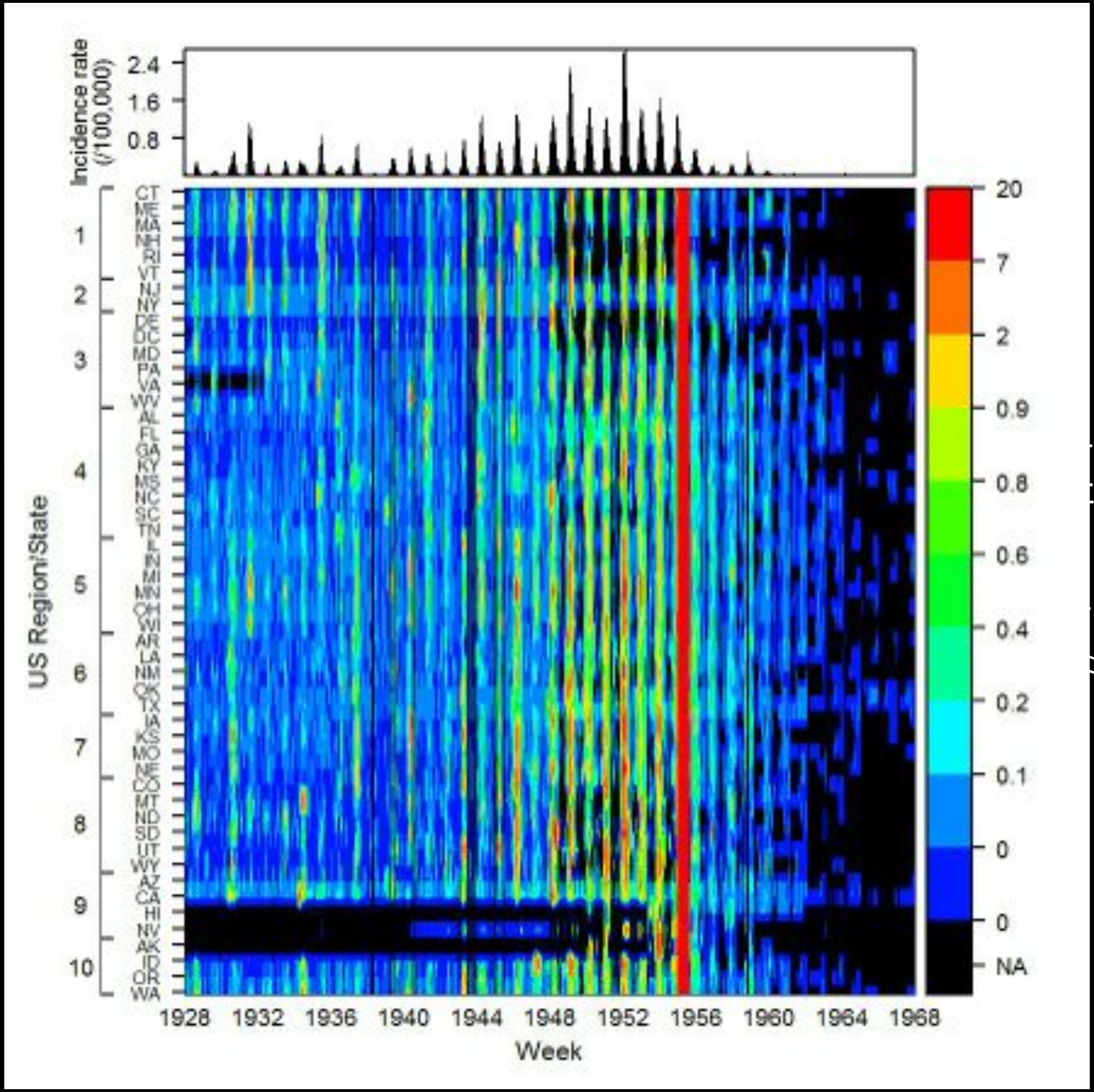
Cases per 10,000 per year



Van Panhuis, et.al. 2013 *NEJM*

Polio Cases in the US

Cases per 10,000 per year



Van Panhuis, et.al. 2013 *NEJM*

What makes a disease easy/hard to control?

- A small R_0
- Do infectious individuals know they're infectious?
- Reservoir (environment or another species)
- Vector-borne transmission
- Available interventions (vaccine, treatment, etc..)

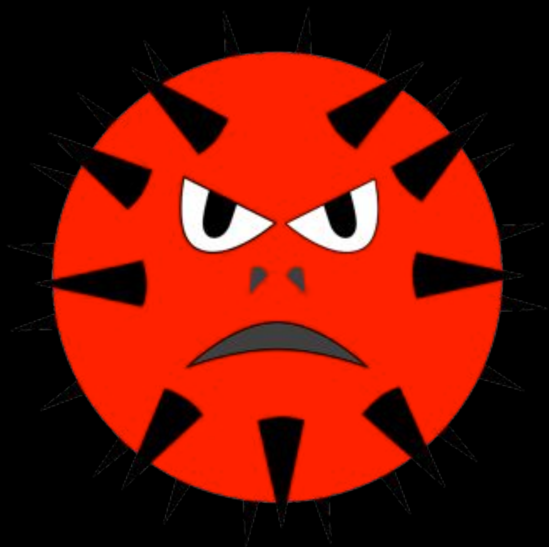
Vaccine-Preventable Pathogens

- Tend to already confer natural immunity
- Usually childhood diseases
- Low strain variability

Why do pathogens cause disease?

~~They hate humans.~~

Evolutionary Consequences



Why do parasites cause disease?

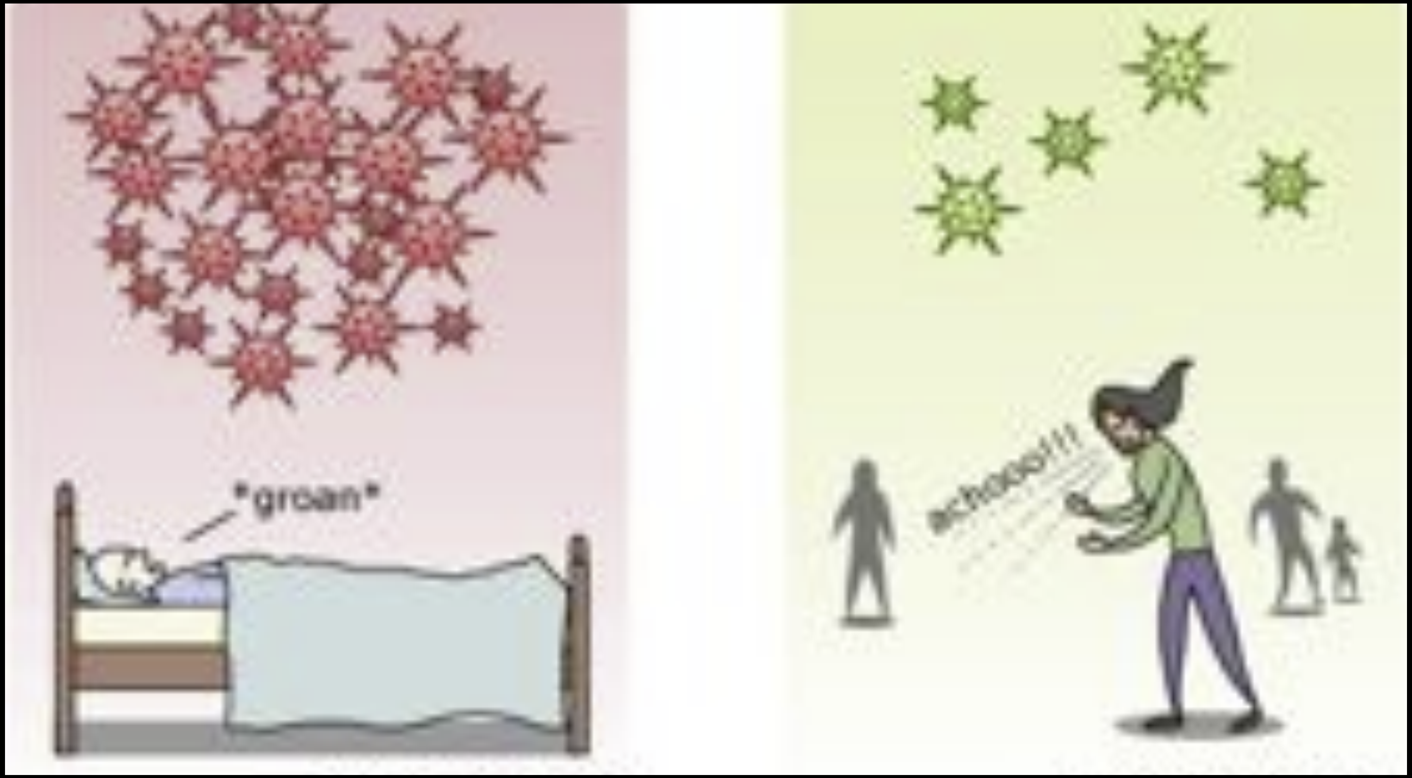
Transmission-Virulence Tradeoff

- Successful pathogens are successful at spreading.
- Mechanisms of spread are often linked to disease.

Coughing spreads whooping cough (pertussis).

Why do parasites cause disease?

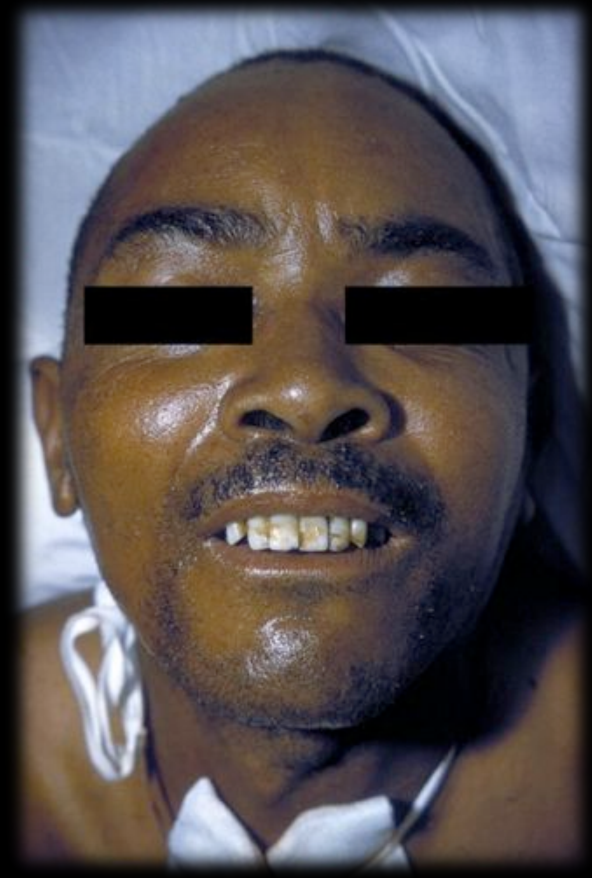
Transmission-Virulence Tradeoff



Why do parasites cause disease?

Accidental

- Toxins adapted for other causes.
- We may be a dead end host.

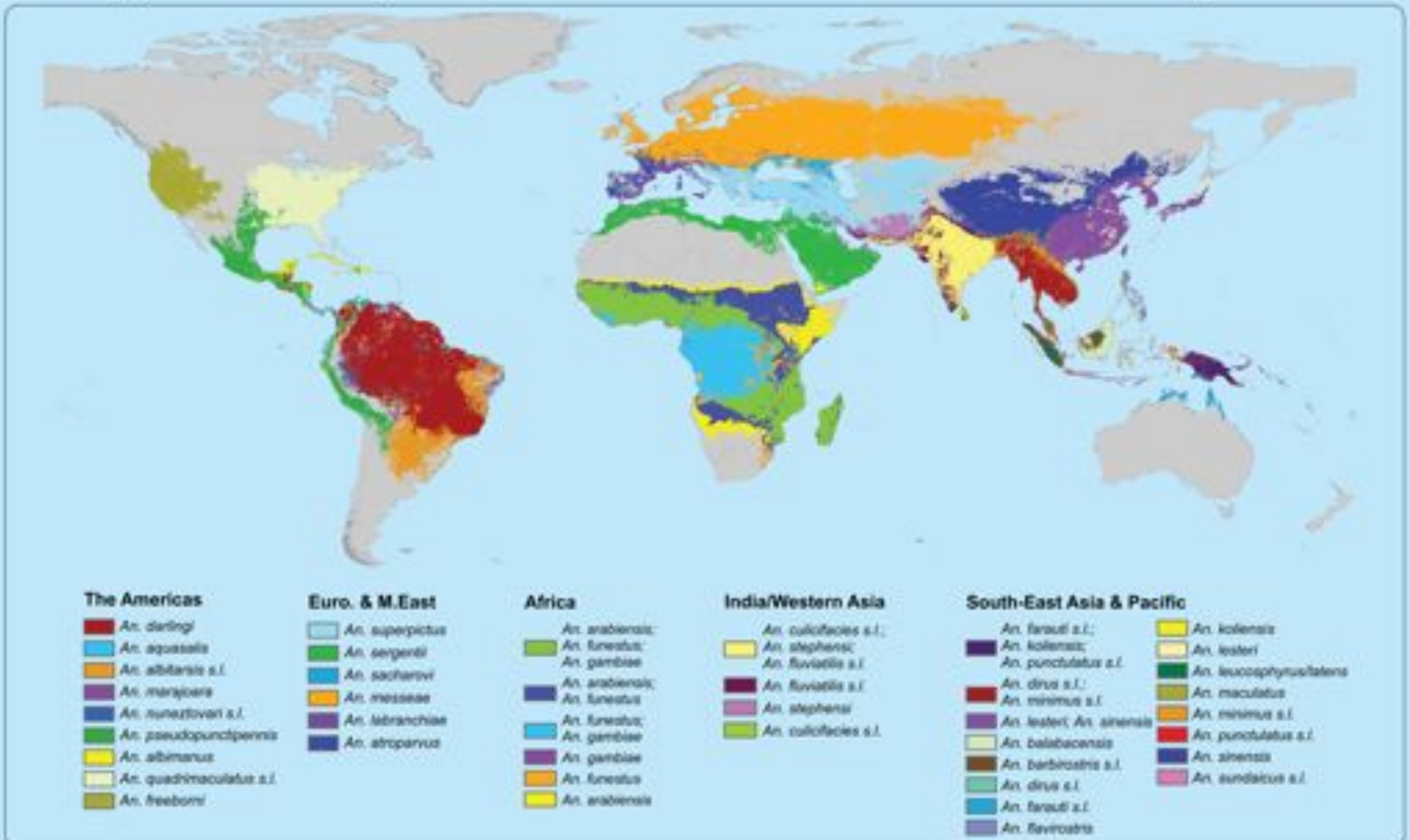


Tetanus caused by the soil-dwelling bacterium *Clostridia tetani*.

Vector-Borne Diseases

- Malaria (*Plasmodium spp.*)
- Dengue
- Chikungunya
- Yellow Fever

A global map of dominant malaria vector species

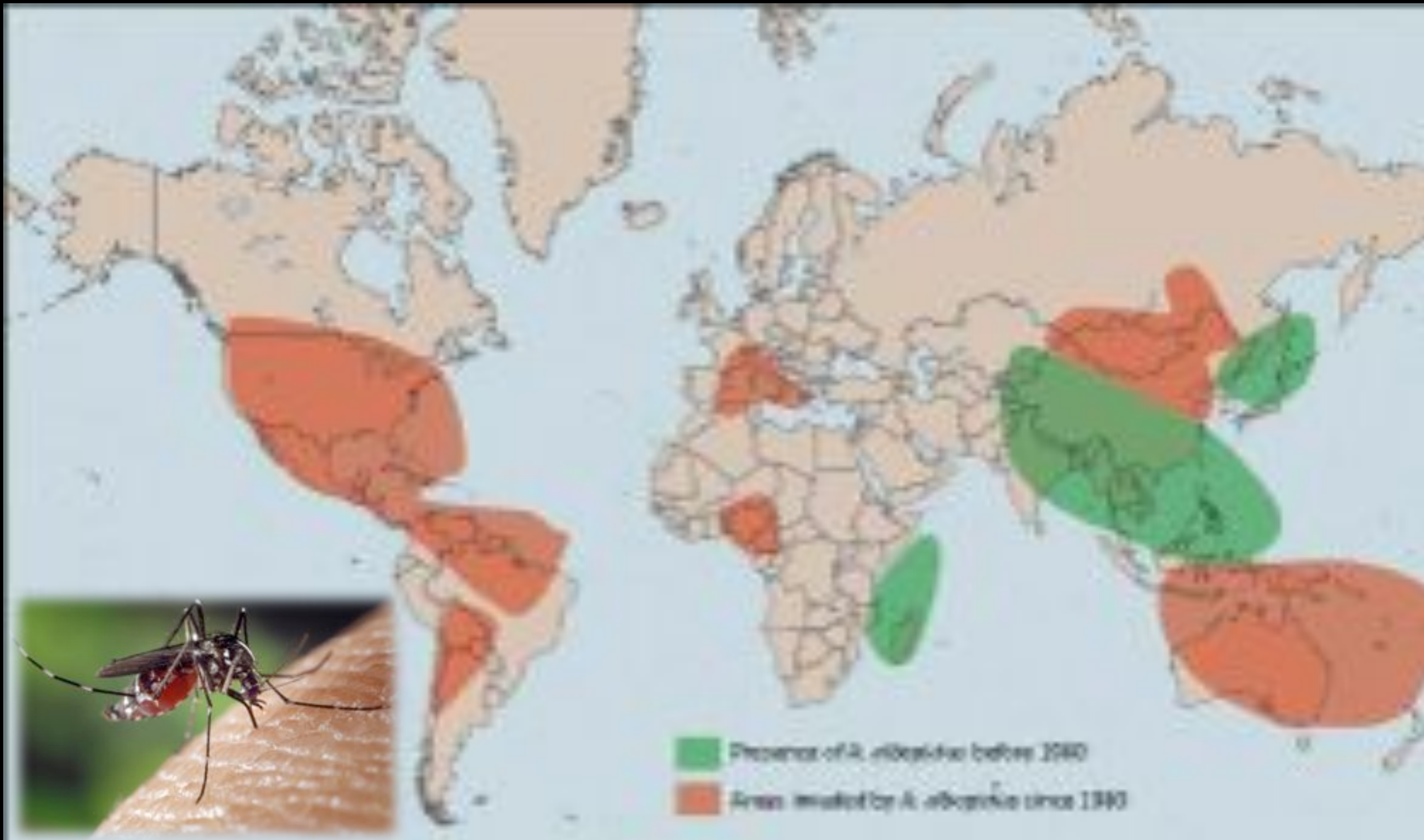


map

Parasites &Vectors

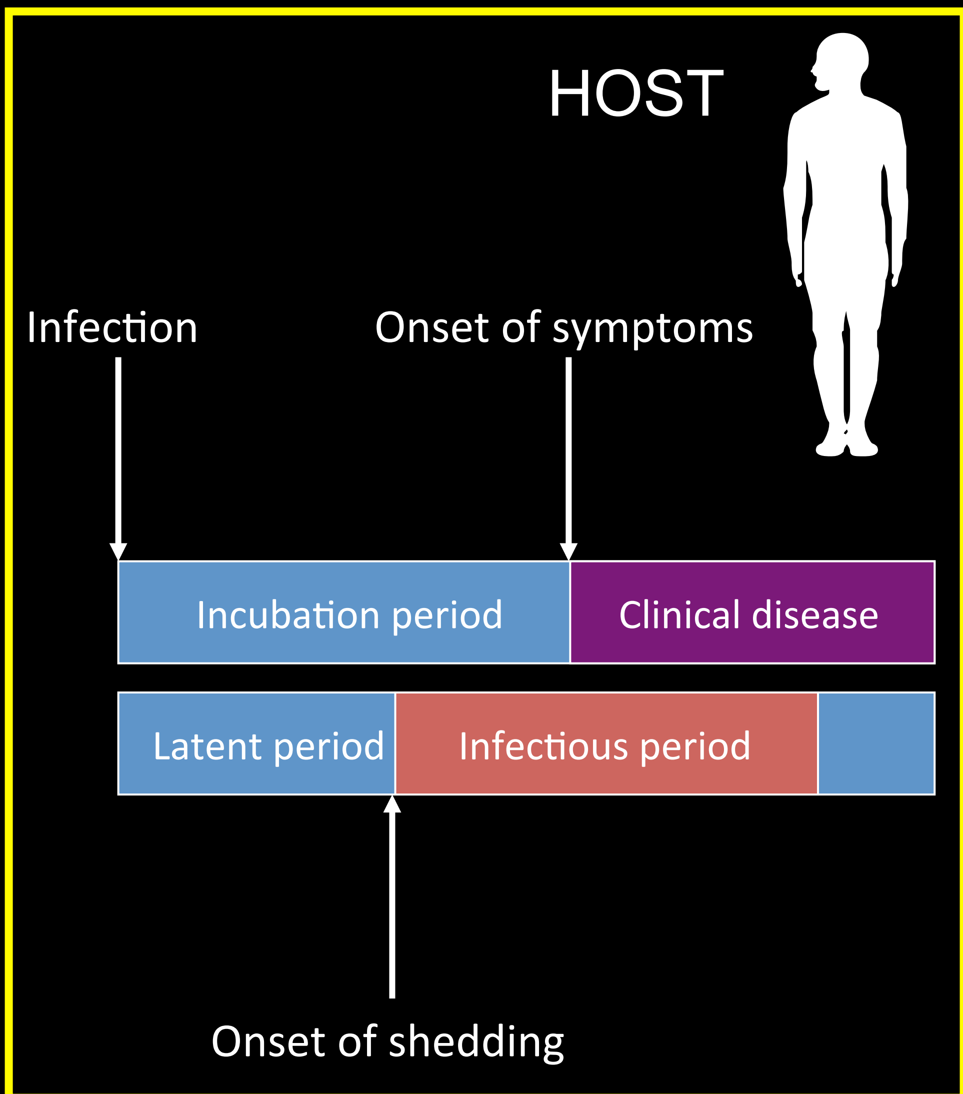
Sinka et al. *Parasites & Vectors*, 2012 5:69

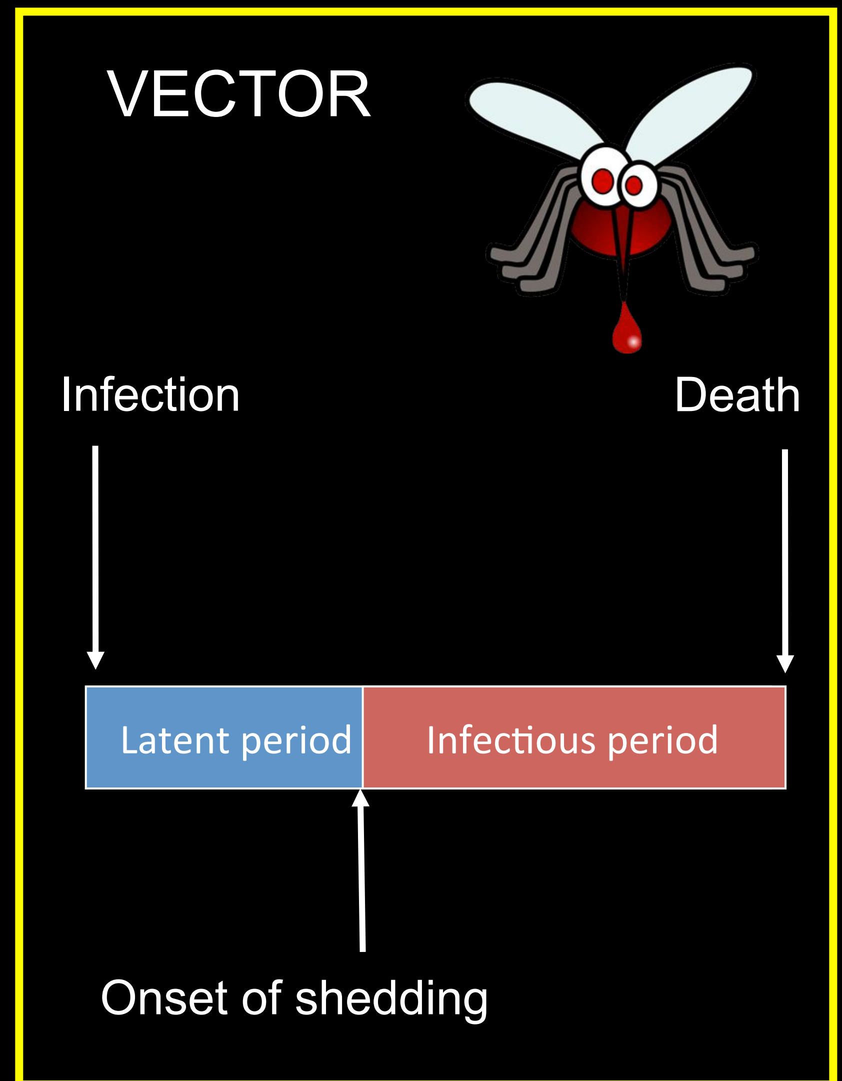
Expansion of the Asian Tiger Mosquito



Vector of dengue virus, yellow fever virus, chikungunya virus

Vector-Borne Diseases

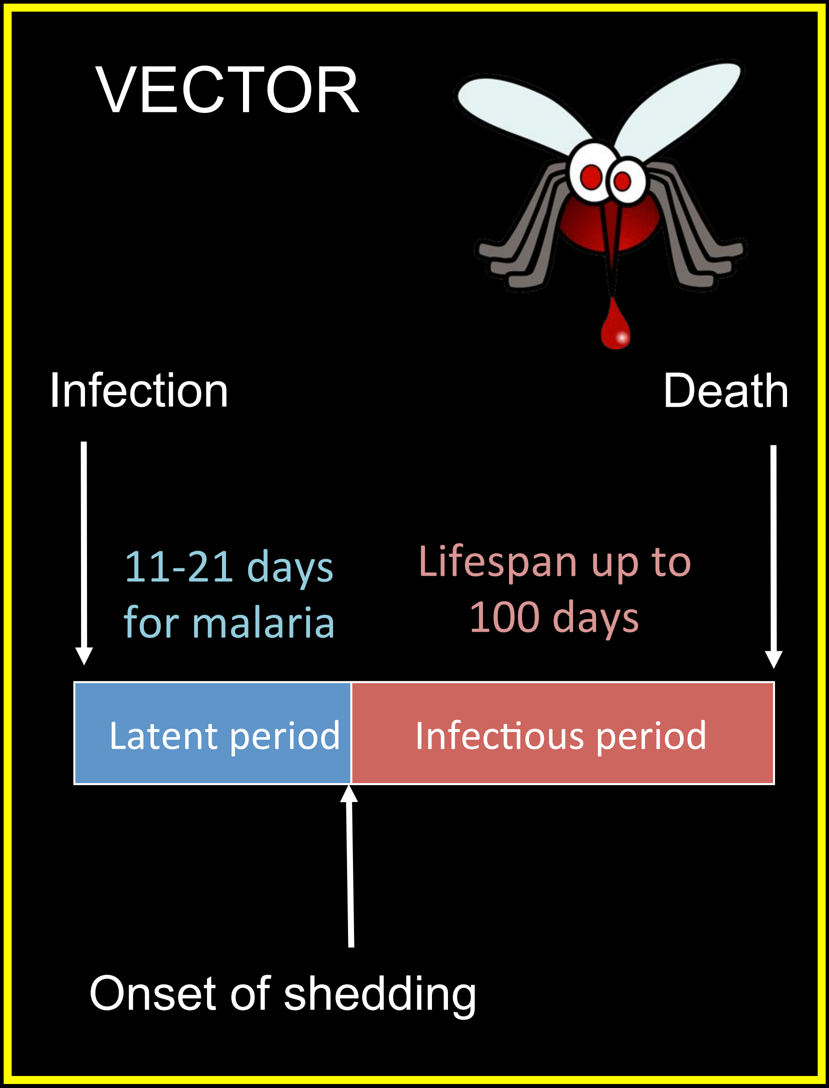




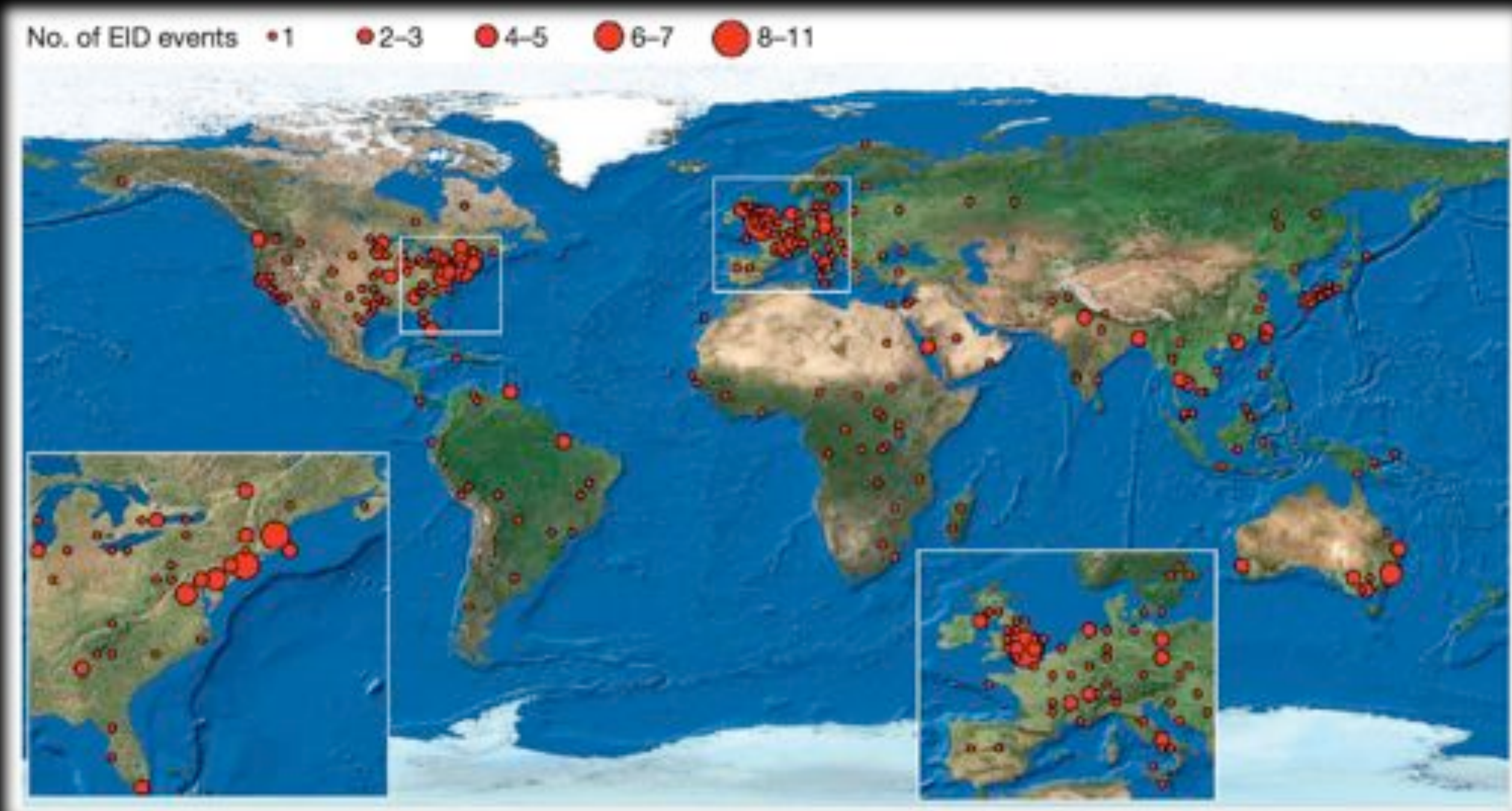
Vector-Borne Diseases

Why does mosquito control work?

- Fewer mosquitoes
- Shortens mosquito lifespan, reducing
    1. Proportion living long enough after becoming infected to become infectious
    2. # days mosquitoes live once infectious



Emerging Infectious Disease Events 1940-2004



Jones et al. (2008) *Nature*

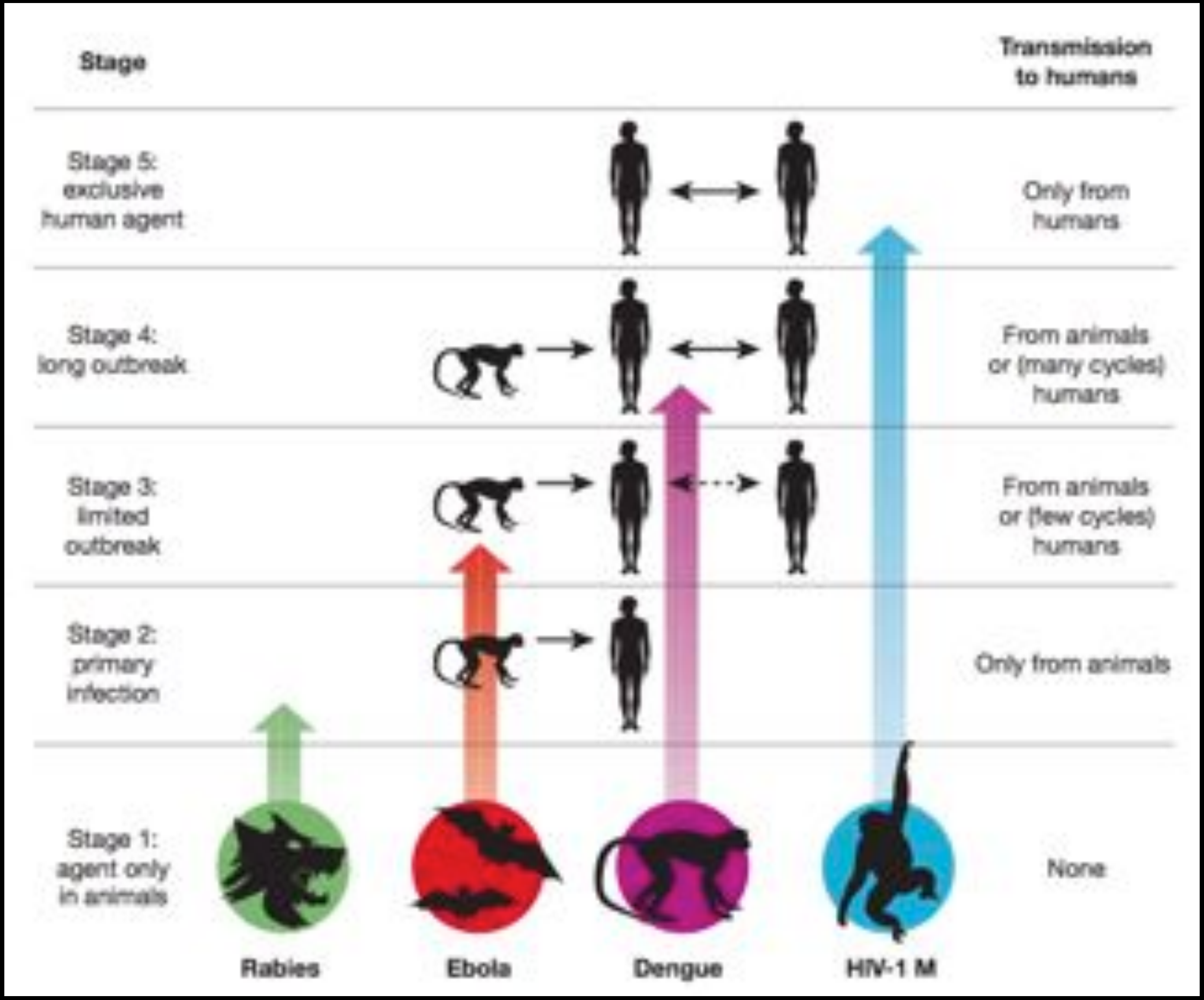
EID risk from animals

from wildlife

from domestic animals

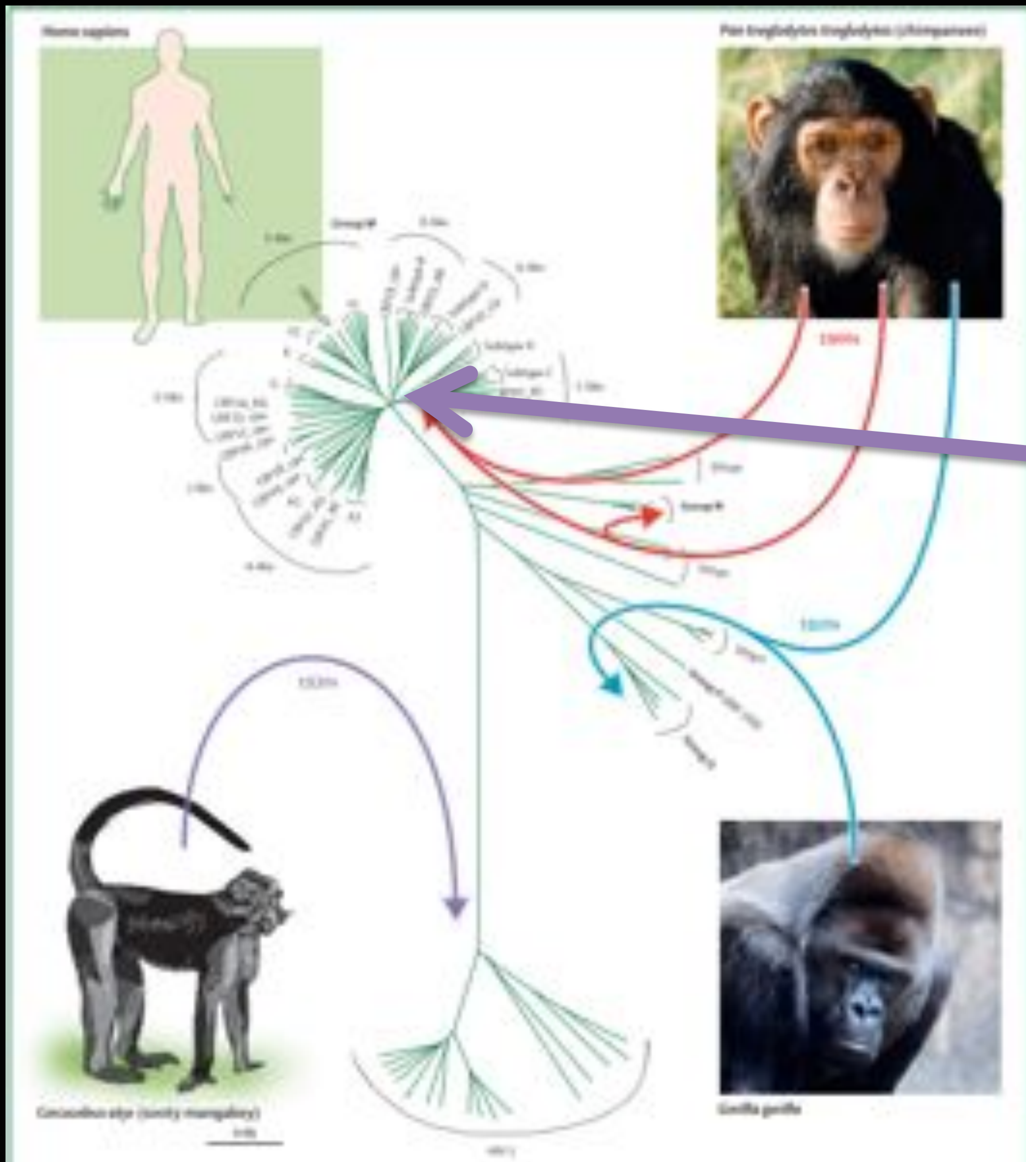
Jones et al. (2008) *Nature*

Stages of Zoonotic Pathogens



Wolfe et al. (2007) *Nature*

HIV Emergence

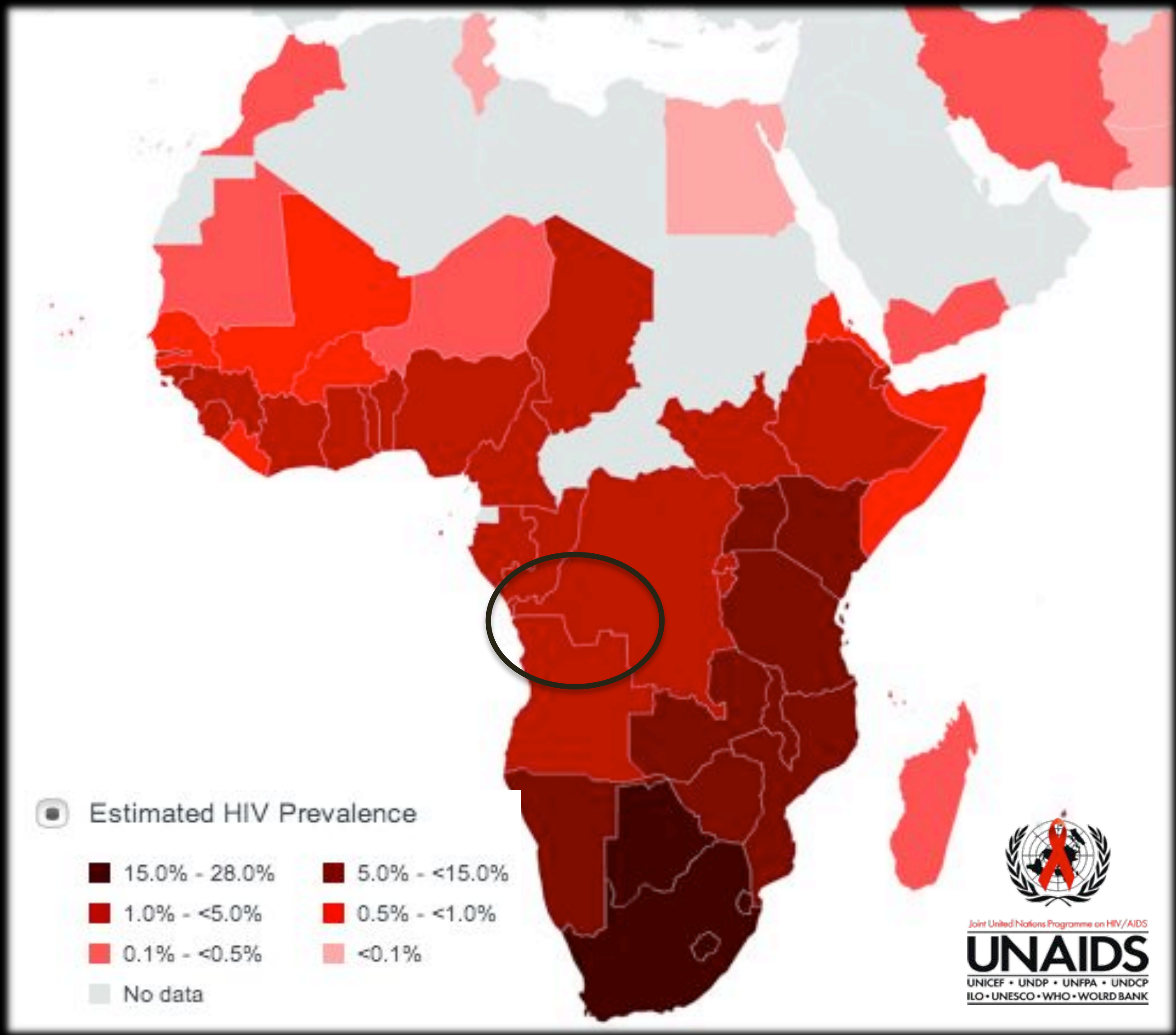


Most recent common ancestor around 1900.

But HIV only discovered in 1981!

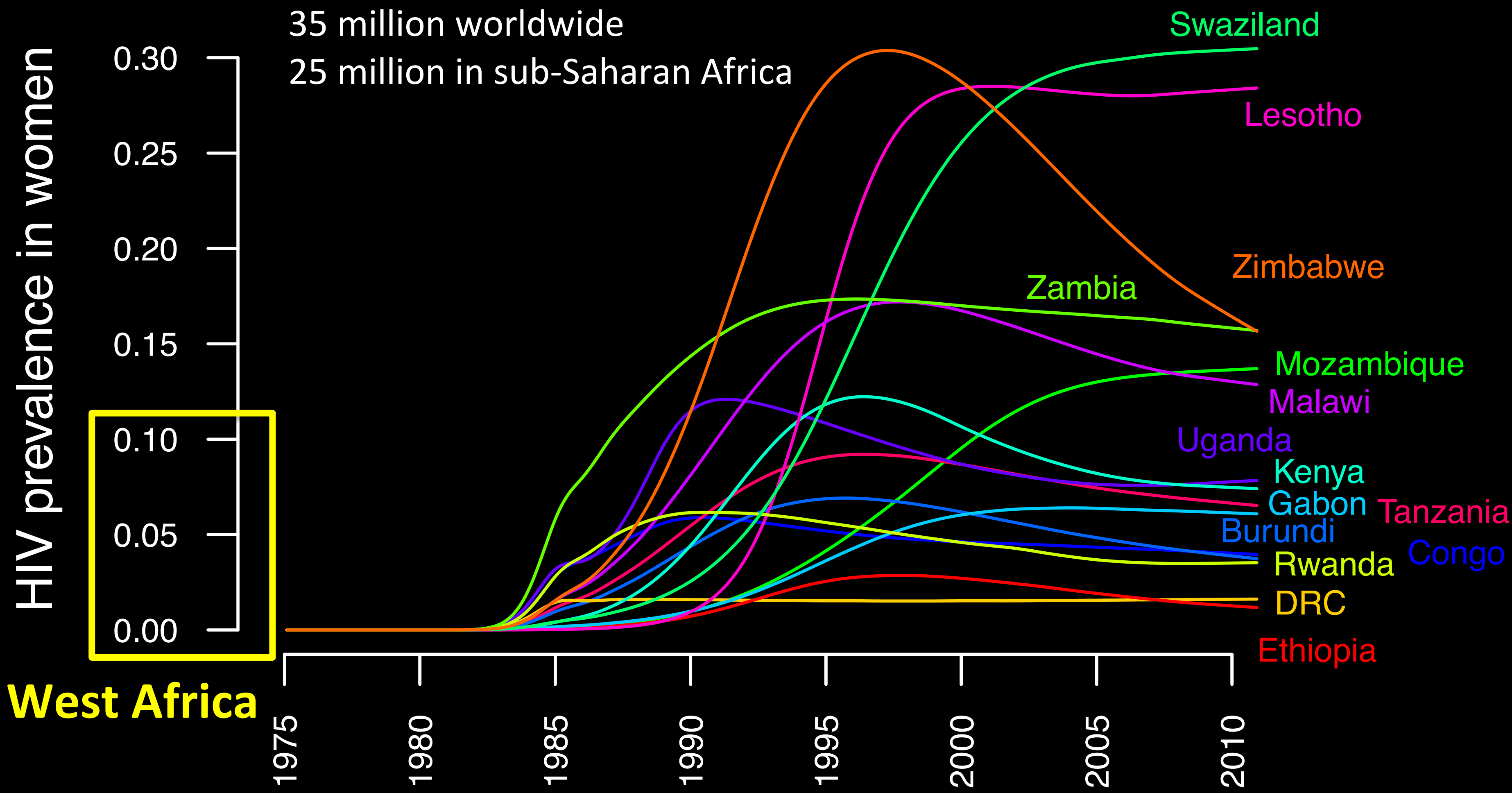
Tebit et al. 2011

HIV Prevalence



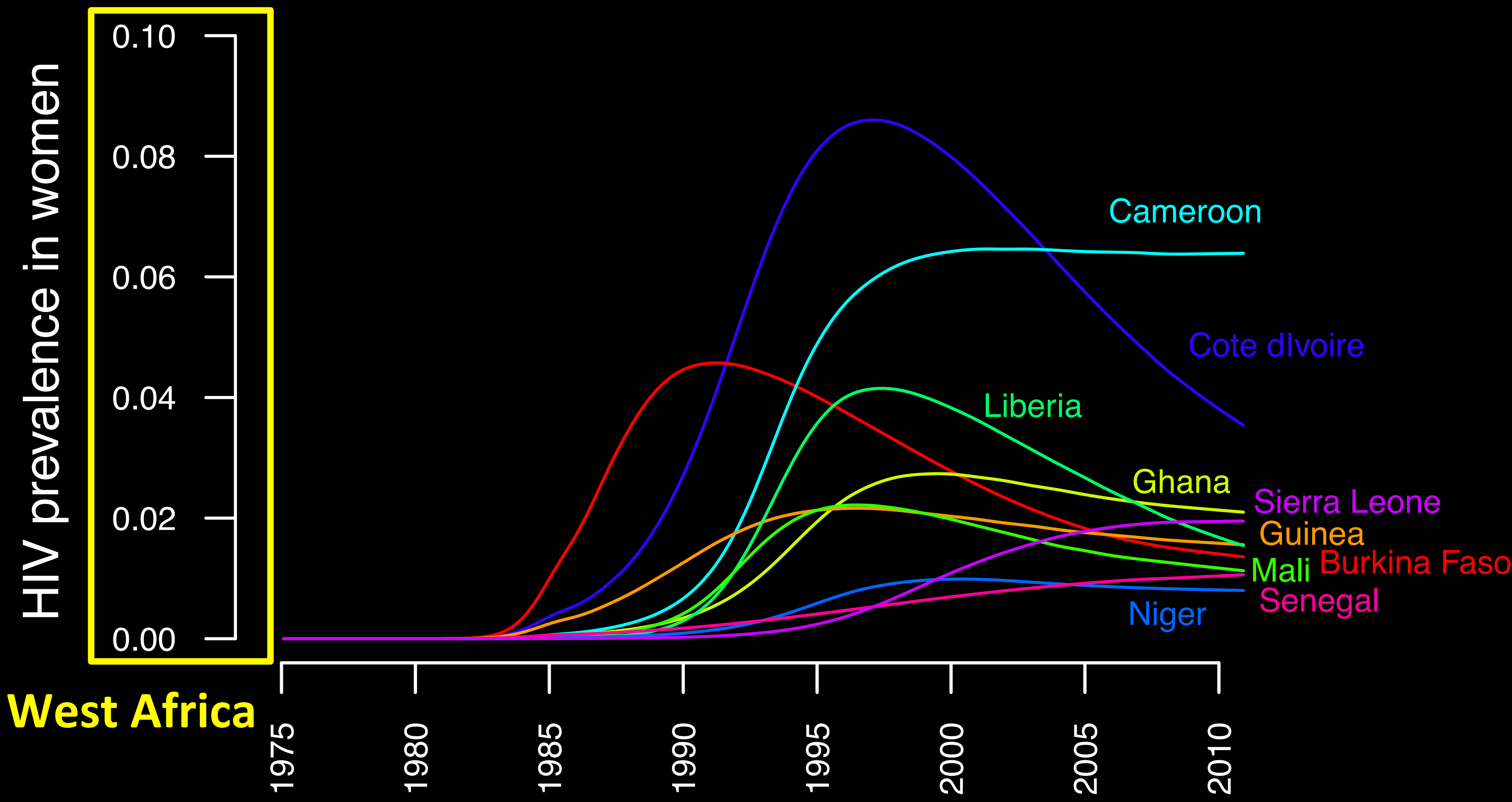
HIV prevalence in Africa

people living with HIV
35 million worldwide
25 million in sub-Saharan Africa



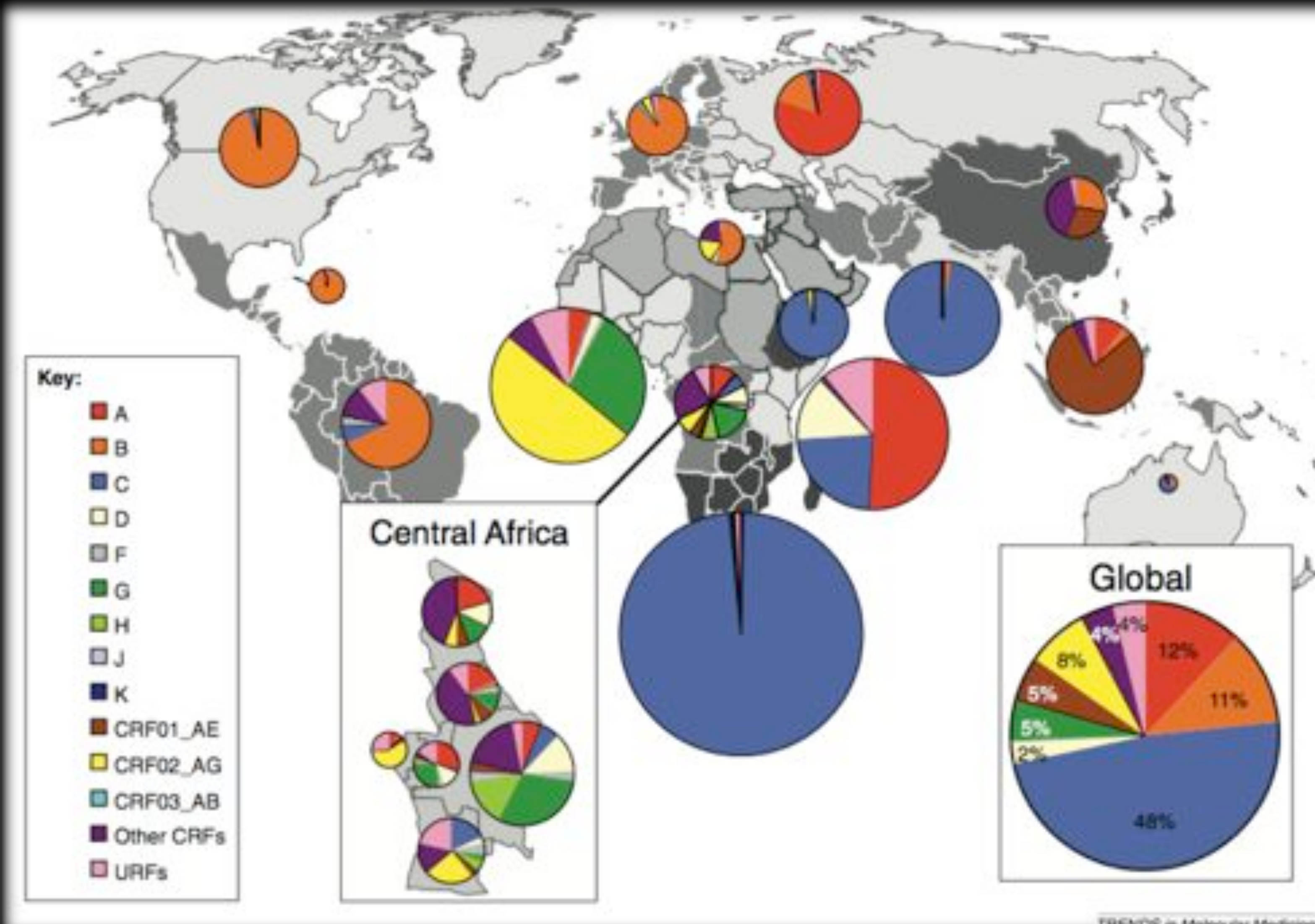
UNAIDS 2013

HIV prevalence in Africa



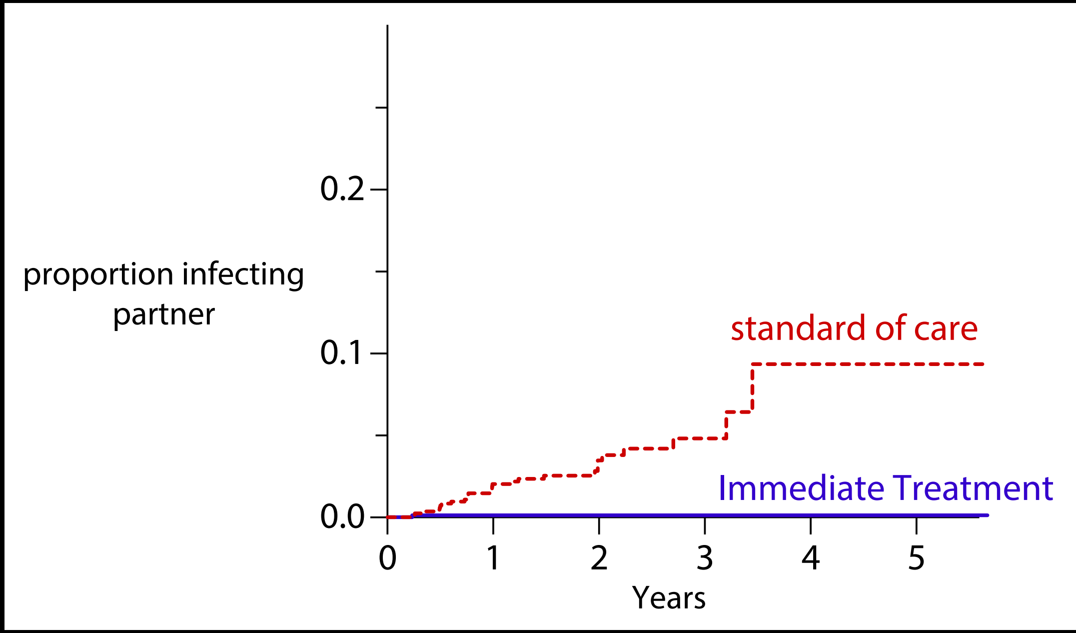
UNAIDS 2013

HIV Diversity Indicates its Origin



Hemelaar et al. 2012

Treatment as Prevention (TasP)

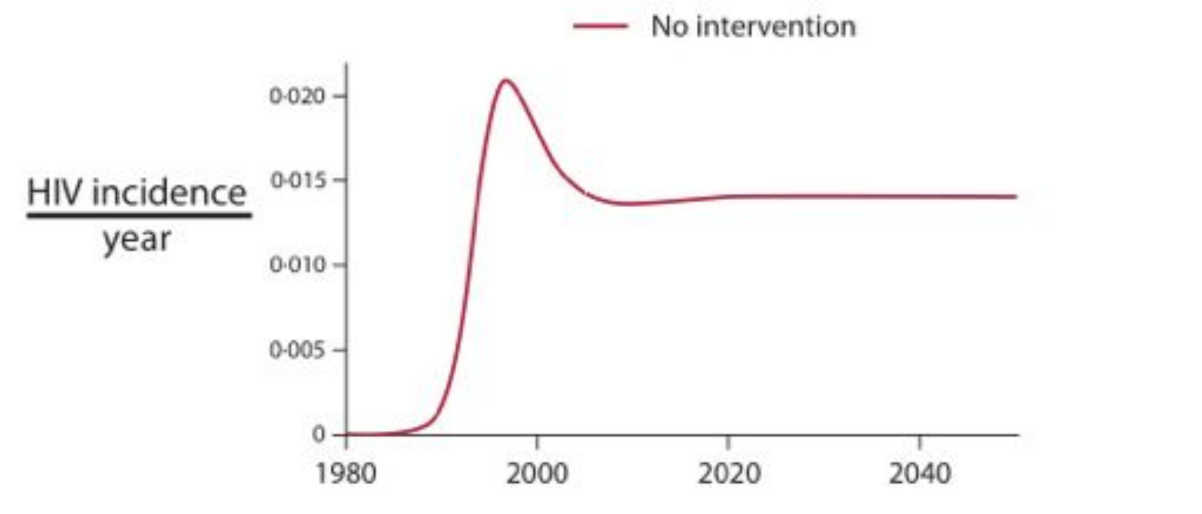


Cohen et al. (2011). *NEJM*.

Antiretroviral therapy suppresses HIV viral load & reduces transmission

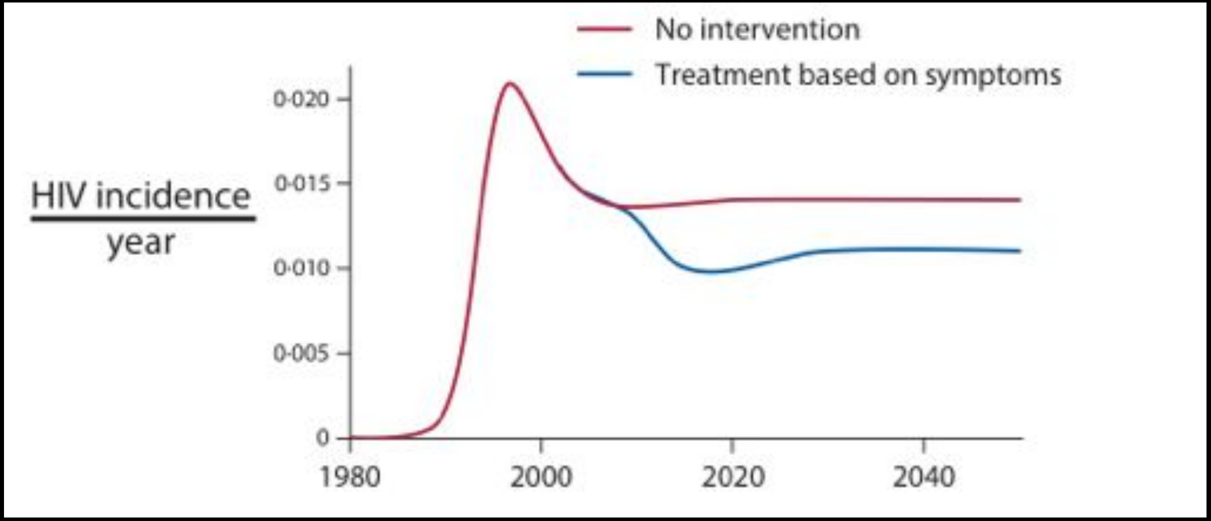
96% reduction in transmission

Universal "Test and Treat"



Granich et al. (2009). *Lancet*.

Universal "Test and Treat"



Granich et al. (2009). *Lancet*.

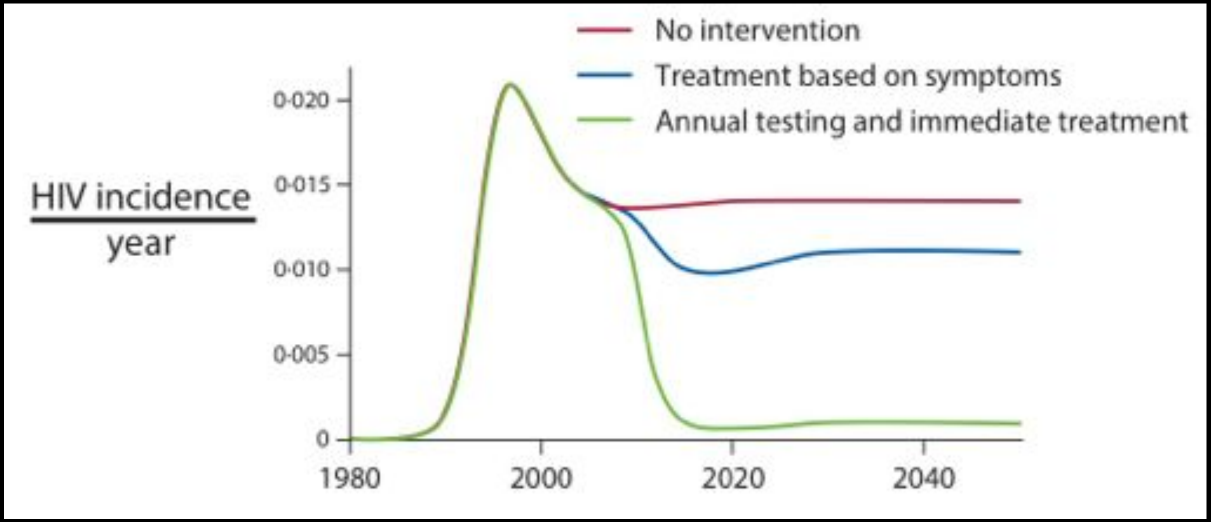
Universal "Test and Treat"

Test annually

Treat immediately

Reduce transmission

Eliminate HIV



Granich et al. (2009). *Lancet*.

cluster randomized controlled trials underway

Will "Test and Treat" work?

- Logistics
- Uptake and adherence
- Drug Resistance
- Early Transmission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PLoS MEDICINE

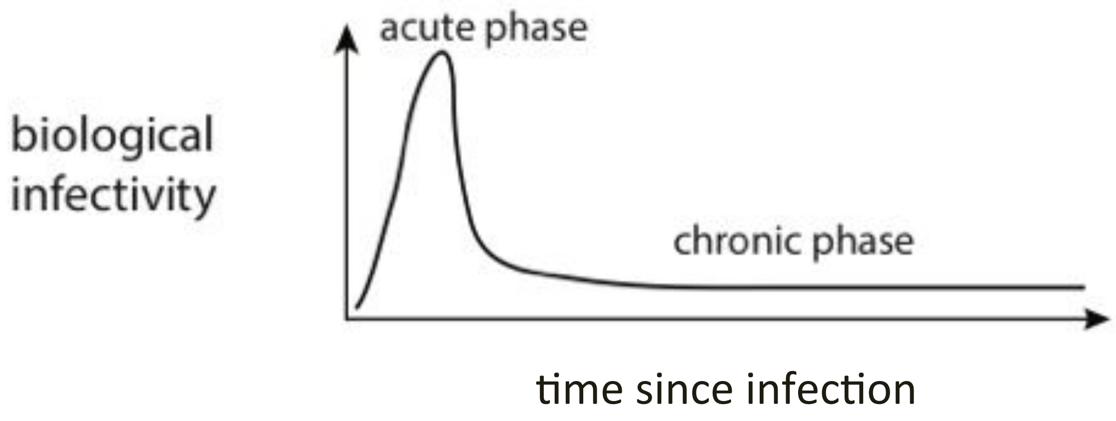
Review

HIV Treatment as Prevention: Debate and Commentary—Will Early Infection Compromise Treatment-as-Prevention Strategies?

Myron S. Cohen[1,2,3¶], Christopher Dye[4¶], Christophe Fraser[5¶*], William C. Miller[2,3¶], Kimberly A. Powers[2,3¶*], Brian G. Williams[6¶*]

How much transmission happens before diagnosis and treatment?

What proportion of transmission occurs early?



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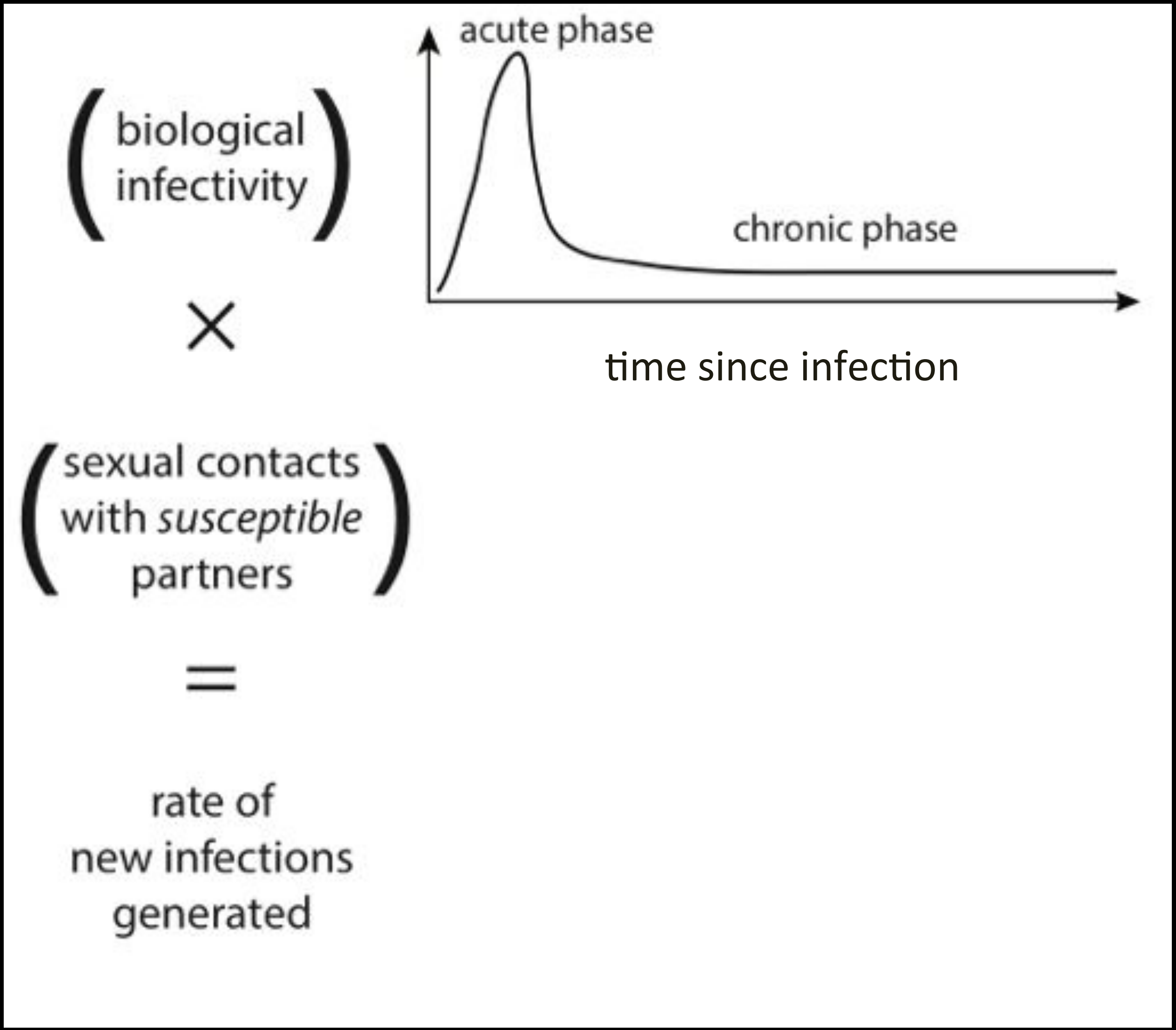

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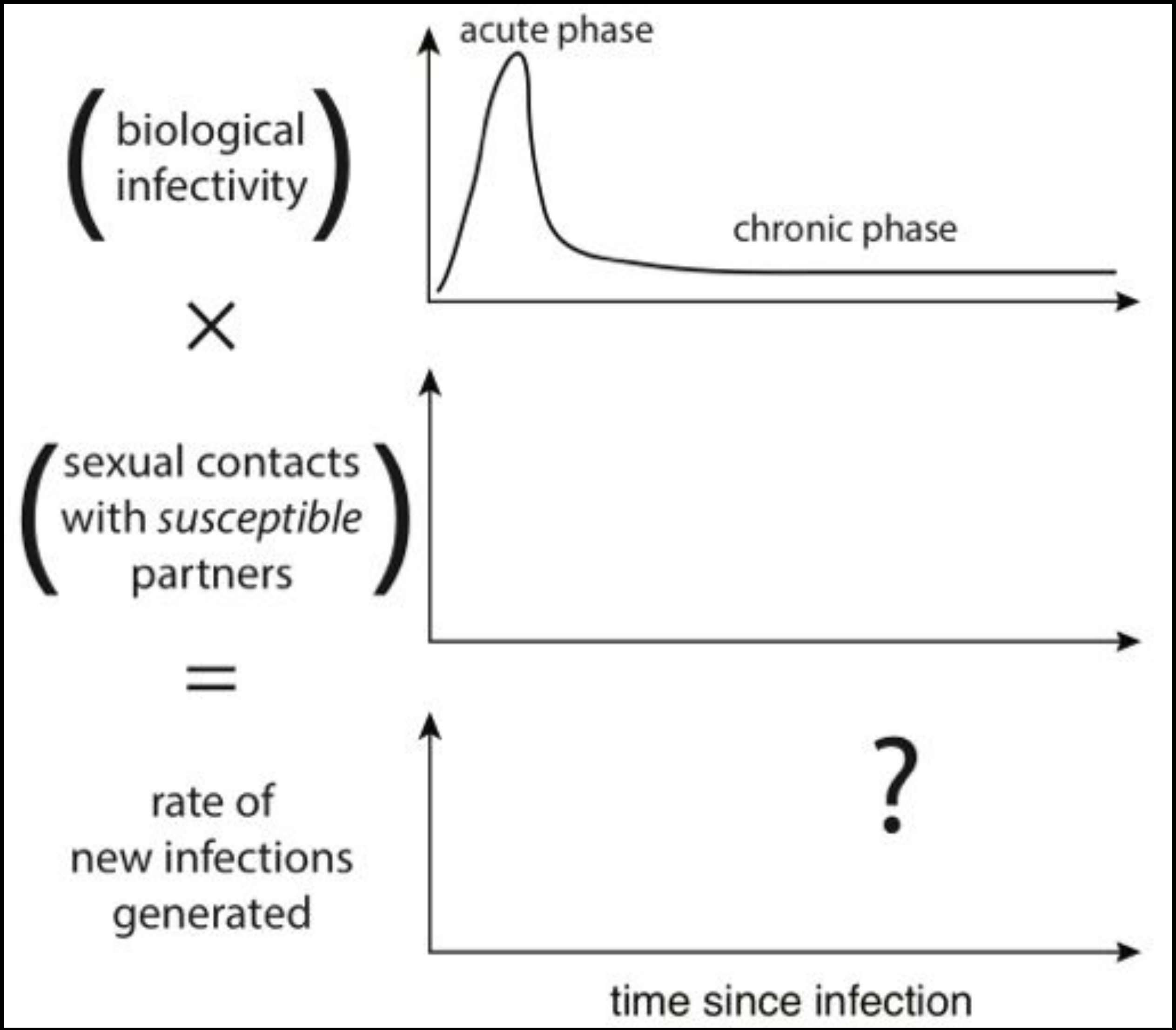

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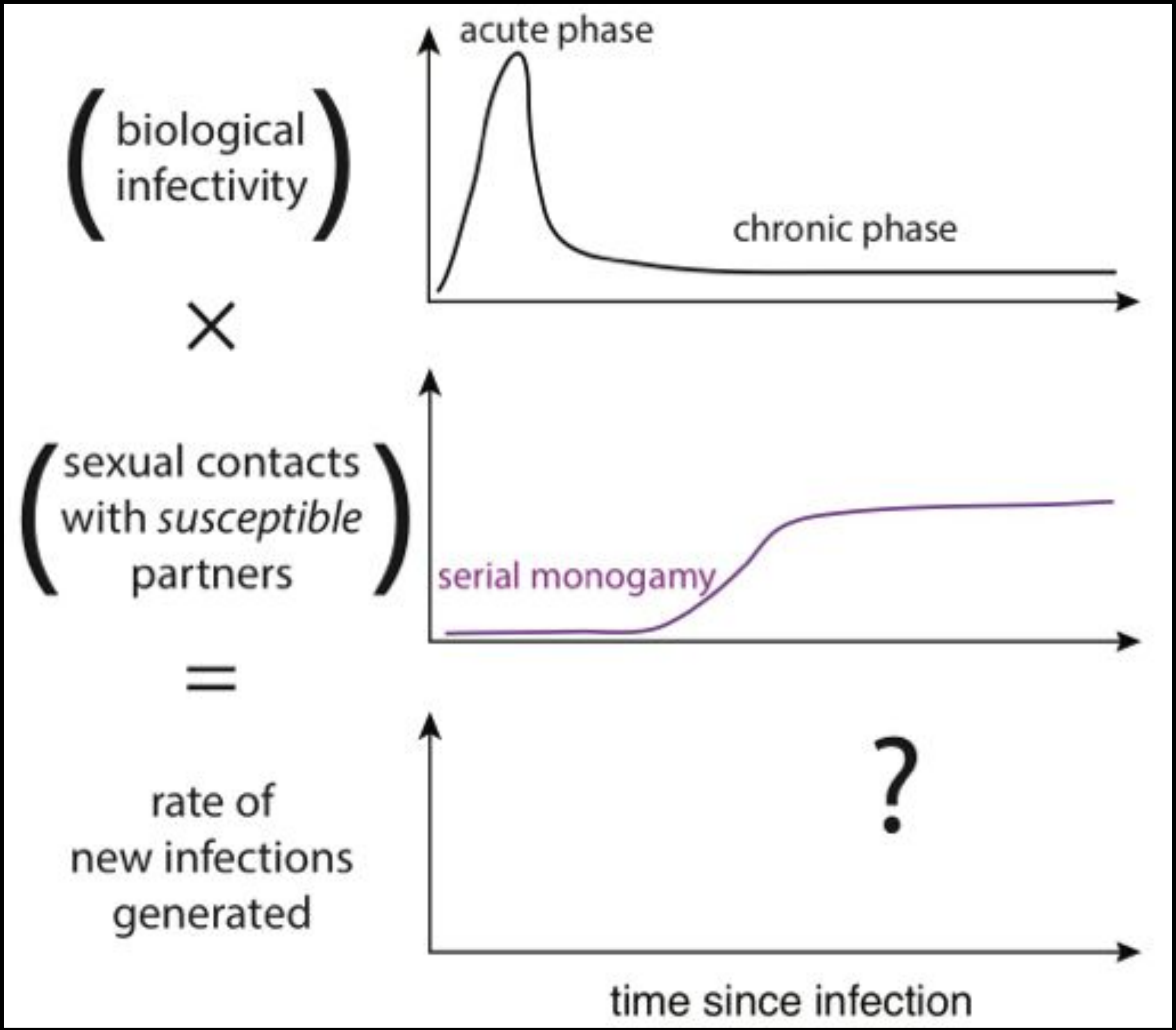

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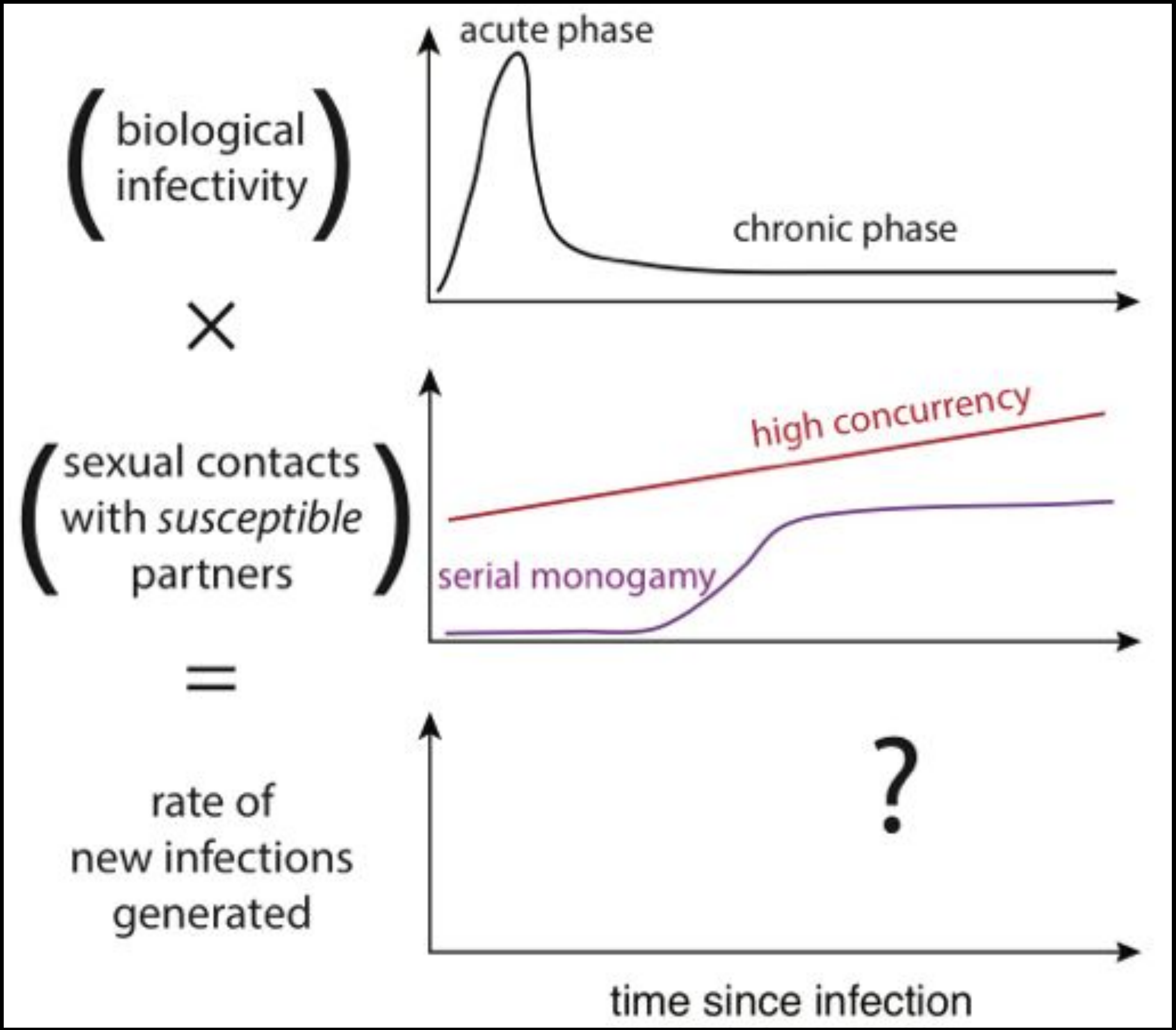

Eaton et al. 2011. *AIDS & Behavior*.

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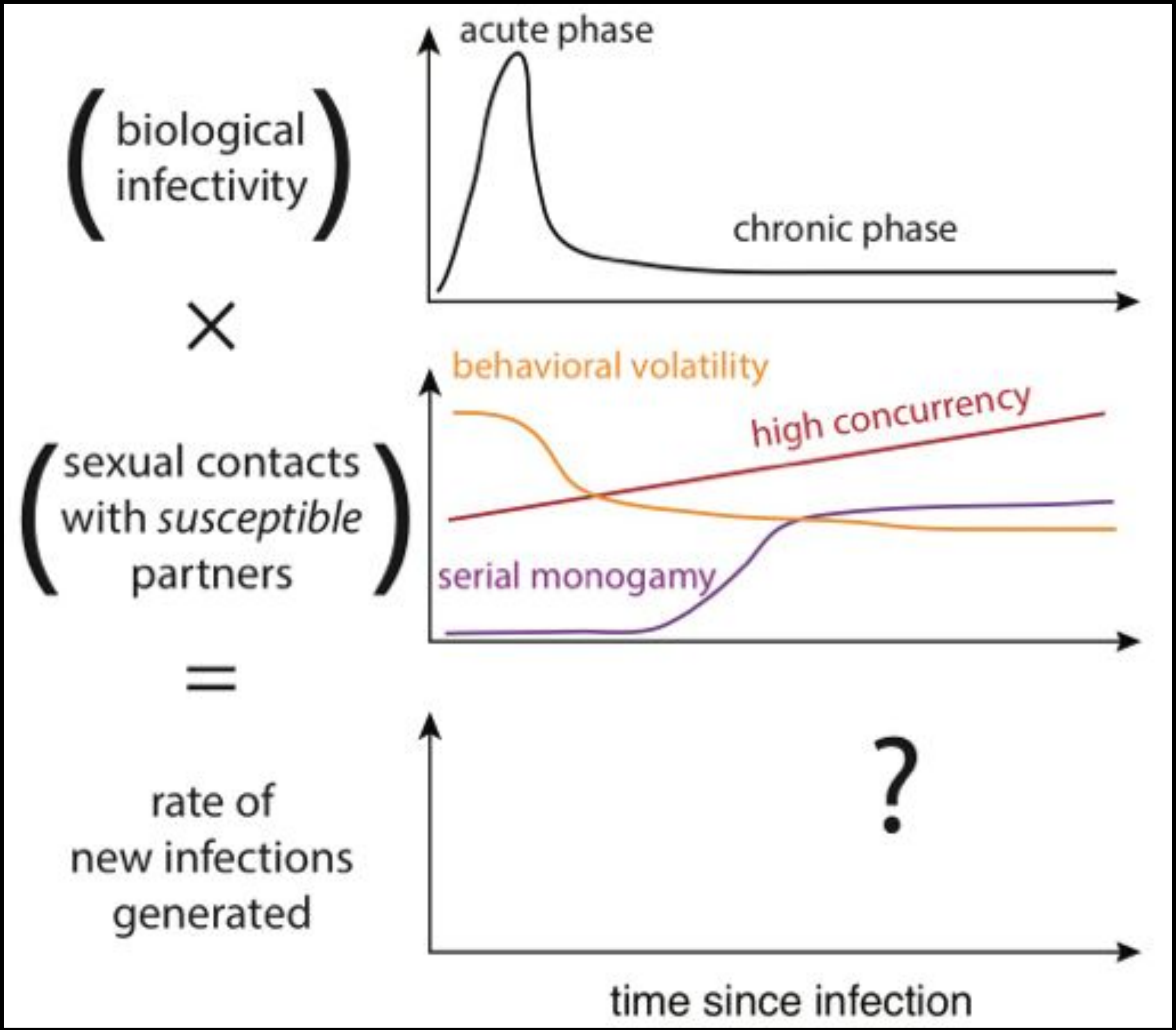

Eaton et al. 2011. *AIDS & Behavior*.

Alam et al. 2013. *Epidemics*.

Romero-Severson et al. 2013. *Epidemiolgy*.

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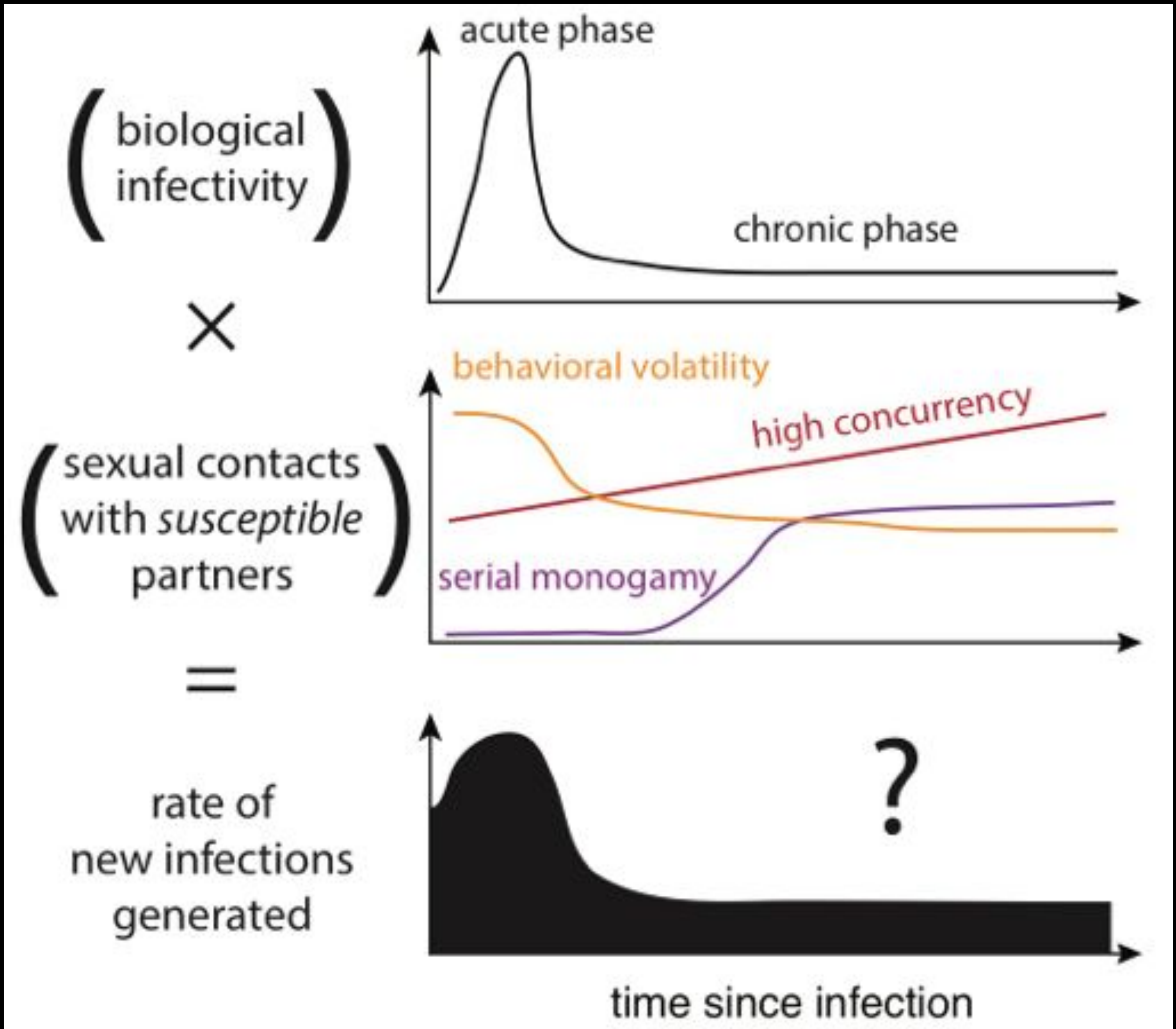

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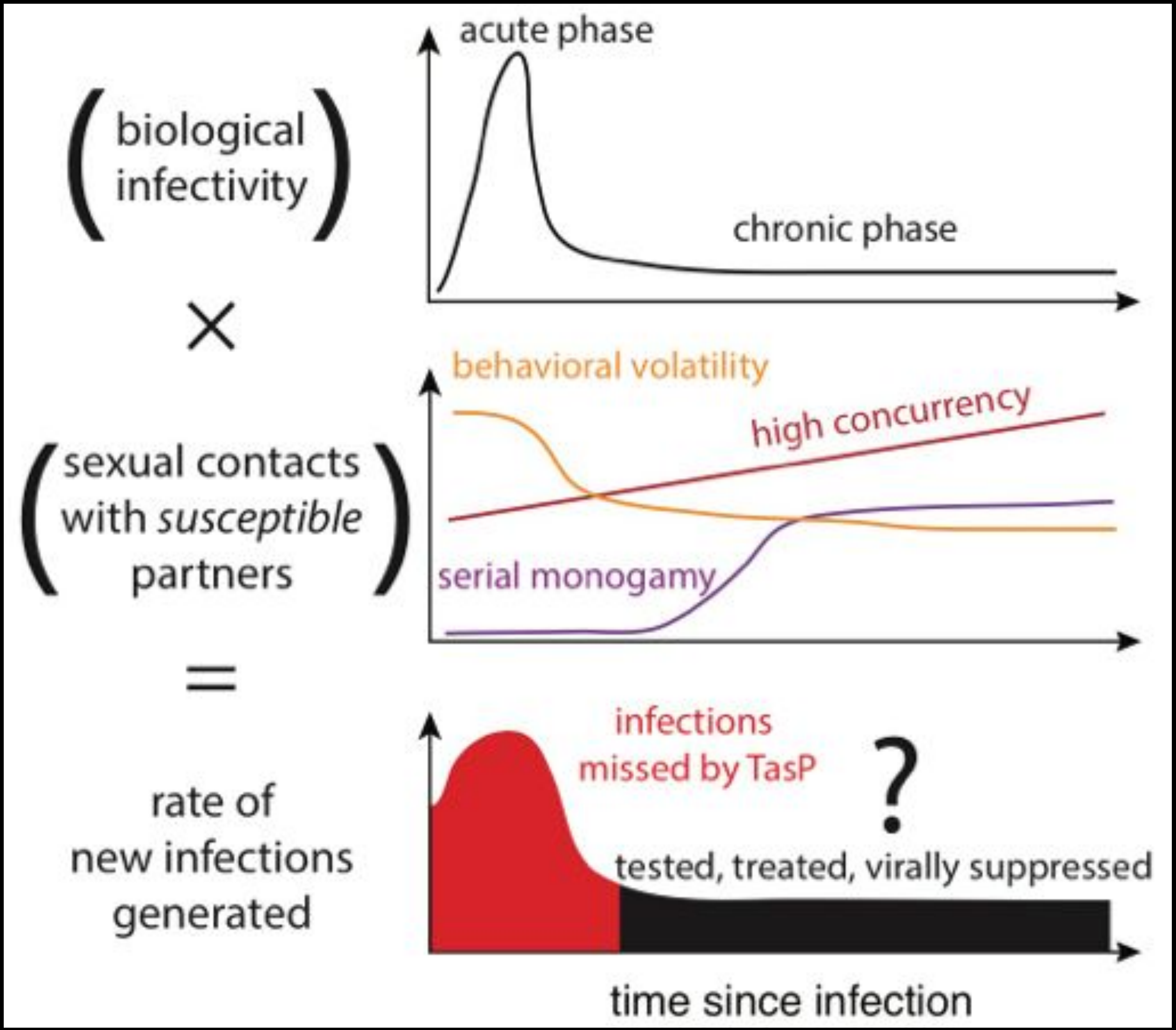

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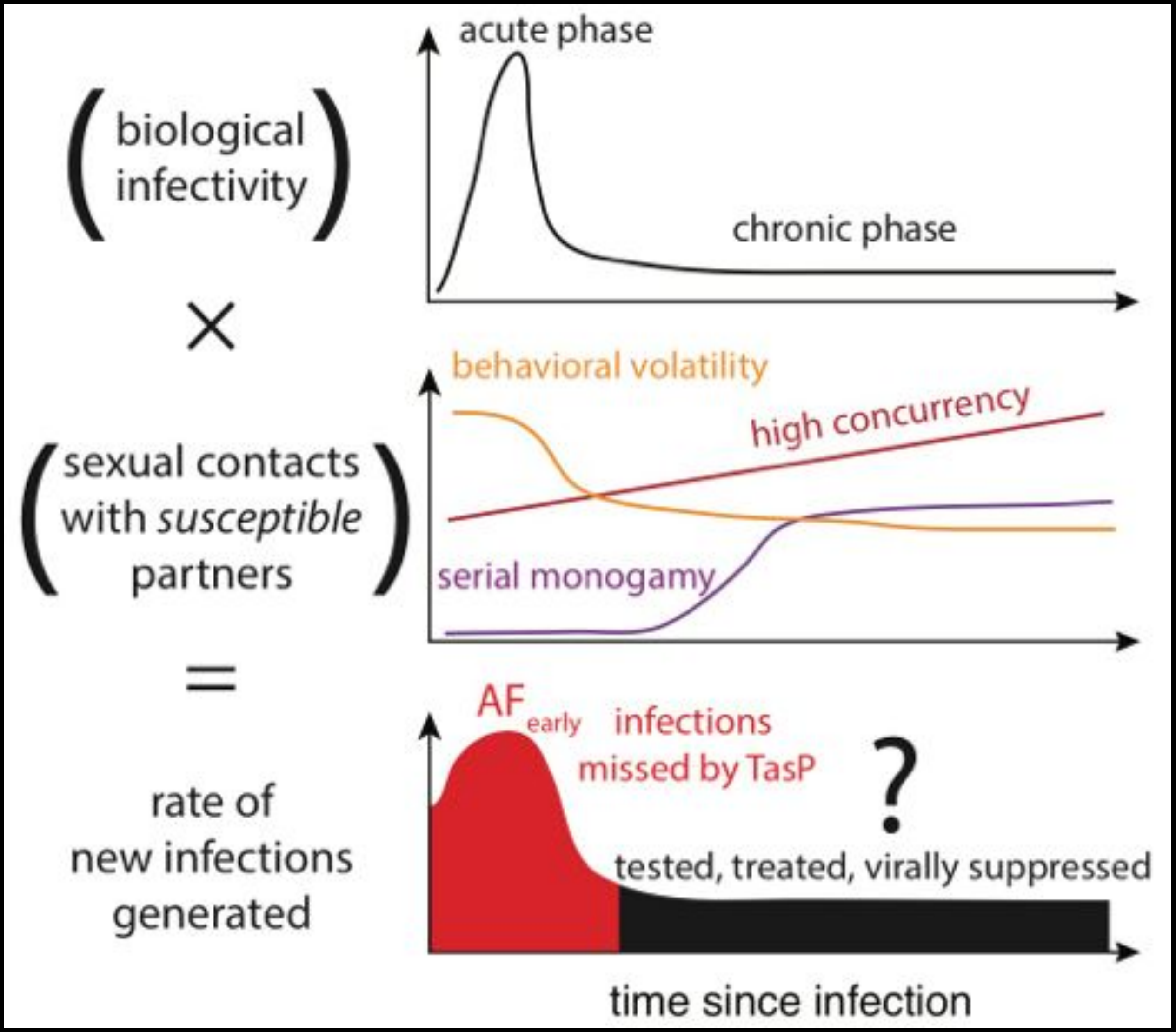

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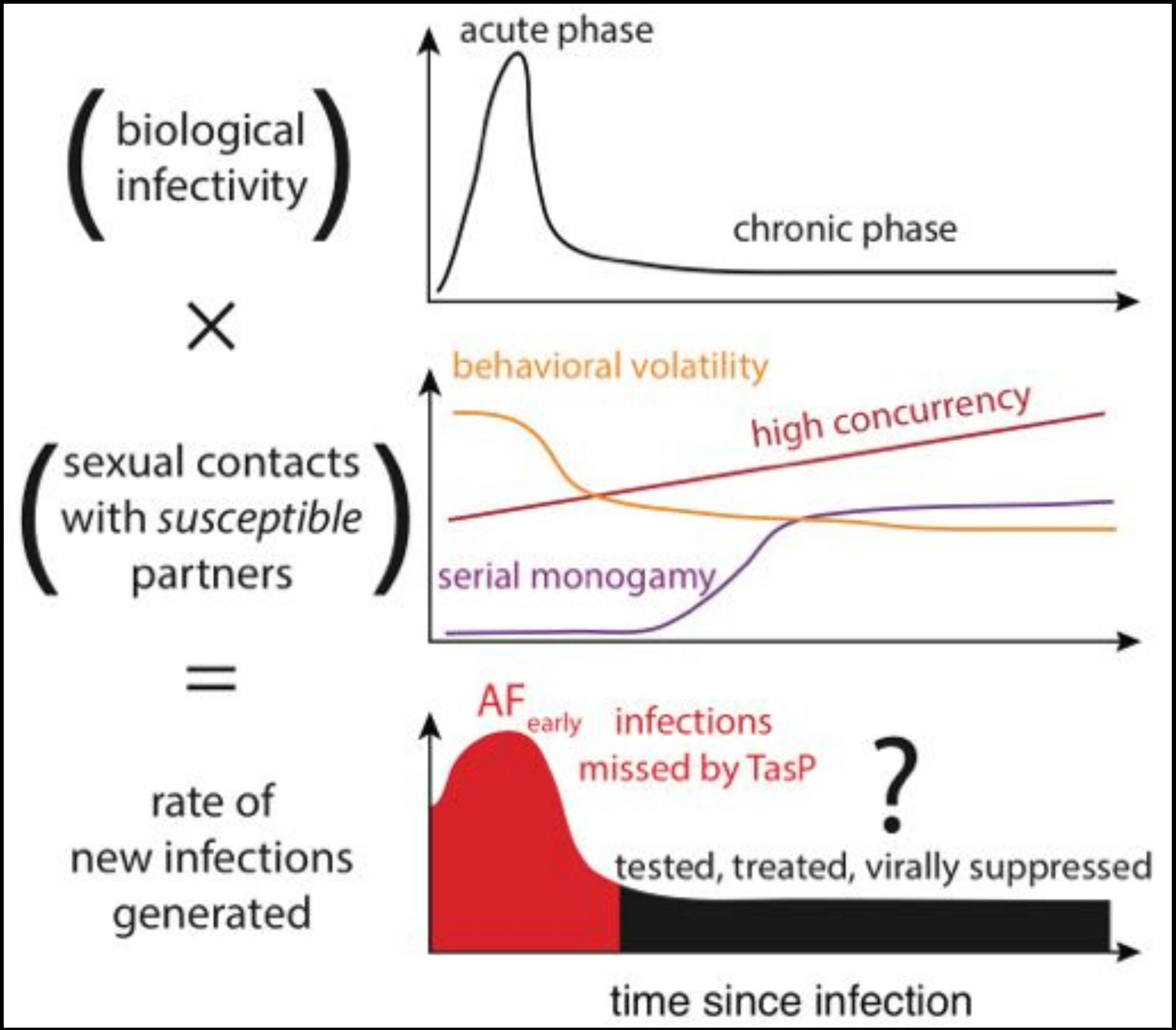

Bellan et al. 2015. *PLOS Medicine*.