

Heterogeneity, contact patterns and modeling options

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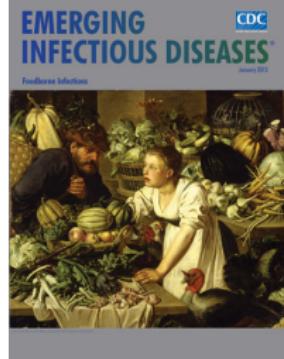
DAIDD 2020

Goals

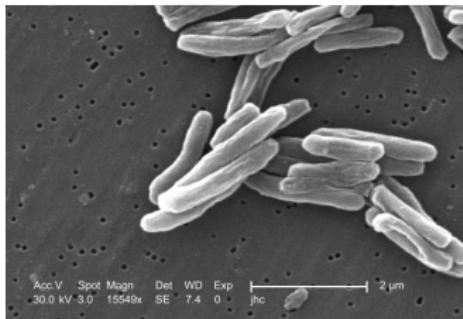
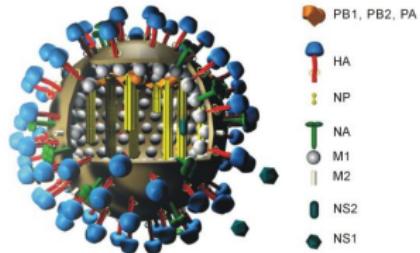
- ▶ Explain the importance of heterogeneity on patterns of disease spread
 - ▶ Focus on different types of human heterogeneity
- ▶ Discuss ways in which homogeneous models fail to match observed dynamics
- ▶ Use simple models to explore qualitative effects of heterogeneity on modeling conclusions
- ▶ Briefly introduce some methods that are used to incorporate heterogeneity in models

The resilience of infectious disease

1967: It's time to close the book on infectious diseases



Pathogen evolution



Human heterogeneity



Human heterogeneity (present)



Human heterogeneity (present)



Outline

Homogeneous disease models

The importance of heterogeneity

Take break

Effects of heterogeneity

Modeling approaches

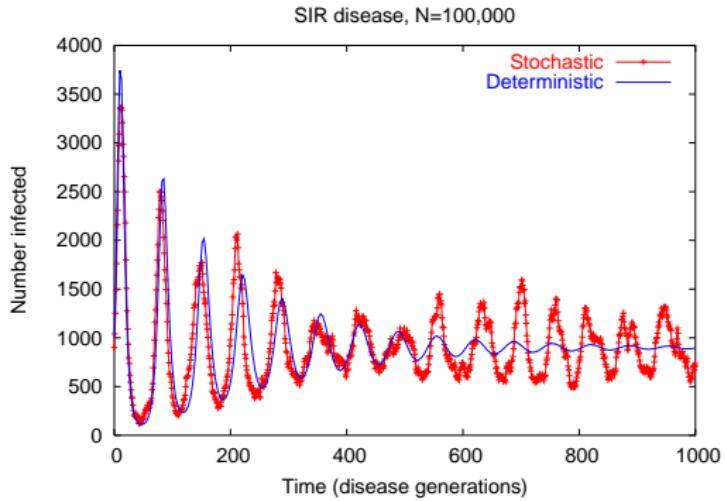
Expanding our models

- ▶ **Homogeneous** models assume everyone has the same:
 - ▶ disease characteristics (e.g. susceptibility, tendency to transmit)
 - ▶ mixing rate
 - ▶ probability of mixing with each person
- ▶ **Heterogeneous** models allow people to be different

The basic reproductive number

- ▶ \mathcal{R}_0 is the number of people who would be infected by an infectious individual *in a fully susceptible population*.
- ▶ $\mathcal{R}_0 = \beta/\gamma = \beta D = (cp)D$
 - ▶ c : Contact Rate
 - ▶ p : Probability of transmission (infectivity)
 - ▶ D : Average duration of infection
- ▶ A disease can invade a population if and only if $\mathcal{R}_0 > 1$.

Equilibrium



- ▶ Equilibrium is worth knowing even if the disease doesn't reach equilibrium
- ▶ System will move around the equilibrium

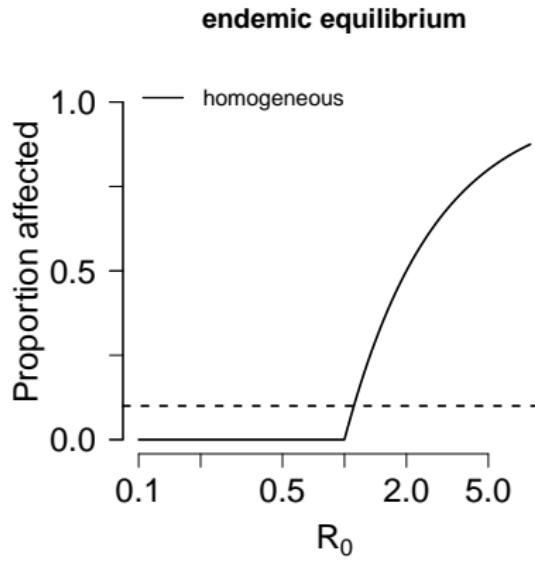
Equilibrium analysis

- ▶ \mathcal{R}_{eff} is the number of people who would be infected by an infectious individual *in a general population*.
- ▶
$$\mathcal{R}_{\text{eff}} = \mathcal{R}_0 \frac{S}{N} = pcD \frac{S}{N}$$
- ▶ At equilibrium: $\mathcal{R}_{\text{eff}} = \mathcal{R}_0 \frac{S}{N} = 1.$
- ▶ Thus: $\frac{S}{N} = 1/R_0.$
- ▶ Proportion ‘affected’ is $V = 1 - S/N = 1 - 1/R_0.$

Proportion affected

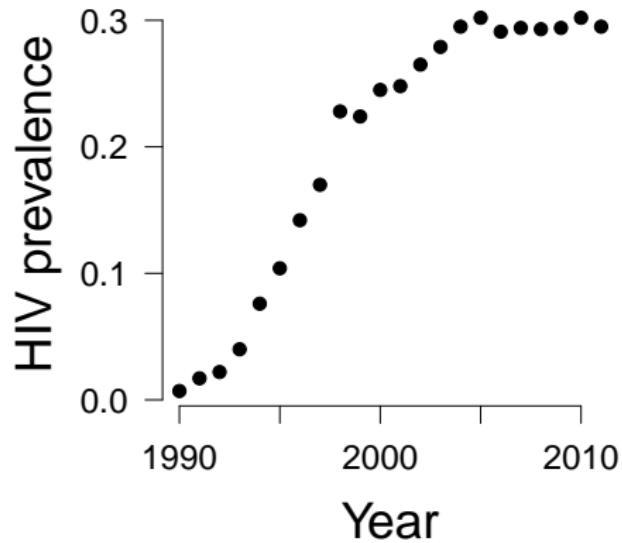
- ▶ Proportion ‘affected’ is $V = 1 - S/N = 1 - 1/R_0$.
 - ▶ * The same formula as the critical vaccination proportion!
 - ▶ * If this proportion is made unavailable, the disease cannot spread
 - ▶ * At least, in the homogeneous case

Homogeneous endemic curve

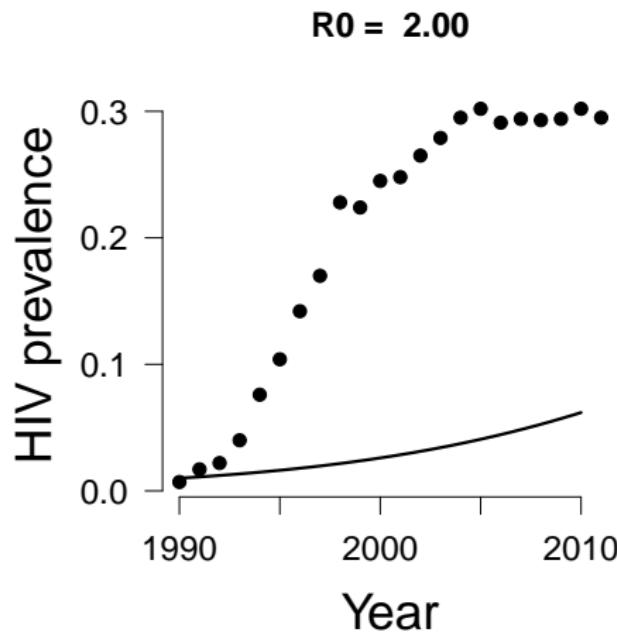


- ▶ Threshold value
- ▶ Sharp response to changes in factors underlying transmission
- ▶ Works – sometimes
- ▶ Sometimes predicts unrealistic sensitivity

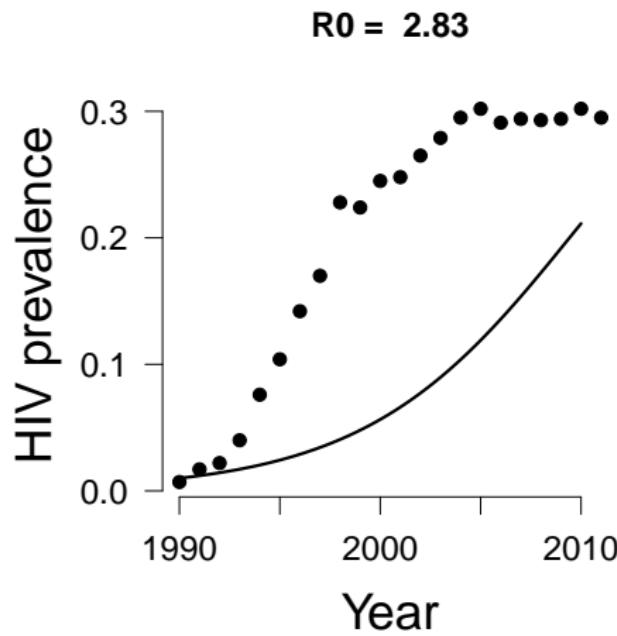
Disease dynamics (present)



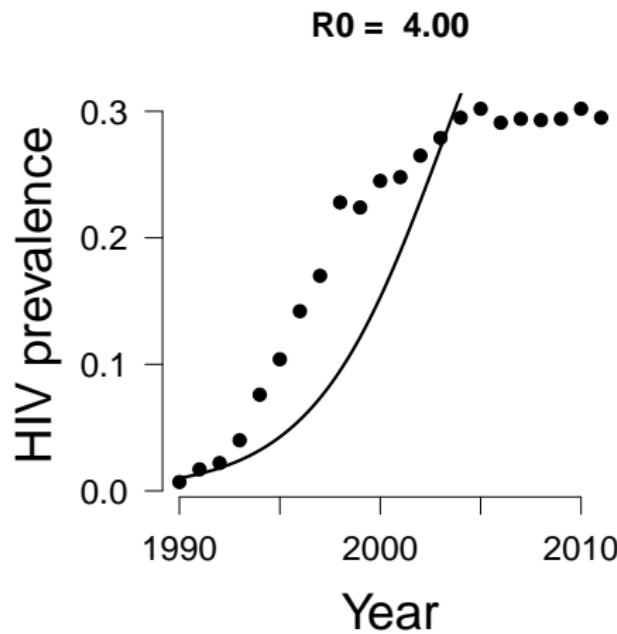
Homogeneous assumptions (present)



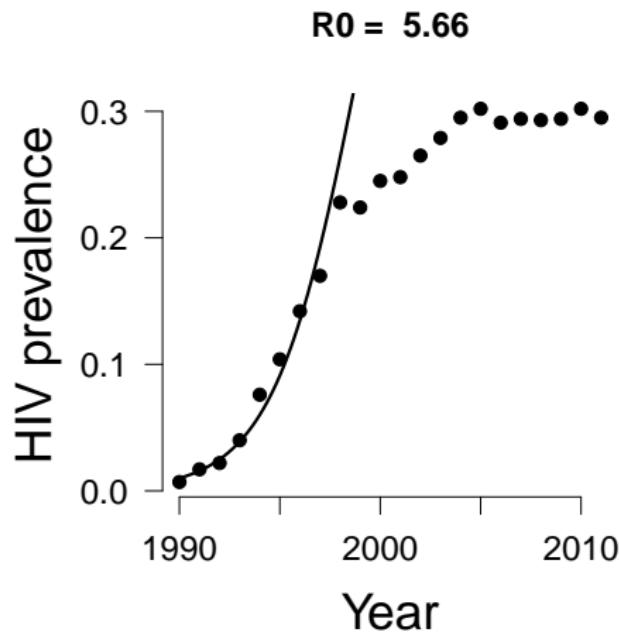
Homogeneous assumptions



Homogeneous assumptions



Homogeneous assumptions



Homogeneous dynamics

- ▶ For many diseases, homogeneous models tend to predict:
 - ▶ Too high of an equilibrium, when matching growth rate
 - ▶ Too low of a growth rate, when matching equilibrium

Outline

Homogeneous disease models

The importance of heterogeneity

Take break

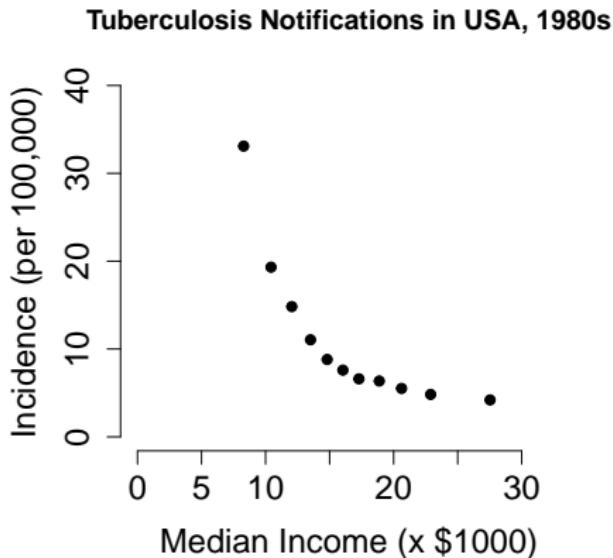
Effects of heterogeneity

Modeling approaches

Beyond homogeneity

- ▶ Flavors of heterogeneity
 - ▶ among hosts
 - ▶ spatial
 - ▶ demographic (discreteness of individuals)
 - ▶ temporal
 - ▶ others

Heterogeneity in TB



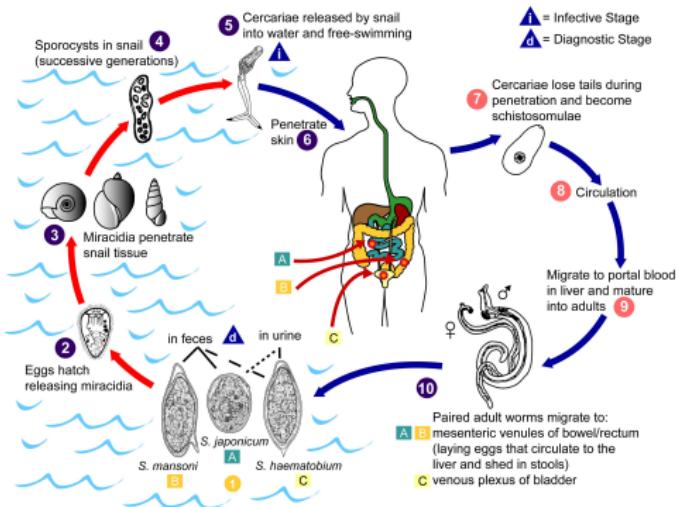
- ▶ **Progression:**
Nutrition, stress
- ▶ **Contact:**
Overcrowding, poor ventilation
- ▶ **Cure:** Access to medical care

Heterogeneity in other diseases

- ▶ **STDs:** Sexual mixing patterns, access to medical care
- ▶ **Influenza:** Crowding, nutrition
- ▶ **Malaria:** Attractiveness to biting insects, geographical location, immune status
- ▶ **Every disease!**

Large-scale heterogeneity

Schistosomiasis



- ▶ For schistosomiasis, the worldwide average $\mathcal{R}_0 < 1$
- ▶ Disease persists because of specific populations with $\mathcal{R}_0 > 1$.
- ▶ This effect operates at many scales.

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Effects of heterogeneity

Modeling approaches

Take break



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Heterogeneity among hosts

- ▶ Differences among people are pervasive, large and often correlated
- ▶ We often consider transmission probability as the product of two components:
 - ▶ The "infector" has tendency to infect τ
 - ▶ The "recipient" has susceptibility σ
- ▶ Then $\mathcal{R}_0 = pcD = (\sigma\tau)cD$,
- ▶ Why do we assume this is multiplicative?
 - ▶ * Convenience, question this assumption

Equilibrium calculations

- ▶ Assume $p = \sigma\tau$ has a susceptibility component and a transmission component:
 - ▶ $\mathcal{R}_0 = \sigma\tau cD$
 - ▶ $\mathcal{R}_{\text{eff}} = \sigma\tau cDS/N$
 - ▶ Equilibrium $S/N = 1/\mathcal{R}_0$
 - ▶ Proportion affected: $1 - 1/\mathcal{R}_0$

Equilibrium calculations with heterogeneity

- ▶ τD applies to infectious individuals $\rightarrow \tau_I D_I$
- ▶ σ applies to susceptible individuals $\rightarrow \sigma_S$
- ▶ c is complicated $\rightarrow c_S c_I / \bar{c}$

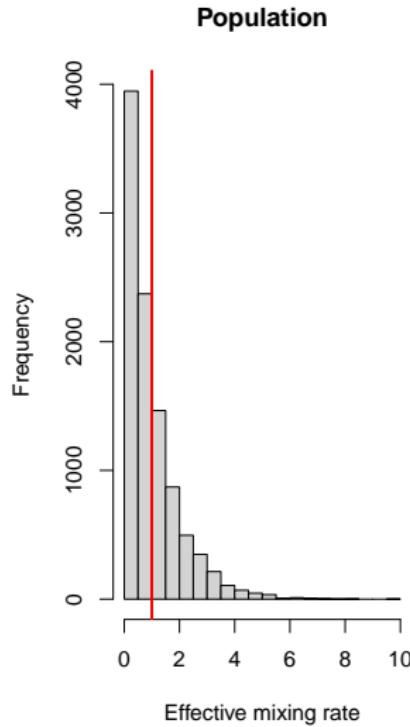
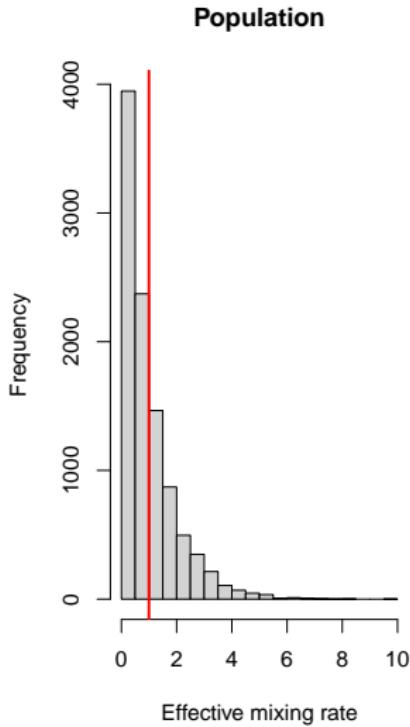
Equilibrium calculations with heterogeneity

- ▶ $\mathcal{R}_0 = \sigma_S \tau_I c_x D_I$ measured during *invasion*
- ▶ $\mathcal{R}_{\text{eff}} = \sigma_S \tau_I c_x D_I S/N$ measured at *equilibrium*
- ▶ Equilibrium $S/N \neq 1/\mathcal{R}_0$

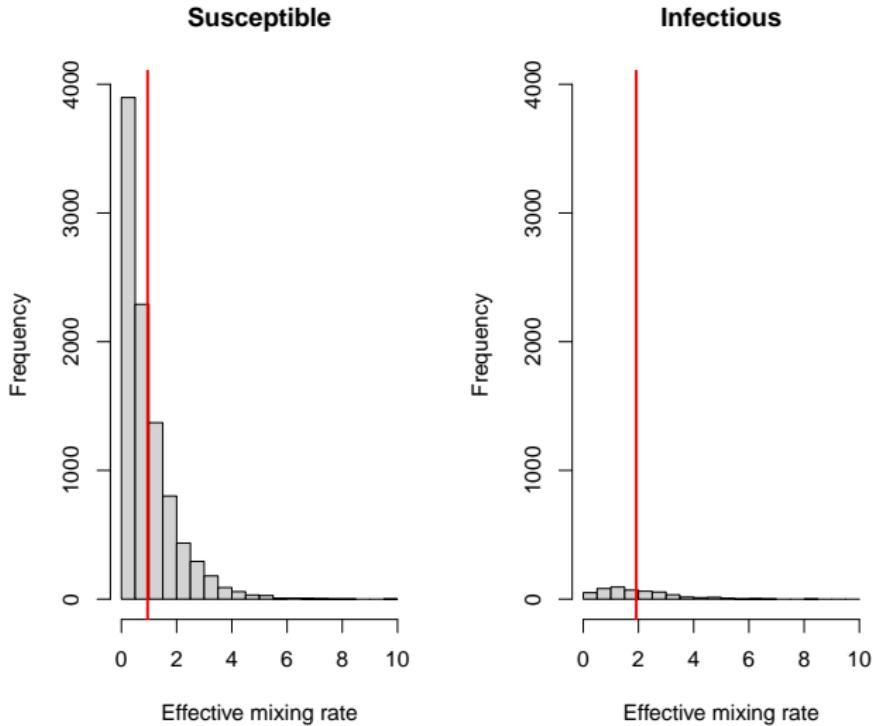
How does \mathcal{R} change?

- ▶ Imagine a disease spread by people who differ only in their effective mixing rates
- ▶ If the disease has just started spreading in the population, how do c_S and c_I compare to \bar{c} ?
 - ▶ $c_S \approx \bar{c}; c_I > \bar{c}$.
- ▶ If the disease is very widespread in the population?
 - ▶ $c_S < \bar{c}; c_I \rightarrow \bar{c}$.

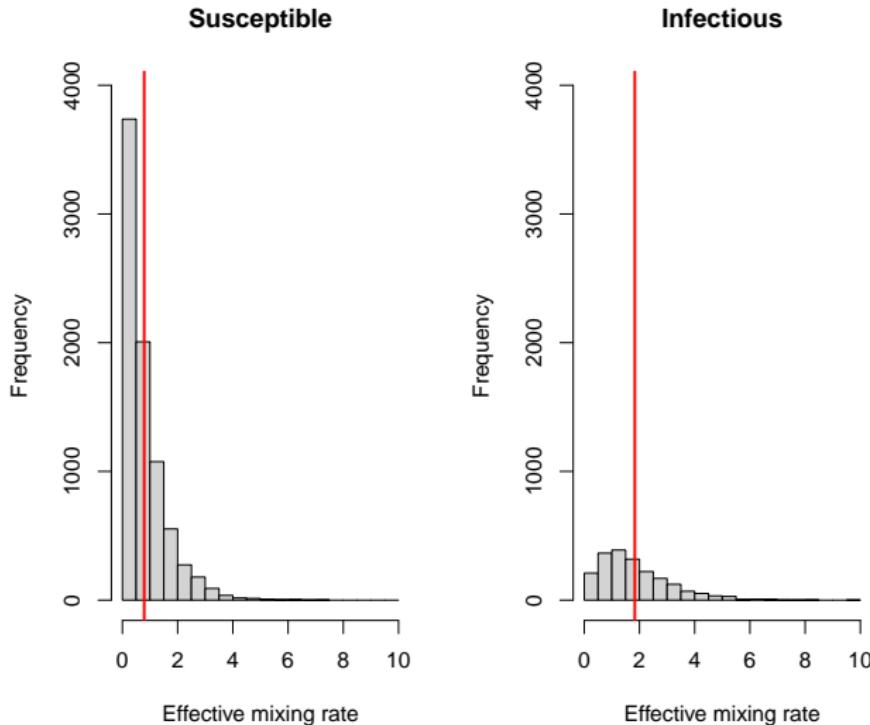
Simulated population



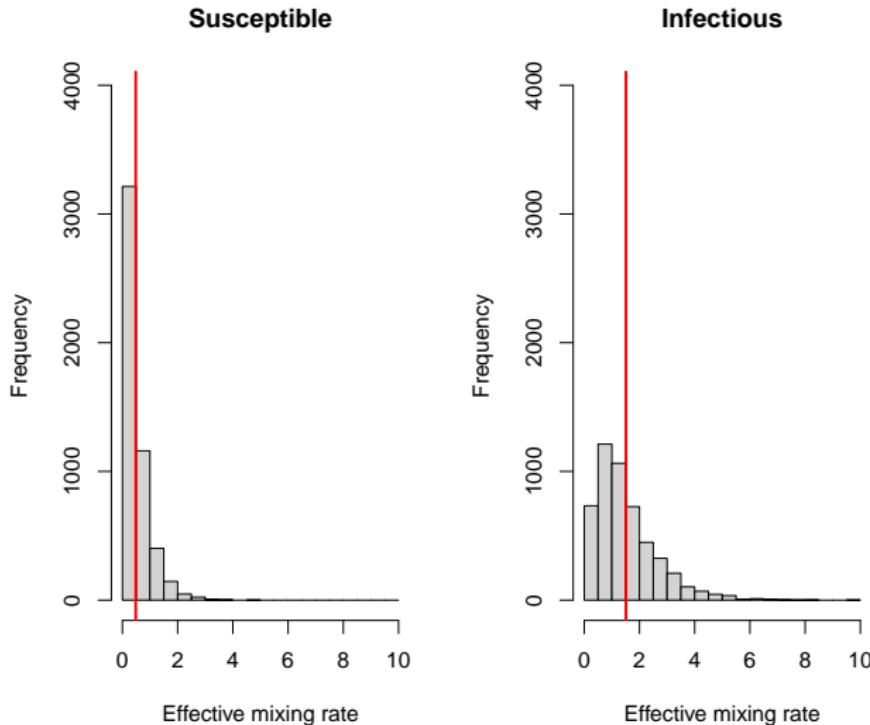
Early (5% infection)



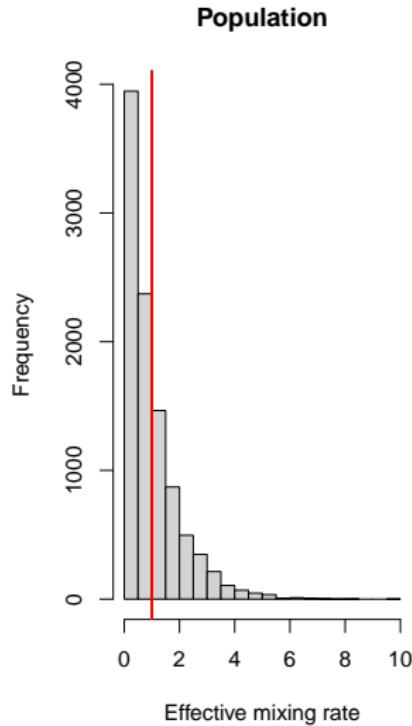
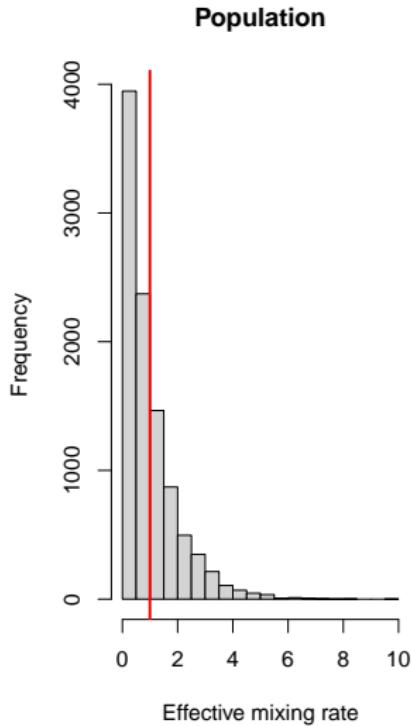
Mid (20% infection)



Mid (50% infection)



Simulated population (repeat)



Simpson's paradox



- ▶ What happens when a peanut farmer is elected to the US Senate?
- ▶ The average IQ goes up in both places!

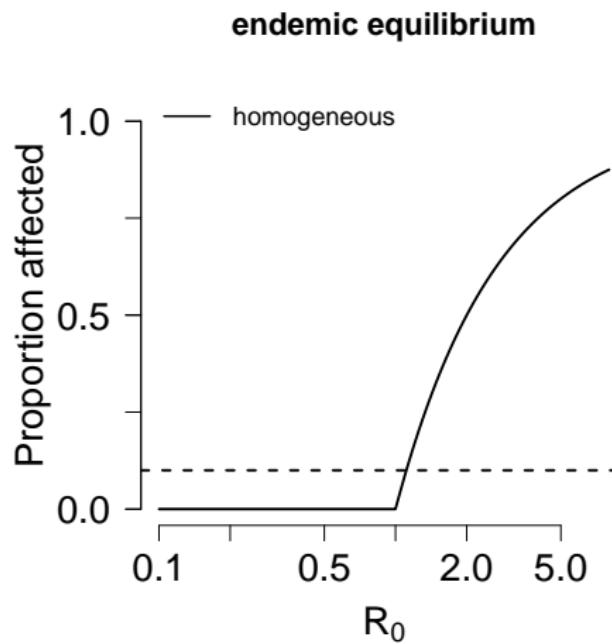
The basic reproductive number

- ▶ When the disease invades:
 - ▶ The susceptible population \approx the general population
 - ▶ The infectious population is likely to have higher values of c , D and/or τ
- ▶ \mathcal{R}_0 is typically greater than you would expect from a homogeneous model

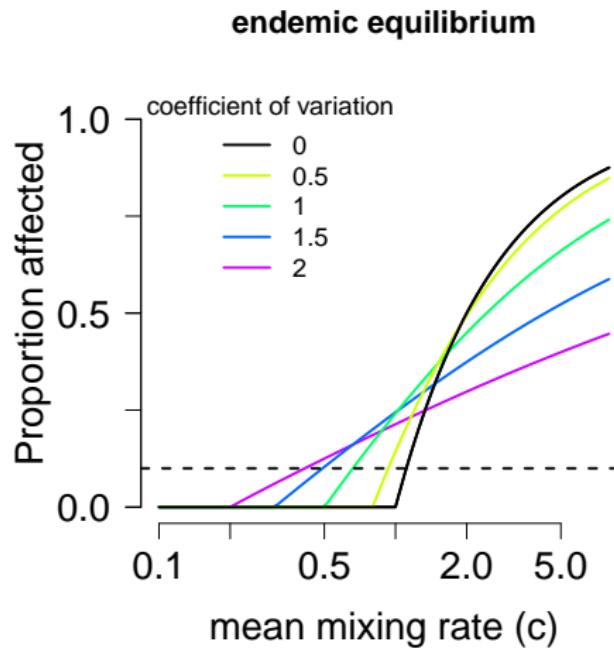
Equilibrium analysis

- ▶ As disease prevalence goes up:
 - ▶ Susceptible pool is the most resistant, or least exposed group
 - ▶ Infectious pool looks more like the general population.
- ▶ → lower proportion affected *for a given value of \mathcal{R}_0 .*

Homogeneous endemic curve (repeat)

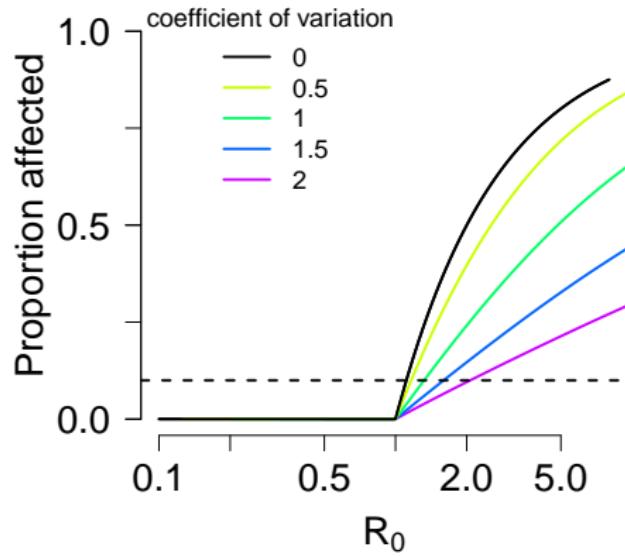


Heterogeneous endemic curves



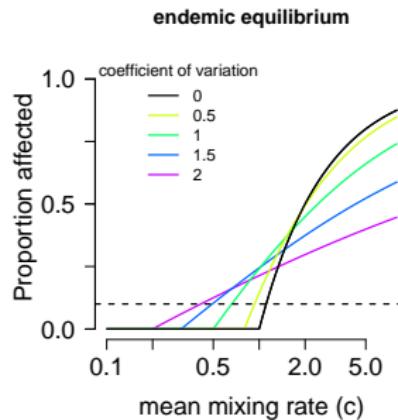
Heterogeneous endemic curves

endemic equilibrium



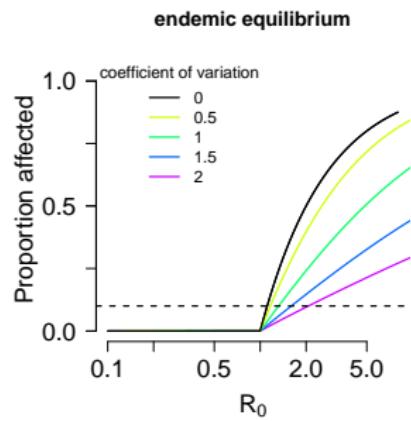
Heterogeneity and disease

- ▶ Heterogeneity has a double-edged effect
 - ▶ Effects of disease are *lower* for a given value of \mathcal{R}_0 .
 - ▶ But \mathcal{R}_0 is *higher* for given mean values of factors underlying transmission



Heterogeneous endemic curves

- ▶ Heterogeneity makes the endemic curve flatter
- ▶ Disease levels are more resistant to change



How diseases reach equilibrium

- ▶ Diseases that invade have high values of \mathcal{R}_0
- ▶ \mathcal{R}_{eff} must be 1 at equilibrium
 - ▶ Potentially infectious contacts are wasted
 - ▶ Many potential contacts are not susceptible (affected by disease)
 - ▶ Those not affected less susceptible than average
 - ▶ Infectious pool less infectious

Spatial and network models

- ▶ Individual-level, or spatial, heterogeneity also usually increases wasted contacts
- ▶ Infectious people meet:
 - ▶ people with similar social backgrounds
 - ▶ people with similar behaviours
 - ▶ people who are nearby geographically or in the contact network
- ▶ More wasted contacts further flatten the endemic curve

Outline

Homogeneous disease models

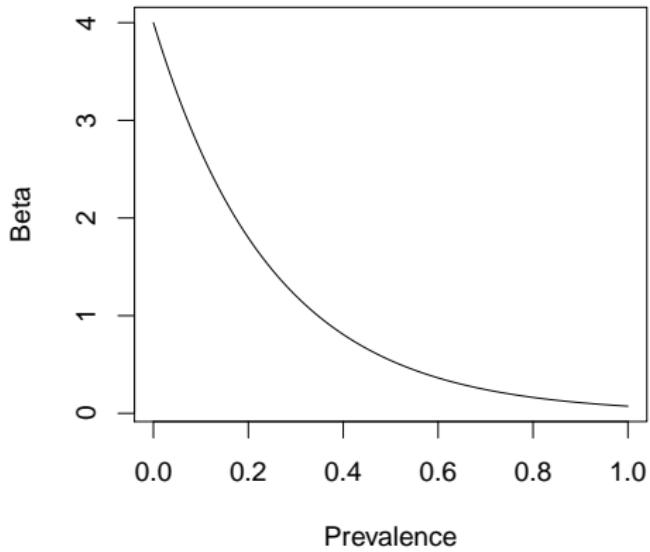
The importance of heterogeneity

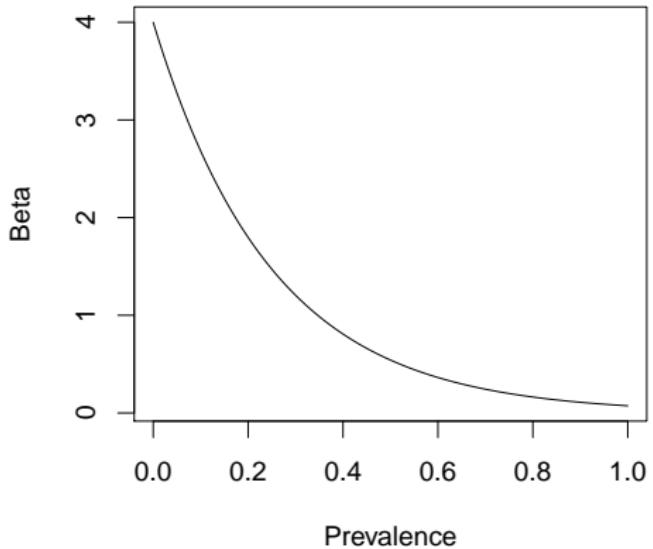
Take break

Effects of heterogeneity

Modeling approaches

Phenomenological





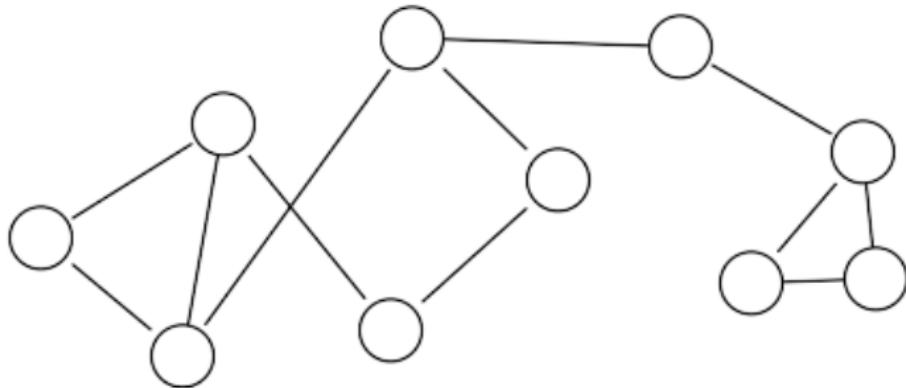
- ▶ Simply make β go down with prevalence,
 $\beta = B \times:$
 - ▶ $e^{-\alpha P}$
 - ▶ $(1 - P)^s$
 - ▶ $(1 - P/s)^{\alpha s}$

Multi-group models

- ▶ Divide the population into groups.
 - ▶ cities and villages
 - ▶ rich and poor
 - ▶ high and low sexual activity
 - ▶ age, gender
 - ▶ ...
- ▶ Even if details are not correct, heterogeneity will emerge and move model in the right direction

Individual-based models

○ **Individual**

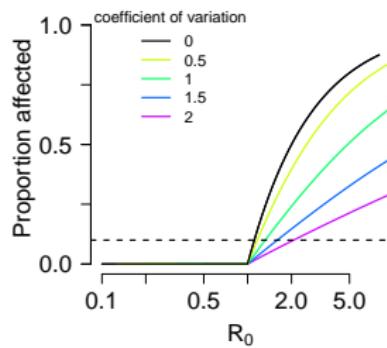


- ▶ Allow many possibilities:
 - ▶ vary individual characteristics
 - ▶ add a network of interactions
 - ▶ let the network change
- ▶ Individual-based approaches require stochastic models

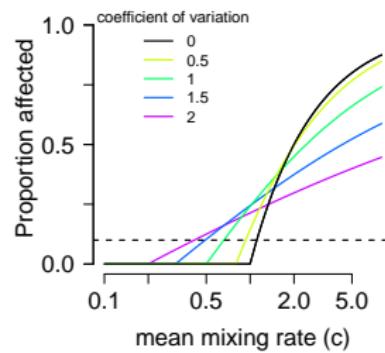
Summary (present)



endemic equilibrium



endemic equilibrium



Summary



- ▶ People are heterogeneous in many ways
 - ▶ ... and on many scales
- ▶ Simple models give us important qualitative insights
 - ▶ Diseases in heterogeneous populations are likely to be more robust to change than expected from homogeneous models
- ▶ More complicated models will often be necessary
 - ▶ And it may be helpful to build complexity gradually



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