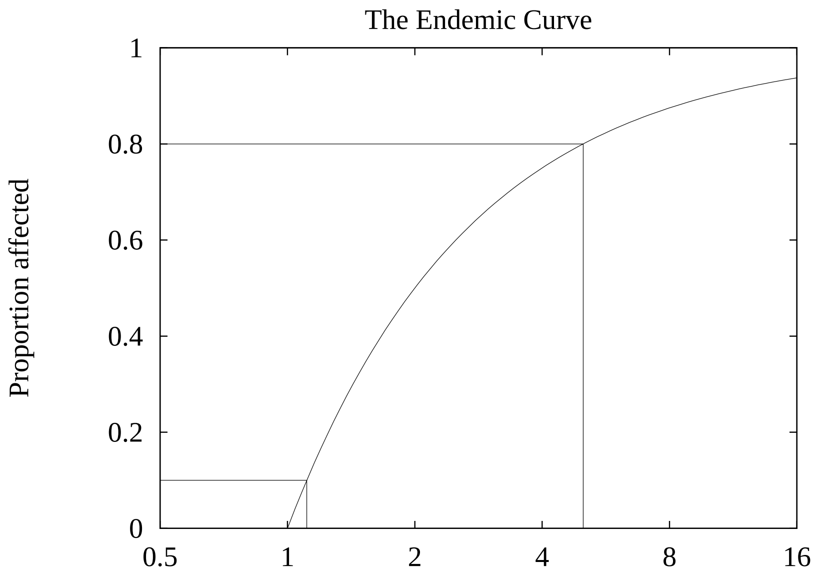
The basic reproductive number

- $\mathcal{R}_0$ is the number of people who would be infected by an infectious individual in a susceptible population.
- $\mathcal{R}_0 = pcD = \beta D = \beta/\gamma$.
  - p: Probability of transmission
  - c: Contact Rate
  - D: Average duration of infection
- A disease can invade a population $\iff \mathcal{R}_0 > 1$.

Equilibrium analysis

- More generally, the number of new cases per case is $\mathcal{R} = pcD\frac{S}{N} = \beta D\frac{S}{N} = \mathcal{R}_0\frac{S}{N}$.
- At equilibrium: $\mathcal{R} = \mathcal{R}_0\frac{S}{N} = 1$.
- Thus: $\frac{S}{N} = 1/R_0$.
- Proportion 'affected' is $V = 1 - S/N = 1 - 1/R_0$.

The endemic curve



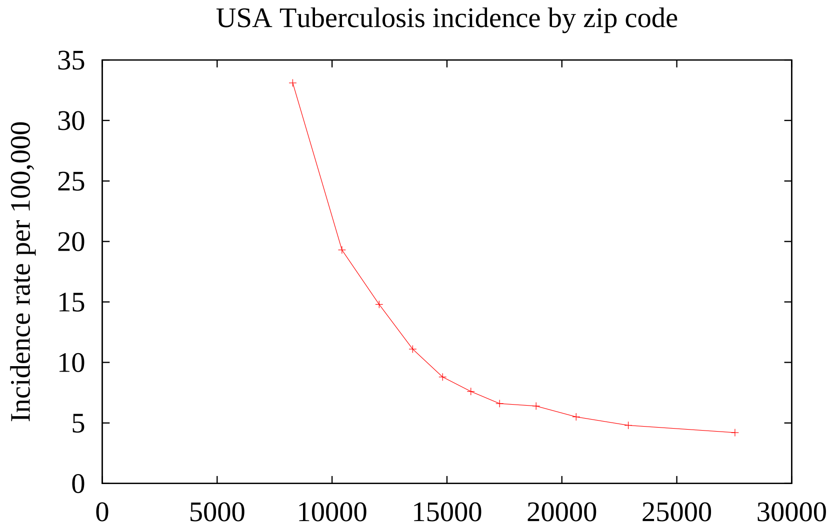
Beyond the homogeneous model

- Heterogeneity among hosts
- Heterogeneity in space
- Demographic heterogeneity (individuality)
- Temporal heterogeneity
  - "waiting" distributions
  - seasonality

Heterogeneity among hosts

- Differences among people are pervasive, large and often correlated
- We break down the transmission probability into a focus and a victim' component
  - $\mathcal{R}_0 = pcD = \sigma\tau cD$,
  - where σ measures intrinsic susceptibility and τ intrinsic tendency to transmit.
  - Why do we assume this is multiplicative?

Heterogeneity in TB



Disease Heterogeneity in TB

- *Progression to Disease*: Nutrition, stress
- *Contact Rate*: Overcrowding, poor ventilation
- *Cure Rate*: 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
- *Many others*

Parametric heterogeneity

Imagine an aspect space indexed by $a \in \mathcal{A}$. Each a is associated with a value for $\sigma(a)$, $\tau(a)$, $c(a)$ and $D(a)$. We can model heterogeneity explicitly, using boxes, or distributions, or seek approximations based on the moments of the parameters: e.g., means, variances and covariances across the aspect space.

$$\bar{c} = \int_{\mathcal{A}} c(a)N(a)da$$

$$\sigma_c^2 = \int_{\mathcal{A}} (c(a) - (\bar{c}))^2 N(a)da$$

Mixing function

- $p(a, b)$ gives the proportion of group a's contacts that are with members of group b.
- $\int p(a, b)db = 1$
- $c(a)N(a)p(a, b) = c(b)N(b)p(b, a)$
- Simplest case is proportional mixing:
  - $p(a, b) = \dfrac{c(b)N(b)}{\bar{c}N}$

Next-generation framework

- We can analyze the relationship between risk factors and equilibria without making assumptions about waiting times, using a next-generation framework:
- *How many new cases are caused by a given case?*
  - $\mathcal{R}_0$ is the expected number of new cases per case along the eigendistribution of cases near the disease-free equilibrium.
  - The endemic equilibrium is where a distribution of cases regenerates itself for the next generation.

Heterogeneity and $\mathcal{R}_0$

Proportional mixing

$$\mathcal{R}_0 = \frac{\left\langle c^2 \sigma \tau D \right\rangle_N}{\langle c \rangle_N}$$

- Heterogeneity in susceptibility, transmissibility or duration alone has no effect on $\mathcal{R}_0$ and thus on whether a disease persists in a population.
- Heterogeneity in contact rate alone increases $\mathcal{R}_0$. The “effective” contact rate is given by $c_e = \bar{c}(1 + V_c^2)$, where V_c is the coefficient of variation of the distribution of c.
- Correlations between other parameters can have a similar effect (e.g., if those who are more susceptible are on average also more able to transmit).

Heterogeneity and $\mathcal{R}_0$

Assortative mixing

- Assortative mixing means the tendency of like to mix with like
- Assortative mixing combined with any kind of heterogeneity will increase $\mathcal{R}_0$.

Heterogeneity and equilibrium

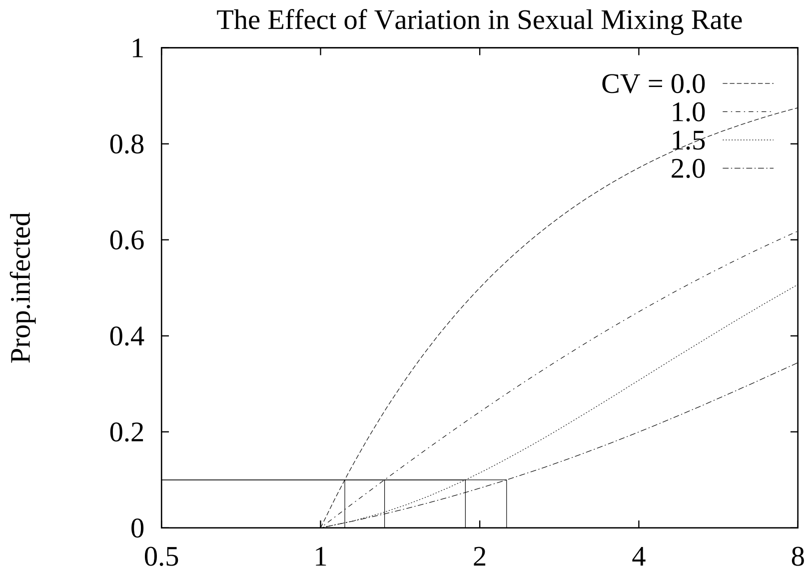
- If a disease persists, in the long term the geometric mean reproductive number $\langle \mathcal{R} \rangle = 1$
- The factors that reduce $\mathcal{R}$ from $\mathcal{R}_0$ to 1 determine the level of equilibrium.
  - If the only factor that changes is S/N, we have the classic endemic curve
- In a heterogeneous population, the infected population and the susceptible population generally both become less risky on average as the disease spreads!
  - Makes equilibrium disease level lower for a given risk
  - Conversely, risk may be higher than you think

Heterogeneity and equilibrium

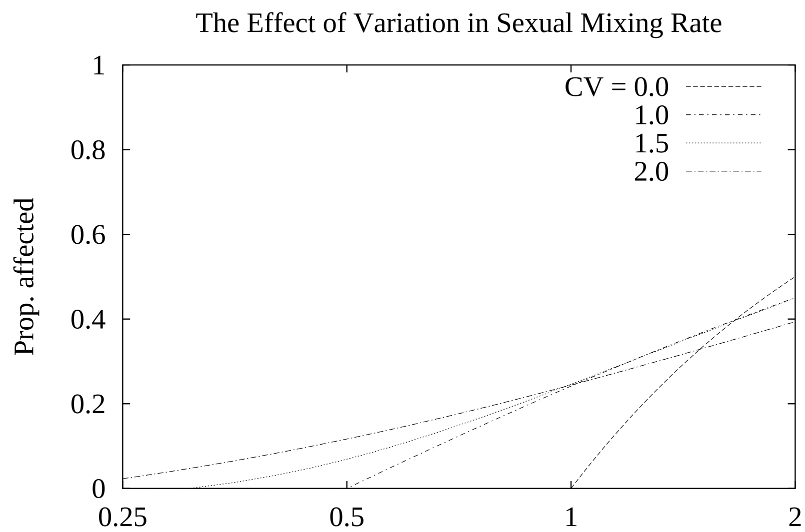
Proportional mixing

- $\mathcal{R}_0 = \langle c\sigma \rangle_N \frac{\langle c\tau D \rangle_{\hat{I}}}{\bar{c}}; \quad 1 = \langle c\sigma \rangle_{\tilde{S}} \frac{\langle c\tau D \rangle_{\tilde{I}}}{\bar{c}} \frac{S}{N}$
- Variation in transmissibility alone has no effect on average transmission, or on the endemic curve.
- Variation in susceptibility alone reduces transmission at equilibrium, thus reduces level of disease (flattens the curve).
- Variation in contact rate alone reduces transmission at equilibrium compared to during invasion (flattens the curve).
  - Effect on equilibrium level of disease is mixed.

Heterogeneous population



Heterogeneous population



Host heterogeneity summary

- Heterogeneity makes diseases harder to eliminate than would be predicted from the basic model
  - Assortative mixing
  - Demographic clustering
- Disease-control strategies should take heterogeneity on a variety of scales into account.
- Simple moment-based approximations can help extend the usefulness of the endemic curve – relationships between risk factors and disease level – to heterogeneous populations.