LIFE DATA EPIDEMIOLOGY

Lecture 5: Risk structure

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Disease-induced mortality

- We found 2 equilibria: disease-free or endemic, the latter if $R_0>1$ (also stable)
  - for frequency-dep:

$$x_\infty = \frac{\nu}{\beta(1-\rho)}(R_0-1) \qquad s_\infty = \frac{\nu+\mu}{\beta(1-\rho)} = 1/R_0$$

also, #individuals $N_\infty = \frac{\lambda}{\nu}\left(\frac{R_0(1-\rho)}{(R_0-\rho)}\right)$

  - for density-dep: $R_0 = (\lambda/\nu)\,\boxed{(1-\rho)\beta / (\nu+\mu)}$

$=1/s_\infty$

Late mortality

- If disease-induced mortality is too high → probability of dying = $\rho \longrightarrow 1$ but then (for both models) R_0 drops to 0
  - also the share of infected at equilibrium is always 0 and the disease is never endemic
  - the reason is that new infected die almost instantly and cannot spread the disease
- We may want another model where people only die at the **end** of the infection

Late mortality

- With late mortality:

(death by the disease are included implicitly, they do not show up as recovered)

$$\frac{ds}{dt} = \lambda - (\beta x + \nu)s$$

$$\frac{dx}{dt} = \beta s x - (\nu + \mu)x$$

$$\frac{dr}{dt} = (1-\rho)\ \mu x - \nu r$$

- This is also analogous to the standard SIR model, with same R_0-related properties

Population control

- Another example:
  - disease always fatal
  - its death rate = μ
  - (no recovered class)
  - we need $N = S+X$

$$\frac{dS}{dt} = \lambda(S+X) - (\beta X + \nu)S$$

$$\frac{dX}{dt} = \beta SX - (\nu + \mu)X$$

- From (2), equilibrium if: $X=0$, or $\beta S = \nu+\mu$
  - disease-free or endemic equilibrium
- But $X=0$ in (1) yields $\lambda S = \nu S$: cannot be!
  - thus, disease-free equilibrium is unstable

Population control

- $X=0$ is unstable as population cannot stay constant→exponential growth with rate $\lambda-\nu$
- What if $S=(\nu+\mu)/\beta$? Then:

  $\lambda(\nu+\mu)/\beta + \lambda X - (\nu+\mu) X + \nu (\nu+\mu)/\beta = 0$

  leading to: $X = (\lambda-\nu)(\nu+\mu) / [\beta (\nu+\mu-\lambda)]$
  - endemic equilibrium... only if $\lambda<\nu+\mu$ otherwise the value of X is negative!
  - if $\lambda>\nu+\mu$ endemic equilibrium is unstable, N grows exponentially with rate $\lambda-\nu-\mu$

Population control

- A further variant
  - same as before but
  - births are only caused by healthy individuals (disease is debilitating)

$$\frac{dS}{dt} = \lambda S - (\beta X + \nu)S$$

$$\frac{dX}{dt} = \beta SX - (\nu + \mu)X$$

- Now $S' = (\lambda - \nu - \beta X)\, S$; $X' = (\beta S - \nu - \mu)\, X$
  - these are the **Lotka-Volterra equations** for population dynamics (predator-prey)

Population control

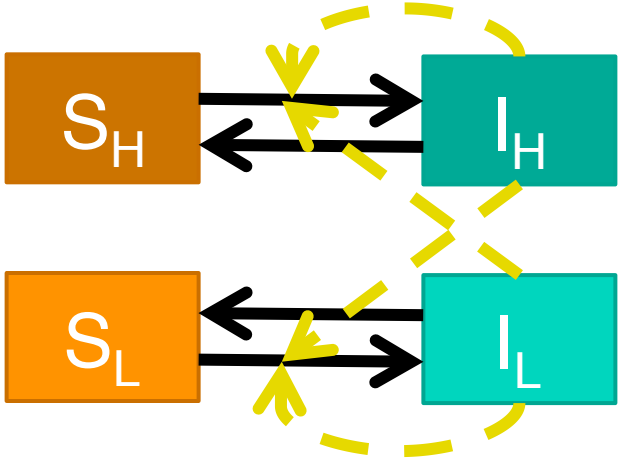
- There must be again two equilibria (unstable disease-free + endemic with
  $S_\infty = (\nu+\mu)/\beta$ and $X_\infty = (\lambda-\nu)/\beta$)
  - but $\Re$[both endemic eigenvalues]=0 meaning cyclically oscillatory dynamics
- This means the system alternates "prevalent S" / "prevalent X" over and over
  - typical behavior of some epidemic plagues

Model heterogeneity

- Some diseases inherently violate the assumption of homogeneous individuals and/or homogeneous mixing
- Diseases may have variable contagious behavior across the population
  - risk-structured diseases (e.g., STDs)
  - age-structured diseases
  - multiple pathogens
  - multiple hosts (vectored, zoonoses)

Risk structure

- These aspects can still be included in a compartmental model with more states
- For example: high/low risk
  - for simplicity consider just an SIS model



- it is like two separate populations that can infect each other

Risk structure

- Instead of parameter β we need matrix $\boldsymbol{\beta}$

$$\boldsymbol{\beta} = \begin{pmatrix} \beta_{HH} & \beta_{HL} \\ \beta_{LH} & \beta_{LL} \end{pmatrix}$$

  - **WAIFW** (who acquires infection from whom)
  - β_{ab} = rate to *a* from *b*

- H="high": $\beta_{HH}+\beta_{HL} > \beta_{LH}+\beta_{LL}$; and usually:
  - individuals are born H or L and stay like that forever: n_H = H/N = $s_H + x_H$, same for L
  - assortative mixing: $\beta_{ii} > \beta_{ij}$ with $i \neq j$
  - symmetry $\beta_{HL} = \beta_{LH}$

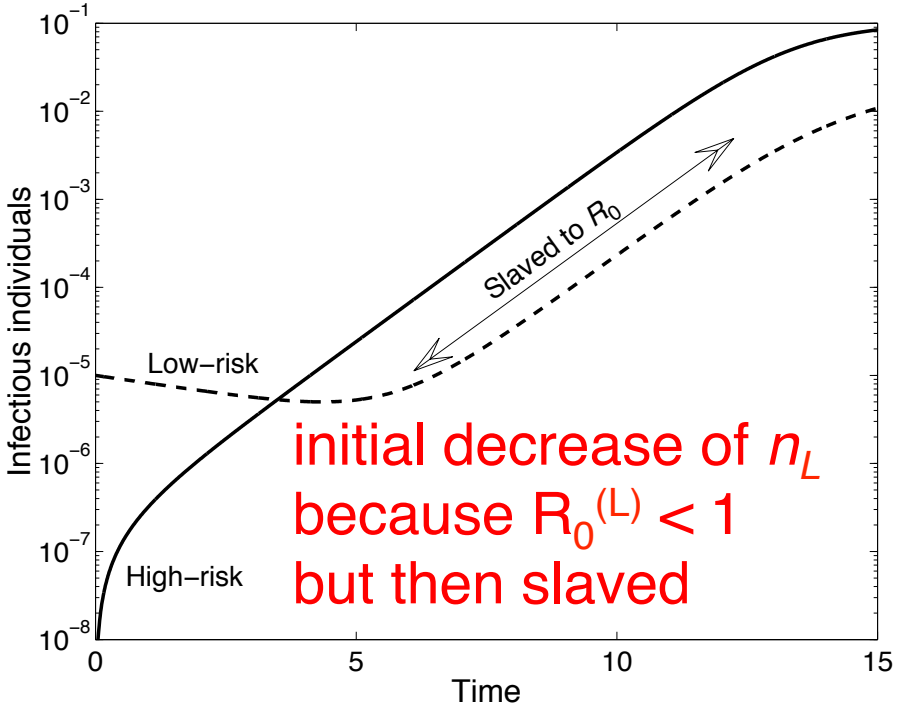
Risk structure

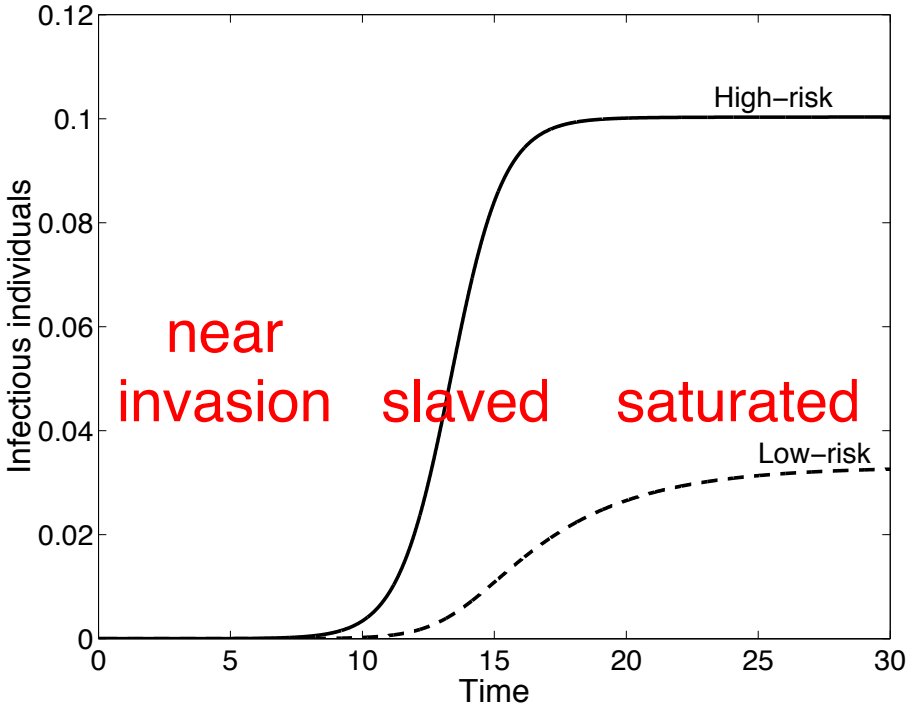
- Usually, the disease has the same course: so just one μ, which is convenient
  - otherwise we need two μs (μ_H and μ_L)

- One possibility is to consider two R_0s:
  - contacts are equally likely, proportional to n_H--n_L split, e.g.: $R_0^{(H)} = (n_H \beta_{HH} + n_L \beta_{LH}) / \mu$
  - depending on the split, maybe $\beta_{LL} > \mu$ but $R_0^{(L)} = (n_H \beta_{HL} + n_L \beta_{LL}) / \mu < 1$

Risk structure

- $R_0^{(H)}$, $R_0^{(L)}$ are meaningful at the start of the invasion but when x_H and x_L increase, group dynamics become slaved (coupled)





R_0 with risk structure

- The system of differential equations is

$$\frac{dx_H}{dt} \approx (\beta_{HH} n_H - \mu) x_H + \beta_{HL} n_H x_L$$

$$\frac{dx_L}{dt} \approx \beta_{LH} n_L x_H + (\beta_{LL} n_L - \mu) x_L$$

  - for a consistent meaning of R_0, redefine it as #secondary infections caused in a naive population **once transient phases ended**

R_0 with risk structure

- The Jacobian matrix ***J*** of this system is:

$$\boldsymbol{J} = \begin{pmatrix} \beta_{HH} n_H - \mu & \beta_{HL} n_H \\ \beta_{LH} n_L & \beta_{LL} n_L - \mu \end{pmatrix}$$

- Its dominant eigenvalue Λ_1 gives the exponential dynamic in the slaved phase

$$x_H \propto e^{\Lambda_1 t} \quad \text{and} \quad x_L \propto e^{\Lambda_1 t}$$

- Spreading out if $\Lambda_1 > 0$ (akin to say: $R_0 > 1$)

R_0 with risk structure

- To compute R_0, define matrix $\boldsymbol{R}$ showing #secondary cases caused by each combination

$$\boldsymbol{R} = \begin{pmatrix} \beta_{HH} n_H / \mu & \beta_{HL} n_H / \mu \\ \beta_{LH} n_L / \mu & \beta_{LL} n_L / \mu \end{pmatrix}$$

- R_0 is the dominant eigenvalue of $\boldsymbol{R}$ and $x_L \propto e^{(R_0 - 1)\mu t}$ as the nonstructured case

R_0 with risk structure

- If no mixing (classes do not infect one another)

$$\boldsymbol{R} = \begin{pmatrix} \beta_{HH} n_H / \mu & 0 \\ 0 & \beta_{LL} n_L / \mu \end{pmatrix}$$

- → R_0 =weighted average of $R_0^{(H)}$ and $R_0^{(L)}$

- But even a not-so-large $\beta_{HL} = \beta_{LH}$ causes infection to mix → coupling → R_0 is higher

R_0 with risk structure

- Since we have an initial invasion and then a slaved trend, dynamics can be variegate
  - in the scenario previously plotted: μ=1, WAIFW is $\beta = \begin{pmatrix} 10 & 0.1 \\ 0.1 & 1 \end{pmatrix}$ and $n_H : n_L = 20:80$
  - here, x_L decreases at first and then catches up when slaved
  - this is because $R_0^{(H)} = 2.08$, $R_0^{(L)} = 0.82$, but the ultimate value is $R_0 = 2.0013$

R_0 with risk structure

- But we can even have the opposite trend
  - if μ=1, still $n_H : n_L$ = 20:80 but we take WAIFW as $\beta = \begin{pmatrix} 1 & 1.5 \\ 1.5 & 0.5 \end{pmatrix}$
  - we see that an initial infected in high-risk causes on average an increase of 1.4 secondary infections
- But the eventual dynamics follows a basic reproductive ratio $R_0 = 0.9083 < 1$

s_∞ and x_∞ with risk structure

- To solve the equilibrium and find e.g. $s_\infty^{(H)}$ (or $x_\infty^{(H)}$ or $s_\infty^{(L)}$ and so on) is in general difficult because of non-linear system
  - still, the system can be solved numerically
- Main practical conclusion: the asymptotic share of infecteds is usually low
  - in the previously shown example: $x_\infty^{(H)} \approx 0.1$, $x_\infty^{(L)} \approx 0.033$, although $R_0 \approx 2$

Eradication with risk structure

- Immediate consequence: a risk-structured disease is **difficult to eradicate**
  - the reason is that the asymptotic fraction of infected is generally low, but eradication requires to push R_0 (actually high) below 1
  - true e.g. for **random** vaccination, but... not for specific vaccination/treatment procedures specifically targeted especially towards **high-risk individuals**

Applications: STDs

- Risk structure is typically adopted when modeling STDs, where our assumptions about “risk” are usually respected
  - risk class easy to associate to #partners
  - connections tend to be assortative
  - persistence of the disease is usually due to few active spreaders in the high risk class
  - we can also think of a further connection with network graphs (sexual network)

Shredders vs. spreaders

- Many airborne infections have a special WAIFW in the presence of either super-shredders or super-spreaders
  - a super-shredder is an individual that is able to contaminate more secondary than usual (but he is not necessarily at high risk)
  - a super-spreader is more frequently in contact with others (he spreads more but he is also at higher risk himself)

Shredders vs. spreaders

- Transmission matrix with super-shredders:

$$\beta = \begin{pmatrix} \beta_{SS} & \beta_{SR} \\ \beta_{RS} & \beta_{RR} \end{pmatrix} = \begin{pmatrix} f\beta & \beta \\ f\beta & \beta \end{pmatrix}$$

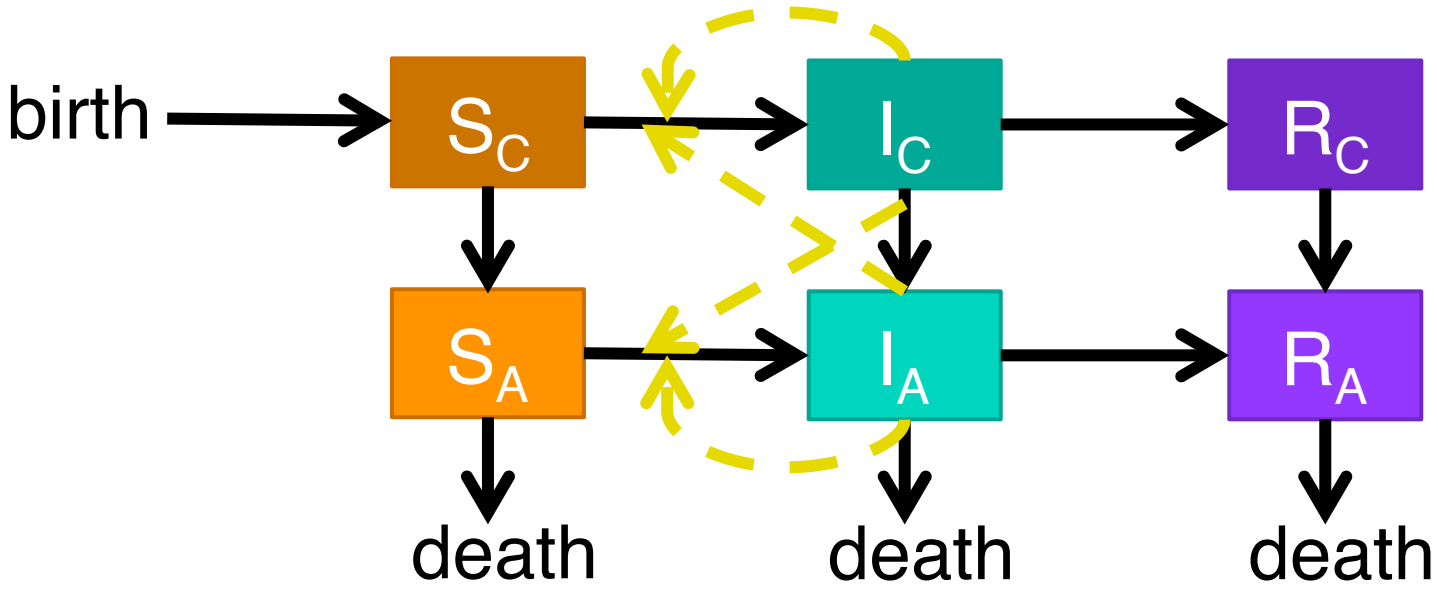
  - (symmetry is broken; factor $f > 1$ for S)

- Transmission matrix with super-spreaders:

$$\beta = \begin{pmatrix} \beta_{SS} & \beta_{SR} \\ \beta_{RS} & \beta_{RR} \end{pmatrix} = \begin{pmatrix} f^2\beta & f\beta \\ f\beta & \beta \end{pmatrix}$$

Age structure

- Other diseases have a different behavior at various ages, so consider population with (C)hildren and (A)dults



Age structure

- We can still write WAIFW matrix $\boldsymbol{\beta}$

$$\boldsymbol{\beta} = \begin{pmatrix} \beta_{CC} & \beta_{AC} \\ \beta_{AC} & \beta_{AA} \end{pmatrix}$$

- Hypotheses that are still reasonable
  - assortative mixing: $\beta_{ii} > \beta_{ij}$ with $i \neq j$
  - symmetry $\beta_{AC} = \beta_{CA}$
- But now it is unclear what class is more at risk, and also class sizes change in time

Age structure

- We may actually be tempted to treat age as a continuous parameter
  - but that makes the equations hard to solve
  - and at the same time, we do not have this many parameters
- Better replicate compartments and divide the population in age classes
  - model is more tractable and we can exploit standard assumptions (e.g. memoryless)

Control by vaccination

- For risk structure, it was more efficient to vaccinate or quarantine high-risk elements as this reduces the actual value of R_0
- In age structure, we do not have a class with "higher risk" (it can be both)
  - individuals partake in the entire dynamics (we expect them to be C, then A in due time)
  - yet, $s_\infty^{(a)} / n_\infty^{(a)} \geq s_\infty^{(b)} / n_\infty^{(b)}$ if $a < b$ (younger than)

Control by vaccination

- This implies that to control the disease spread, most of the individual's lifespan should be immune; thus, it is generally best to vaccinate the **youngest** group
  - just a general rule, though (it depends on the numbers and also on waning immunity)
- If children are vaccinated, $1-1/R_0$ still well approximates the minimal vaccination rate
  - often used for measles and baby-diseases