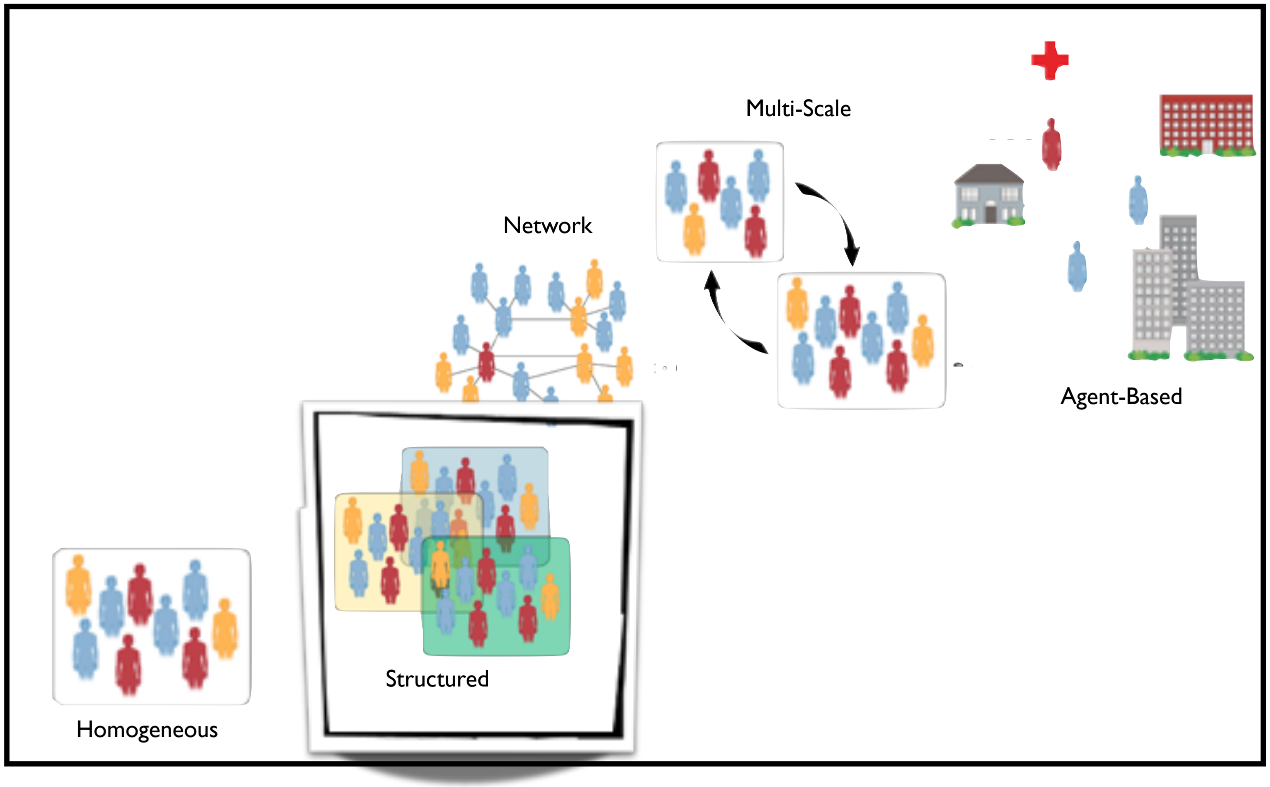
# Heterogeneity in Contacts

Behaviour & Age

# Realism Vs Transparency



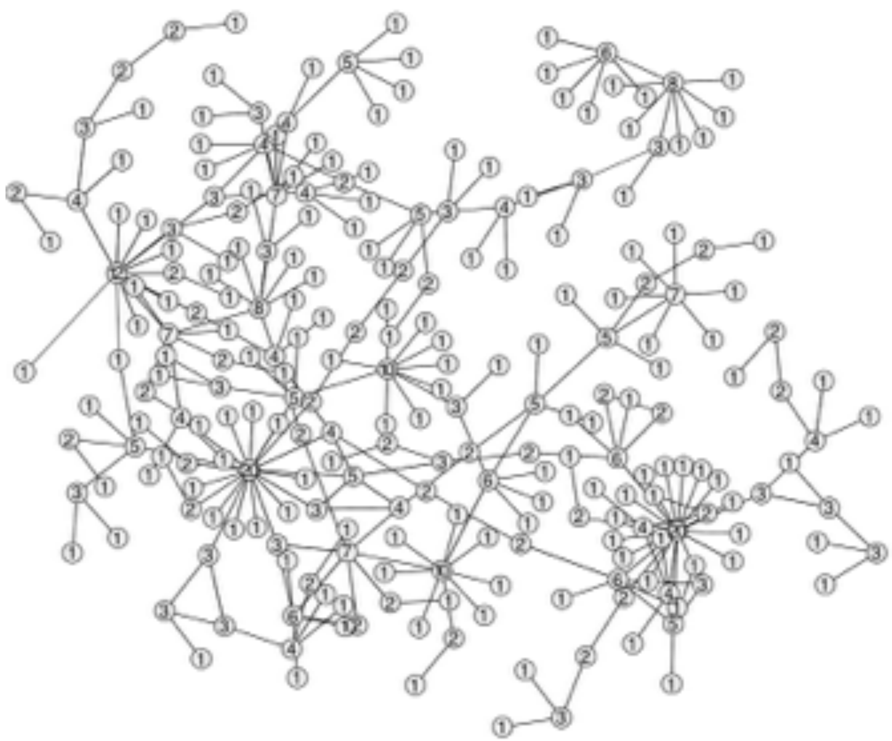
# Sources of Heterogeneity in Contacts

Individual exposure and infection hazard may be heterogeneous for a number reasons:

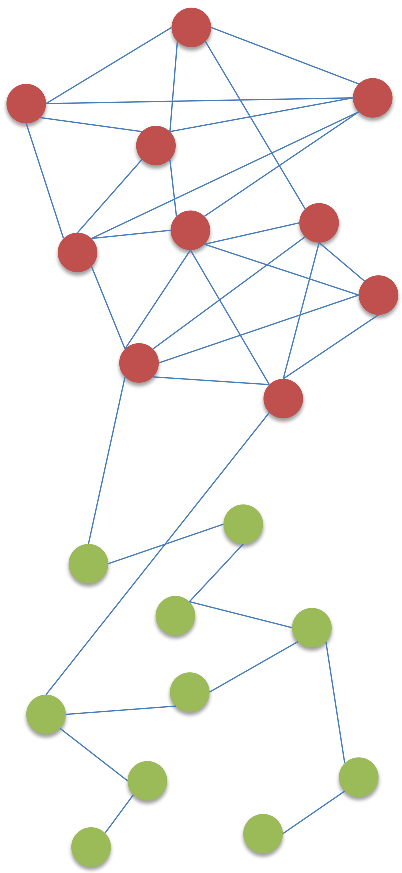
1. Risk structure
   - Determined by behavioural patterns
   - Or related to occupation
2. Age-determined contacts
   - Childhood diseases
3. Seasonality
   - Time-dependent contact rates result in sustained oscillations

# Simple contact heterogeneities

* Contact tracing to examine HIV transmission network in Colorado Springs:



# More Generally

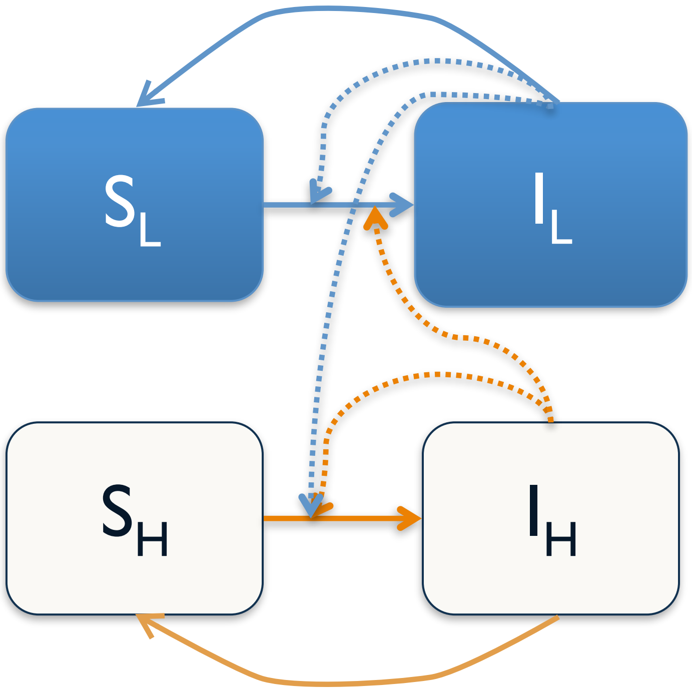


High risk group

Low risk group

# Modeling Risk Structure

Introduce a model consisting of individuals whose behaviour/work places them in one of two *kinds* of groups: Low risk and High risk




Use an extension of simple SIS model

$$\frac{dS_L}{dt} = \gamma_L I_L - \beta_{LL} S_L I_L - \beta_{LH} S_L I_H$$
$$\frac{dI_L}{dt} = -\gamma_L I_L + \beta_{LL} S_L I_L + \beta_{LH} S_L I_H$$

$$\frac{dS_H}{dt} = \gamma_H I_H - \beta_{HH} S_H I_H - \beta_{HL} S_H I_L$$
$$\frac{dI_H}{dt} = -\gamma_H I_H + \beta_{HH} S_H I_H + \beta_{HL} S_H I_L$$

# What's $R_0$?

- Instead of a single transmission rate ($\beta$), we now have a matrix of transmission parameters ($\boldsymbol{\beta}$)

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

- This is called WAIFW (Who Acquires Infection From Whom) matrix
- Typically, it's assumed $\beta_{LH} = \beta_{HL}$
- And high assortativity, such that $\beta_{HH} > \beta_{LL} > \beta_{HL}$

# What's $R_0$?

- At disease-free equilibrium

$$(S_H^*, I_H^*, S_L^*, I_L^*) = (1, 0, 1, 0)$$

- $\mathcal{F}$ = new infections
- $\mathcal{F}_H = \beta_{HH} S_H I_H + \beta_{HL} S_H I_L$
- $\mathcal{F}_L = \beta_{LL} S_L I_L + \beta_{LH} S_L I_H$
- $\mathcal{V}$ = pathogen progression
- $\mathcal{V}_H = \gamma_H I_H$
- $\mathcal{V}_L = \gamma_L I_L$

$$F = \begin{pmatrix} \beta_{HH} S_1^* & \beta_{HL} S_1^* \\ \beta_{HL} S_2^* & \beta_{LL} S_2^* \end{pmatrix} \qquad V = \begin{pmatrix} \gamma_H & 0 \\ 0 & \gamma_L \end{pmatrix}$$

# What's $R_0$?

- Next generation operator, K, given by

$$FV^{-1} = \begin{pmatrix} \beta_{HH} & \beta_{HL} \\ \beta_{HL} & \beta_{LL} \end{pmatrix} \begin{pmatrix} \frac{1}{\gamma_H} & 0 \\ 0 & \frac{1}{\gamma_L} \end{pmatrix}$$

$$K = FV^{-1} = \begin{pmatrix} \frac{\beta_{HH} S_1^*}{\gamma_H} & \frac{\beta_{HL} S_1^*}{\gamma_L} \\ \frac{\beta_{LH} S_2^*}{\gamma_H} & \frac{\beta_{LL} S_2^*}{\gamma_L} \end{pmatrix}$$

$$\det(K - \Lambda I) = \begin{vmatrix} \frac{\beta_{HH}}{\gamma_H} - \Lambda & \frac{\beta_{HL}}{\gamma_L} \\ \frac{\beta_{LH}}{\gamma_H} & \frac{\beta_{LL}}{\gamma_L} - \Lambda \end{vmatrix} = 0$$

- Solve for largest $\Lambda$

# Worked example

- Let $\gamma_H = \gamma_L = 50$,
- with WAIFW matrix give by $\beta = \begin{pmatrix} 45 & 20 \\ 20 & 35 \end{pmatrix}$

$$K = FV^{-1} = \begin{pmatrix} 45 & 20 \\ 20 & 35 \end{pmatrix} \begin{pmatrix} \frac{1}{50} & 0 \\ 0 & \frac{1}{50} \end{pmatrix}$$

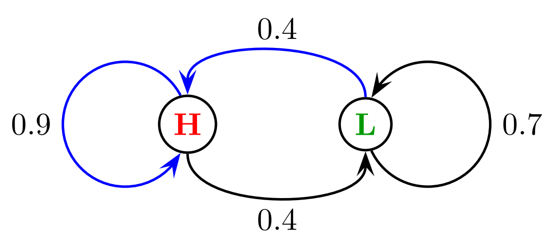
$$= \begin{pmatrix} .9 & .4 \\ .4 & .7 \end{pmatrix}$$

$$\det(K = \Lambda I) = \begin{vmatrix} .9 - \Lambda & .4 \\ .4 & .7 - \Lambda \end{vmatrix} = \Lambda^2 - 1.6\Lambda + 0.47$$

- So $\Lambda = 1.21$ or $.39 \Rightarrow R_0 = 1.21$

# Limitations

- $R_0$ quantifies overall transmission
- Not target specific
- What if interested in focusing on high risk group?




- Control measures could be aimed at, for example, paths leading to High risk group

# Target Reproduction Number

- Suppose we target *q* paths of transmission
  $j_1 \to i_1, j_2 \to i_2, \ldots, j_q \to i_q$

❖ Let X be set of all targeted paths

'recipient' classes $x_1 = \{i_1, i_2, \ldots, i_q\}$, $x_2 = \{j_1, j_2, \ldots, j_q\}$ 'donour' classes

❖ The Target Reproduction Number is

$$\mathcal{T}_X = \rho(P_{x_1} K P_{x_2}(1 - K + P_{x_1} K P_{x_2})^{-1})), \text{if } \rho(K - P_{x_1} K P_{x_2}) < 1$$

- where $P_{x_i}$ is a projection matrix ($P_{k,k} = 1$ if $k \in x_i$).

# Special Case: Type Reproduction Number

- **Type reproduction Number, $T_i$**

  **- All paths leading to *i* targeted**

  $1 \to i, 2 \to i, \ldots, p \to i.$

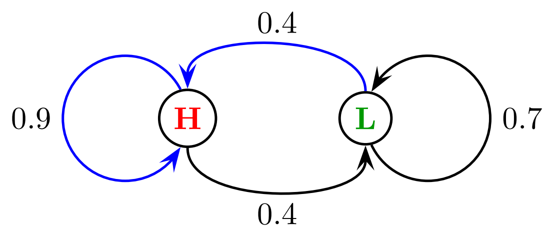
- Then

  - $x_1=\{i\}$, $x_2=\{1, \ldots, n\}$ and $T_i = \mathcal{T}_{1\to i,\, 2\to i,\, \ldots,\, n\to i}$.

- **Basic reproduction Number, $R_0$:** all possible paths are targeted

  - $x_1=\{1,2, \ldots, n\}$, $x_2=\{1, \ldots, n\}$

# Targeting $S_H$




- Target paths: H → H, L → H.
- $x_1=\{H\}$, $x_2=\{H, L\}$
- Target reproduction number:

$$T_H = \mathcal{T}_{H\to H,\ L\to H}$$
$$= \rho(P_{x_1} K P_{x_2}(1 - K + P_{x_1} K P_{x_2})^{-1})), \text{if } \rho(K - P_{x_1} K P_{x_2}) < 1$$

$$K = \begin{pmatrix} 0.9 & 0.4 \\ 0.4 & 0.7 \end{pmatrix} \quad P_{x_1} = \begin{pmatrix} 1 & 0 \\ 0 & 0 \end{pmatrix} \quad P_{x_2} = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}$$

# Targeting $S_H$

$$P_{x_1}KP_{x_2} = \begin{pmatrix} 1 & 0 \\ 0 & 0 \end{pmatrix}\begin{pmatrix} 0.9 & 0.4 \\ 0.4 & 0.7 \end{pmatrix}\begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} = \begin{pmatrix} 0.9 & 0.4 \\ 0 & 0 \end{pmatrix}$$

- Check: $\rho(K - P_{x_1}KP_{x_2}) = 0.7$ ✓

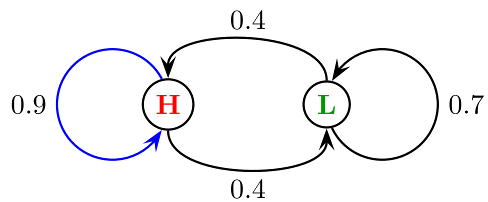
$$(P_{x_1}KP_{x_2})\Big(I - K + (P_{x_1}KP_{x_2})\Big)^{-1}$$

$$= \begin{pmatrix} 0.9 & 0.4 \\ 0 & 0 \end{pmatrix}\left[\begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} - \begin{pmatrix} 0.9 & 0.4 \\ 0.4 & 0.7 \end{pmatrix} + \begin{pmatrix} 0.9 & 0.4 \\ 0 & 0 \end{pmatrix}\right]^{-1}$$

$$= \begin{pmatrix} 1.43 & 1.33 \\ 0 & 0 \end{pmatrix}$$

- Hence, $T_H = \mathcal{T}_{H \to H,\, L \to H} = 1.43$
- Need to vaccinate *H* susceptibles: $1-1/T_H = 1-1/1.43 = 0.3$

# Lowering H➤H transmission




- Target paths: H → H.
- $x_1$={H}, $x_2$={H}
- Target reproduction number: $T_H = \mathcal{T}_{H \to H}$

$$= \rho(P_{x_1} K P_{x_2} (1 - K + P_{x_1} K P_{x_2})^{-1})), \text{if } \rho(K - P_{x_1} K P_{x_2}) < 1$$

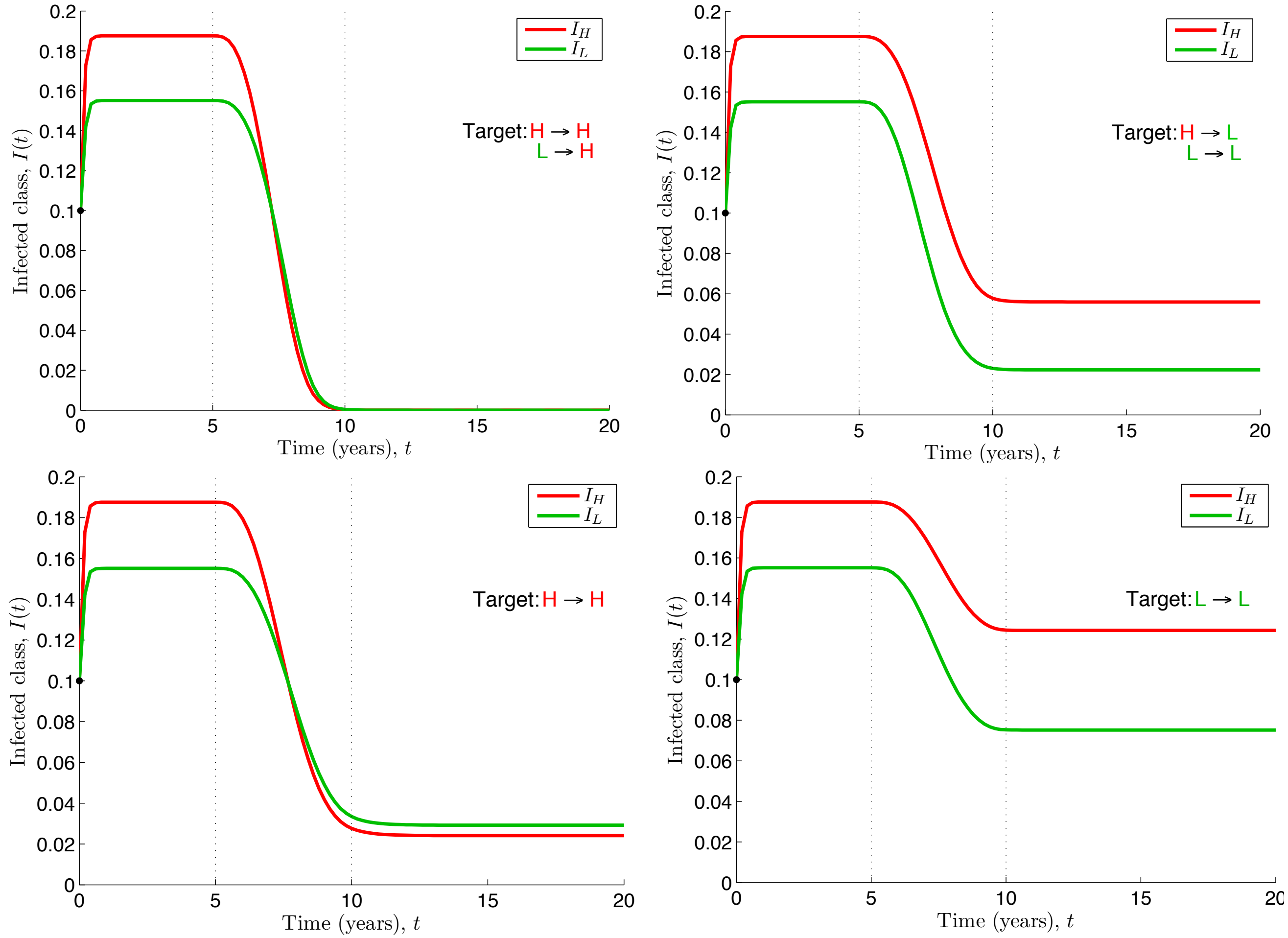
$$K = \begin{pmatrix} 0.9 & 0.4 \\ 0.4 & 0.7 \end{pmatrix} \quad P_{x_1} = \begin{pmatrix} 1 & 0 \\ 0 & 0 \end{pmatrix} \quad P_{x_2} = \begin{pmatrix} 1 & 0 \\ 0 & 0 \end{pmatrix}$$

- Hence, $T_H = \mathcal{T}_{H \to H} = 1.93$
- Need to reduce contact by $1 - 1/T_H = 1 - 1/1.93 = 0.48$

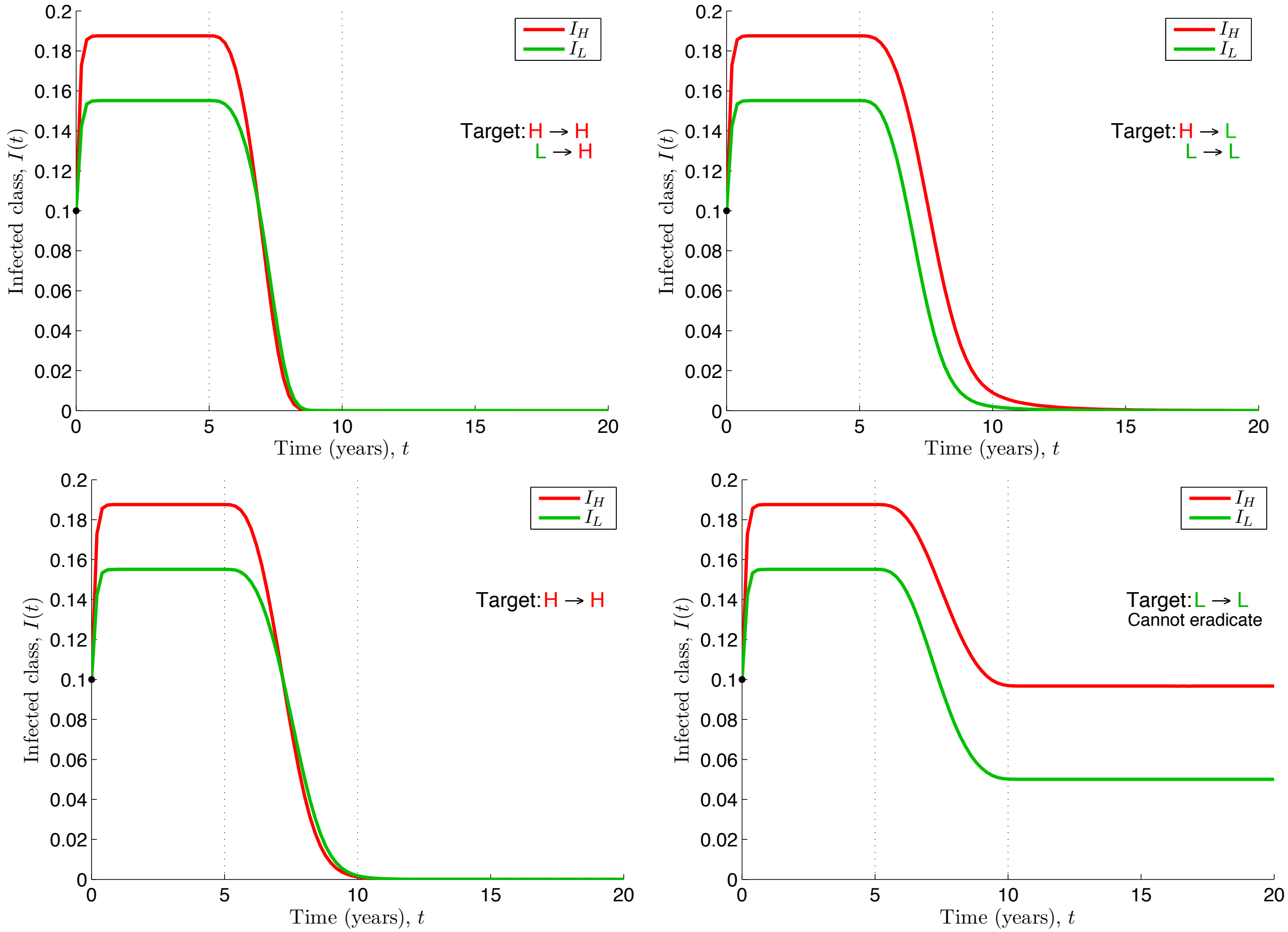
# More Generally

| Target Paths | $x_1$ | $x_2$ | Target Reproduction | Reduction | Vaccination |
|---|---|---|---|---|---|
| All | H, L | H, L | $R_0 = 1.21$ | 0.17 | 17% H<br>17% L |
| H → H<br>L → H | H | H, L | $T_H = 1.43$ | 0.3 | 30% H<br>0% L |
| H → L<br>L → L | L | H, L | $T_L = 2.30$ | 0.57 | 0% H<br>57% L |
| H → H | H | H | 1.93 | 0.48 | - |
| L → L | L | L | Not Defined | - | - |
| L → H | H | L | 5.33 | 0.81 | - |
| H → L | L | H | 5.33 | 0.81 | - |

# Reduce targeted transmission by 40%



# Reduce targeted transmission by 60%



# Summary

- Target reproduction number informative for heterogeneous populations
- Behavioural risk (core groups)
- Vectors & Hosts
- Age structure
- Spatial structure

# Modeling Age Structure

- So far, looked at heterogeneity arising in contacts, due to behavioural differences (risk structure)

- Now, we consider changing risk due to age structure, motivated by childhood diseases (ie SIR)

- Initially, assume only two age groups: Low risk (Adults) and High risk (Children)

- Differences from previous model: (i) SIR not SIS, (ii) individuals eventually move from class $C$ to class $A$ in SIR model

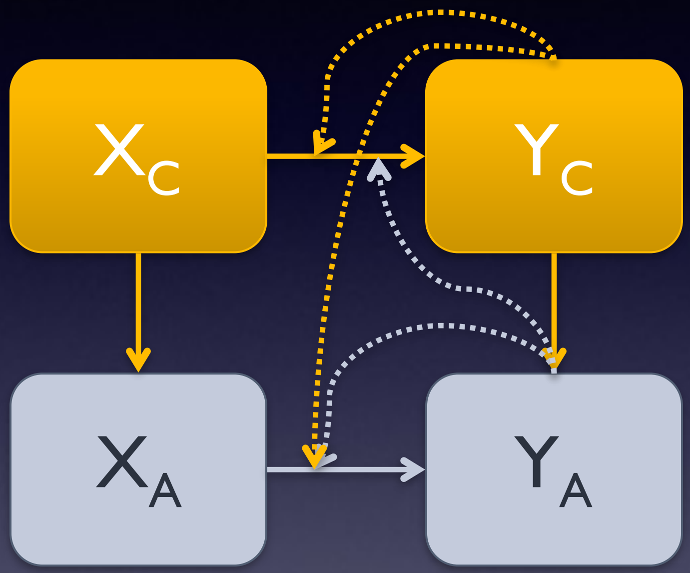
# Modeling Risk Structure

$$\frac{dX_C}{dt} = \nu - (\beta_{CC}Y_C + \beta_{CA}Y_A)X_C - \mu_C X_C - \tau_C X_C$$

$$\frac{dY_C}{dt} = (\beta_{CC}Y_C + \beta_{CA}Y_A)X_C - \gamma Y_C - \mu_C Y_C - \tau_C Y_C$$

$$\frac{dX_A}{dt} = \tau_C X_C - (\beta_{AC}Y_C + \beta_{AA}Y_A)X_A - \mu_A X_A$$

$$\frac{dY_A}{dt} = \tau_C Y_C + (\beta_{AC}Y_C + \beta_{AA}Y_A)X_A - \gamma Y_A - \mu_A Y_A$$




$$N = N_C + N_A = (X_C + Y_C + Z_C) + (X_A + Y_A + Z_A)$$

# Initial Dynamics

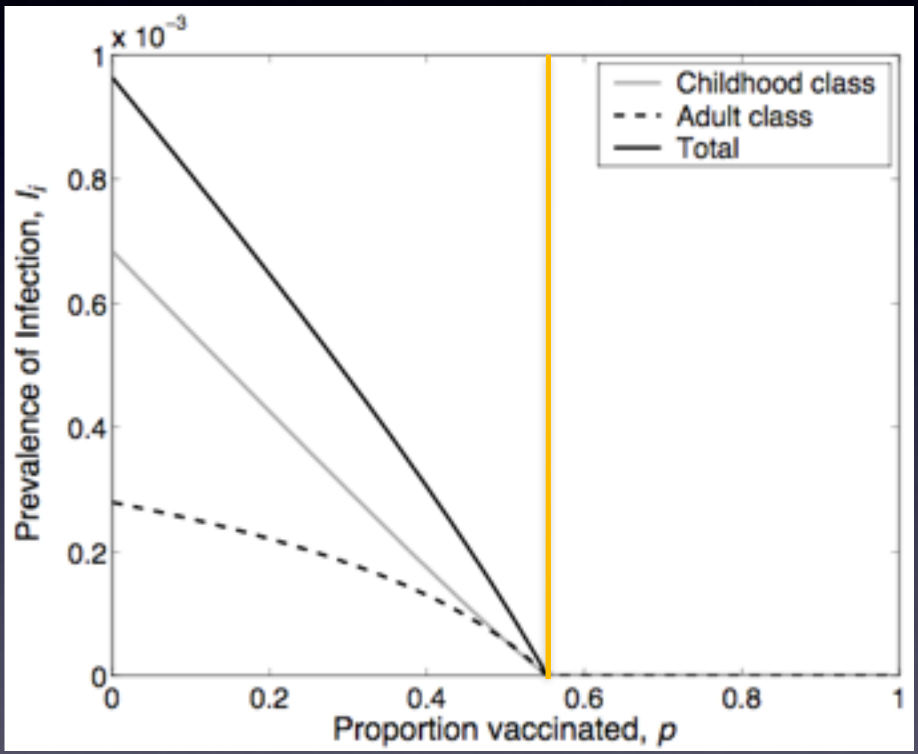
- Again, key thing is WAIFW matrix, which we'll assume to take following form

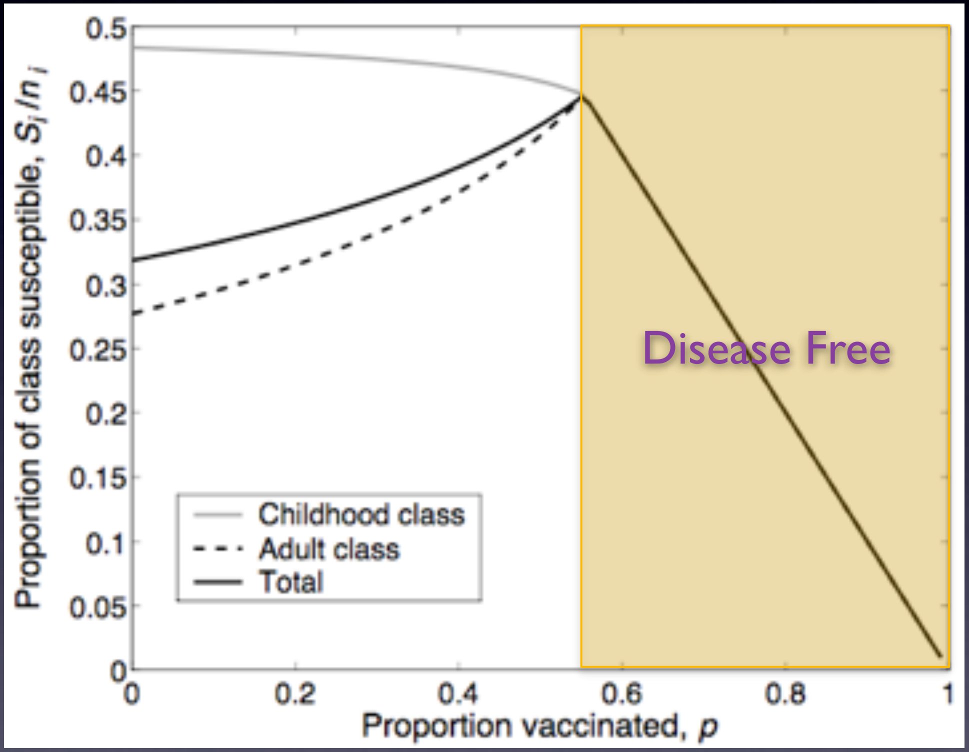
$$\beta = \begin{pmatrix} 100 & 10 \\ 10 & 20 \end{pmatrix}$$

- Let's assume $1/\tau_C$ = 15 years & $1/\tau_A$ = 60 years
- So, $N_C/N$ = 0.2 and $N_A/N$ = 0.8
- Using same eigenvalue approach as before, we get $R_0$ ~2.2

# Paediatric Vaccination

$P_c \sim 0.55$




- Prevalence much higher in *C* class than *A* class
- Vaccination threshold same as in unstructured model (!!)
- Low levels of immunization *increase* fraction of population

# Which WAIFW?

- So far, we have used hypothetical WAIFW matrices
- In reality, we may have data on disease prevalence in *C* and *A* classes, but our matrix β has 4 entries we need to estimate!
- Pragmatic assumption has been to simplify WAIFW along intuitive/sensible lines, eg

$$\beta = \begin{pmatrix} \beta_1 & \beta_2 \\ \beta_2 & \beta_2 \end{pmatrix}$$

- Often, reasonably obvious what's not a plausible WAIFW matrix

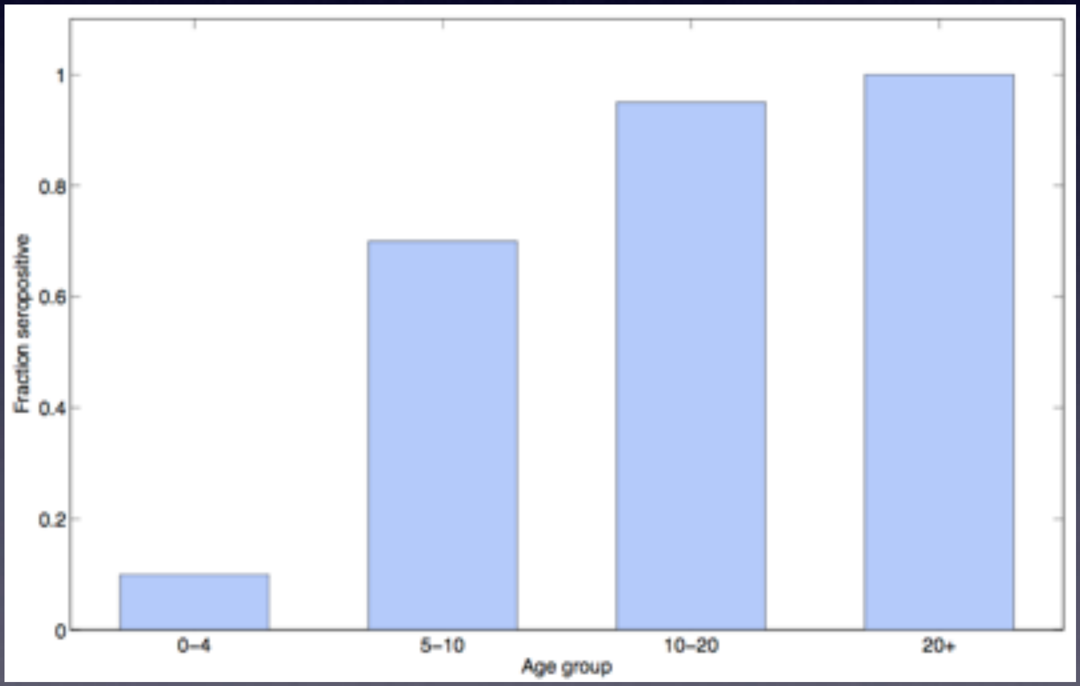
$$\beta_{\text{unlikely}} = \begin{pmatrix} \beta_1 & \beta_2 \\ \beta_2 & \beta_1 \end{pmatrix}, \begin{pmatrix} \beta_1 & 0 \\ 0 & \beta_1 \end{pmatrix}, \begin{pmatrix} \beta_1 & 0 \\ \beta_2 & 0 \end{pmatrix}, \ldots$$

# Application to Childhood Diseases

- Some of earliest discrete age-class (RAS) models developed for measles (Schenzle 1984)
- Make pragmatic assumption: transmission, especially in pre-vaccine era, primarily driven by school dynamics
- Need four age groups
  - Pre-school (0-4 years)
  - Primary school (5-10 years)
  - Secondary school (11-16 years)
  - Adults (16+)
- We're now faced with old problem of which WAIFW?

# Typical age-specific data

Given $n$ age classes, age-specific transmission matrix has $n^2$ elements … correcting for reciprocity, we still have $n(n-1)/2$ term




Often, only have information on age-specific prevalence or serology

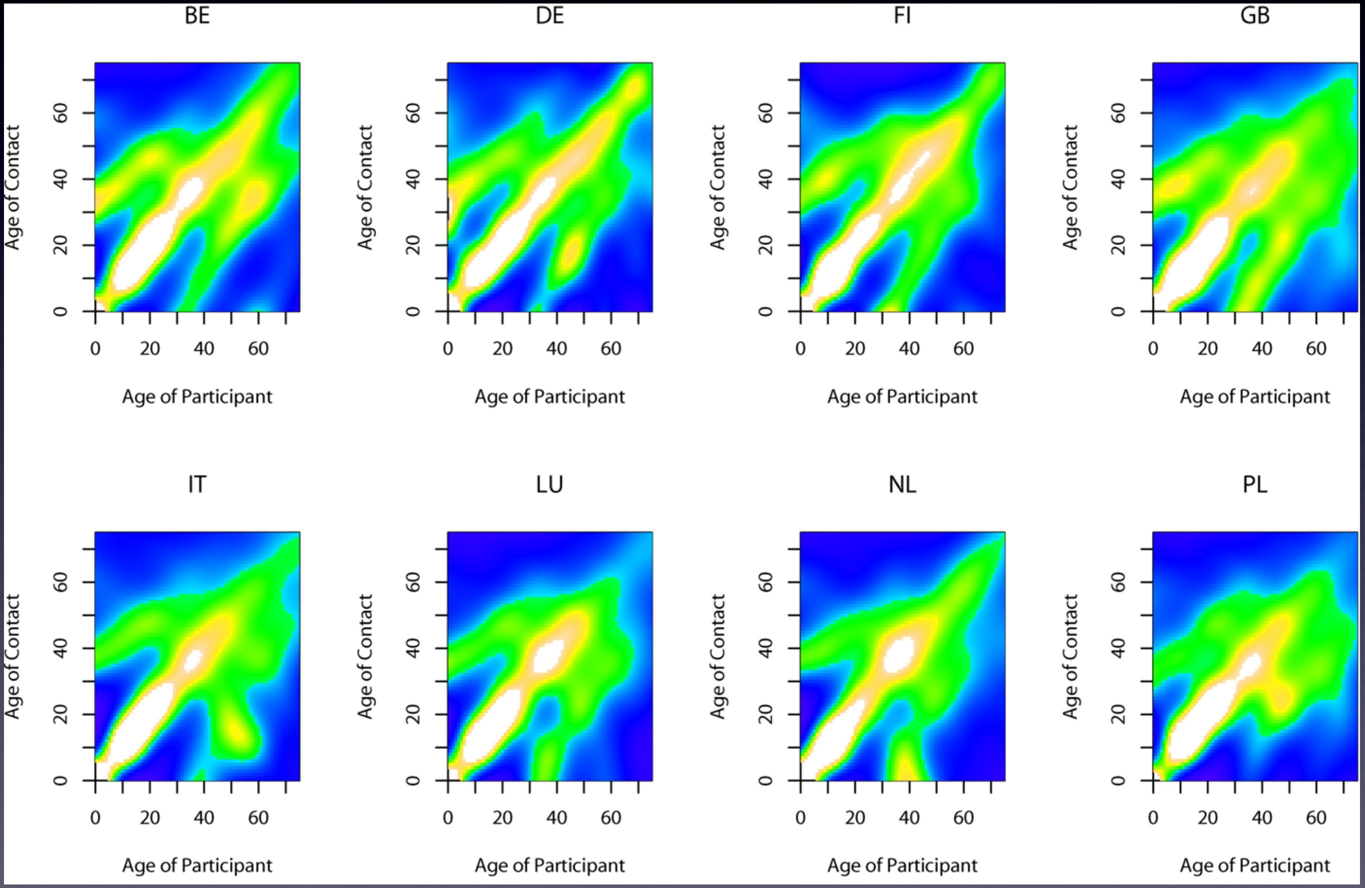
# Which WAIFW?

- Two seemingly sensible WAIFW matrices are

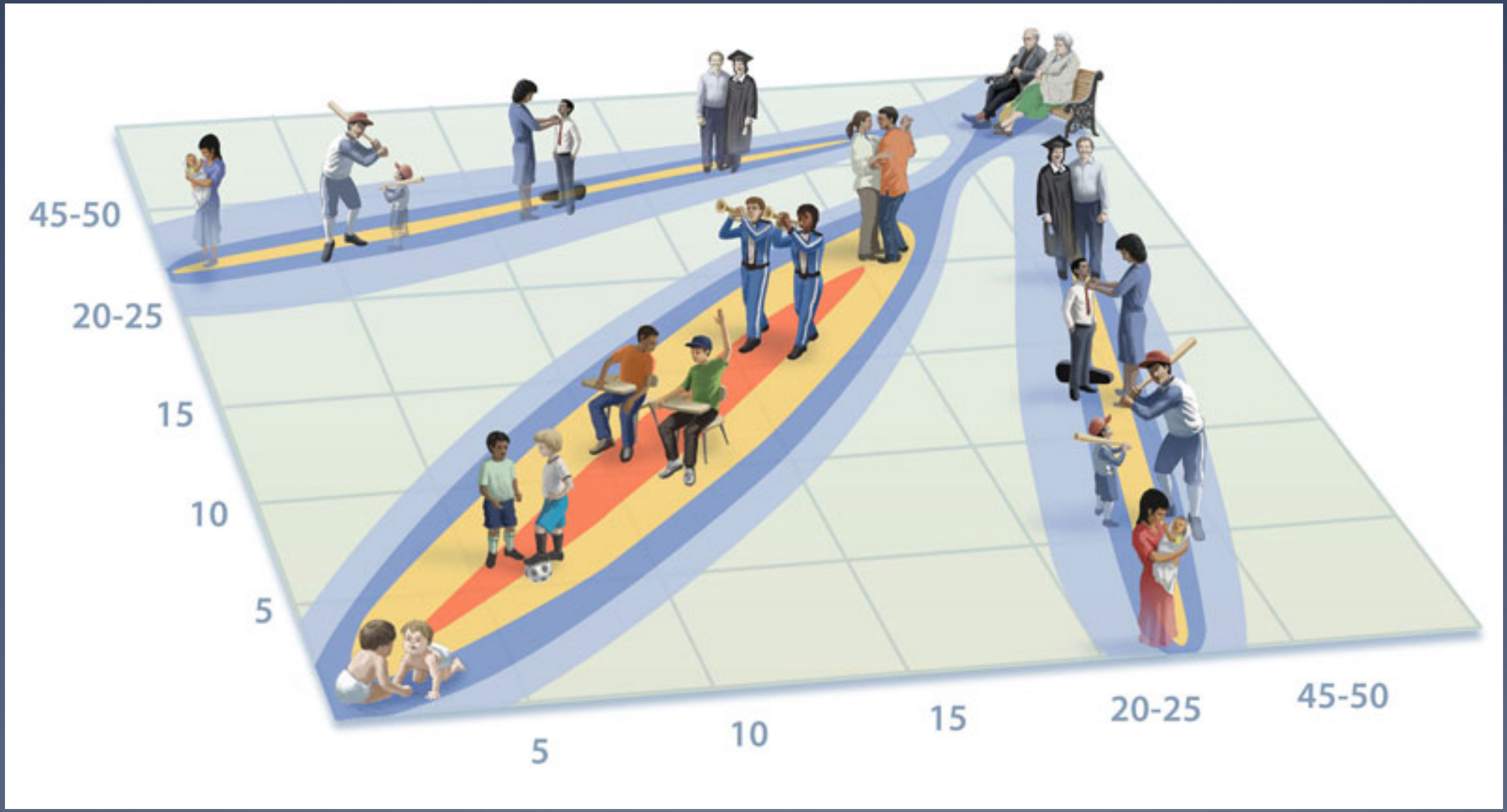
$$\beta = \begin{pmatrix} \beta_2 & \beta_2 & \beta_3 & \beta_4 \\ \beta_2 & \beta_1 & \beta_3 & \beta_4 \\ \beta_3 & \beta_3 & \beta_3 & \beta_4 \\ \beta_4 & \beta_4 & \beta_4 & \beta_4 \end{pmatrix} \beta = \begin{pmatrix} \beta_2 & \beta_4 & \beta_4 & \beta_4 \\ \beta_4 & \beta_1 & \beta_4 & \beta_4 \\ \beta_4 & \beta_4 & \beta_3 & \beta_4 \\ \beta_4 & \beta_4 & \beta_4 & \beta_3 \end{pmatrix}$$

With $\beta_1 > \beta_2 > \beta_3 > \beta_4$

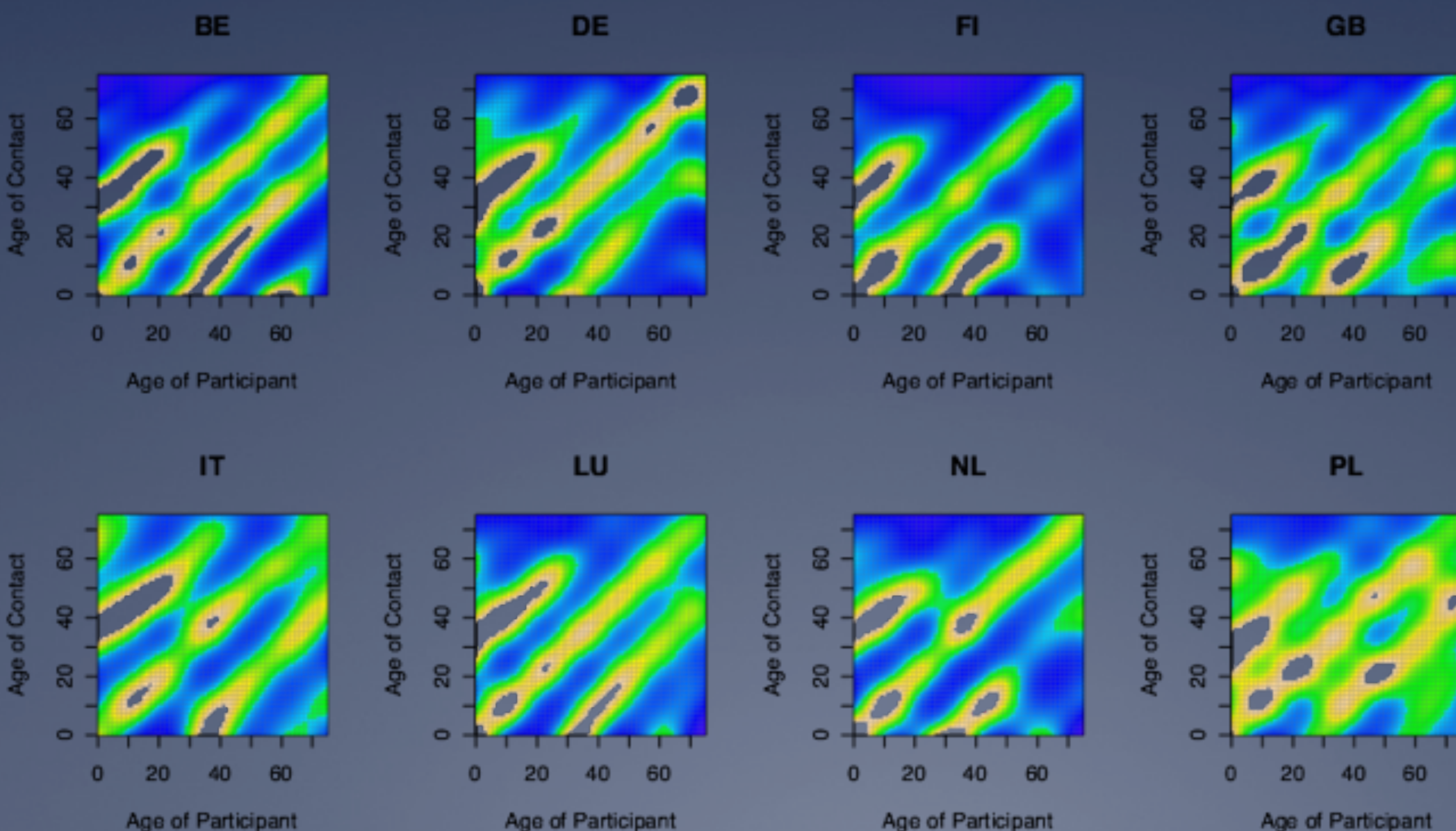
# Mossong *et al.* (2008)



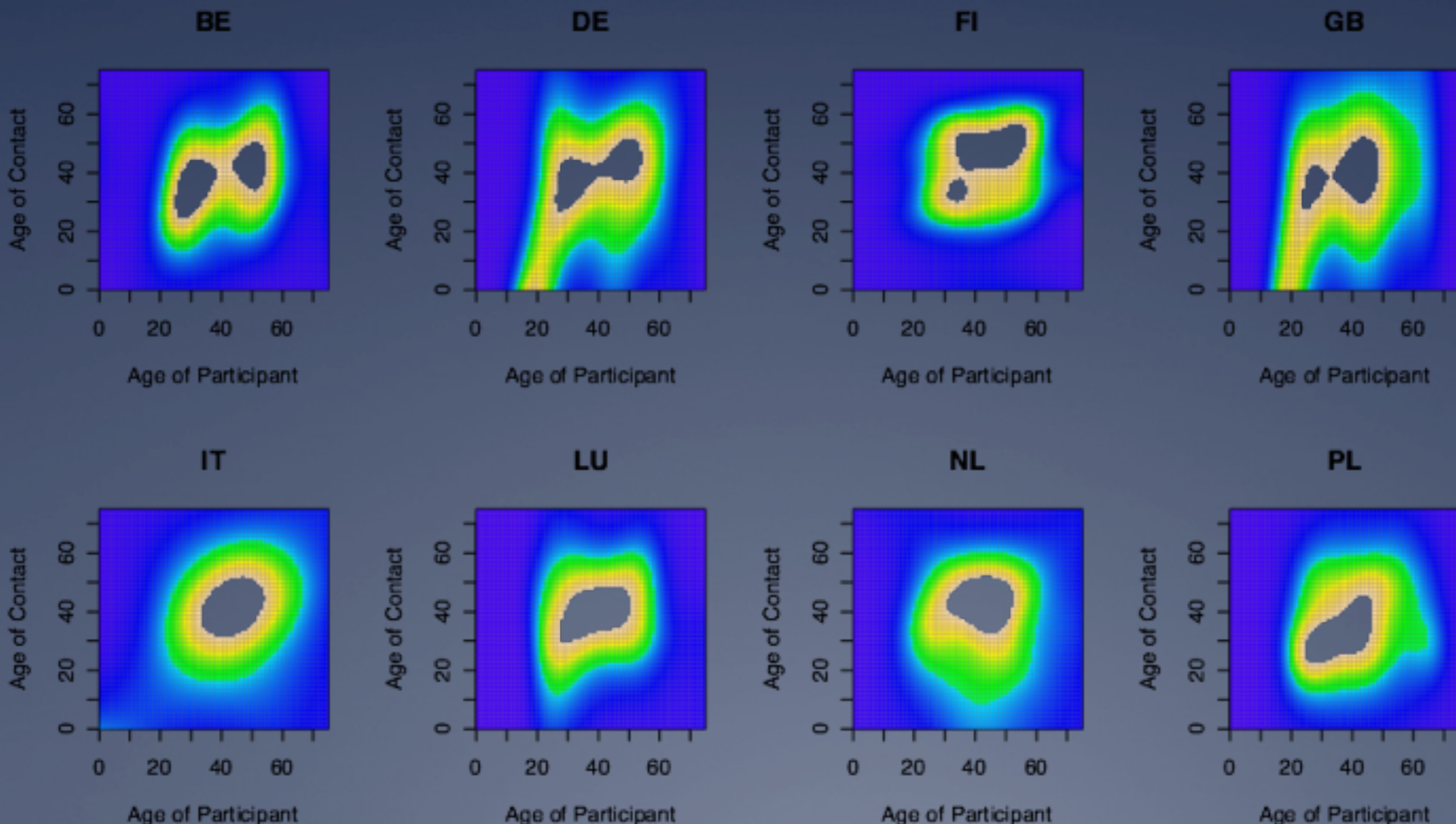
# Age-specific contacts



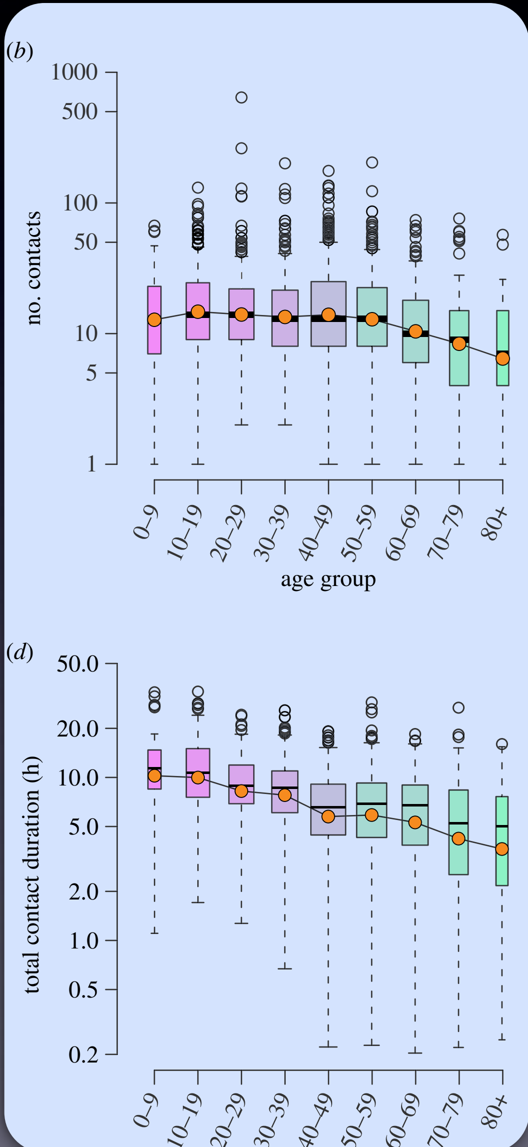
# Contacts at home



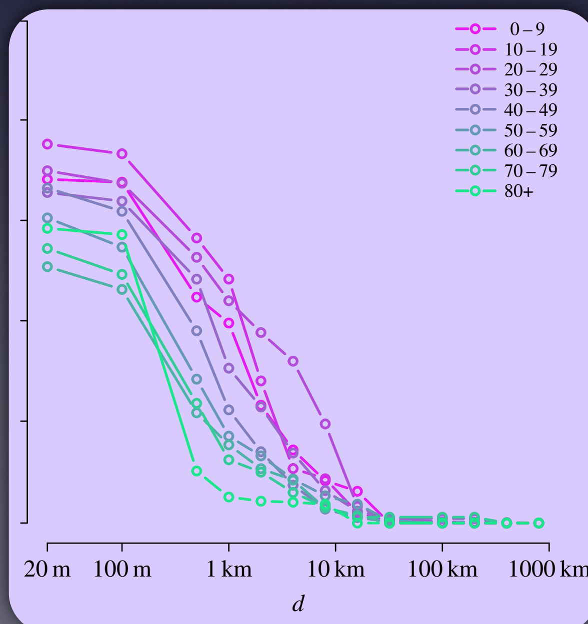
# Contacts at work

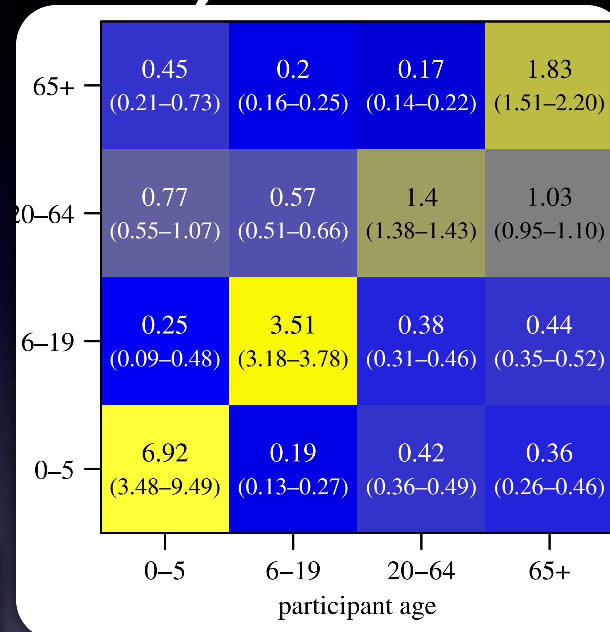


# Read et al. (2014)

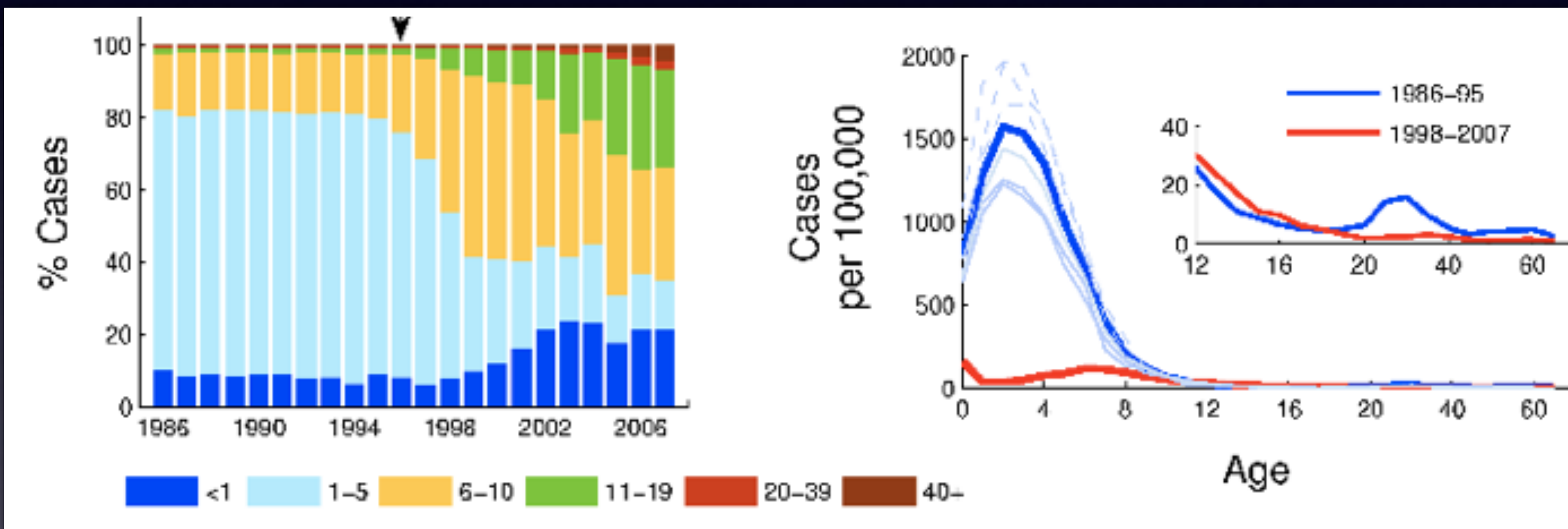



Social mixing data from urban & rural China



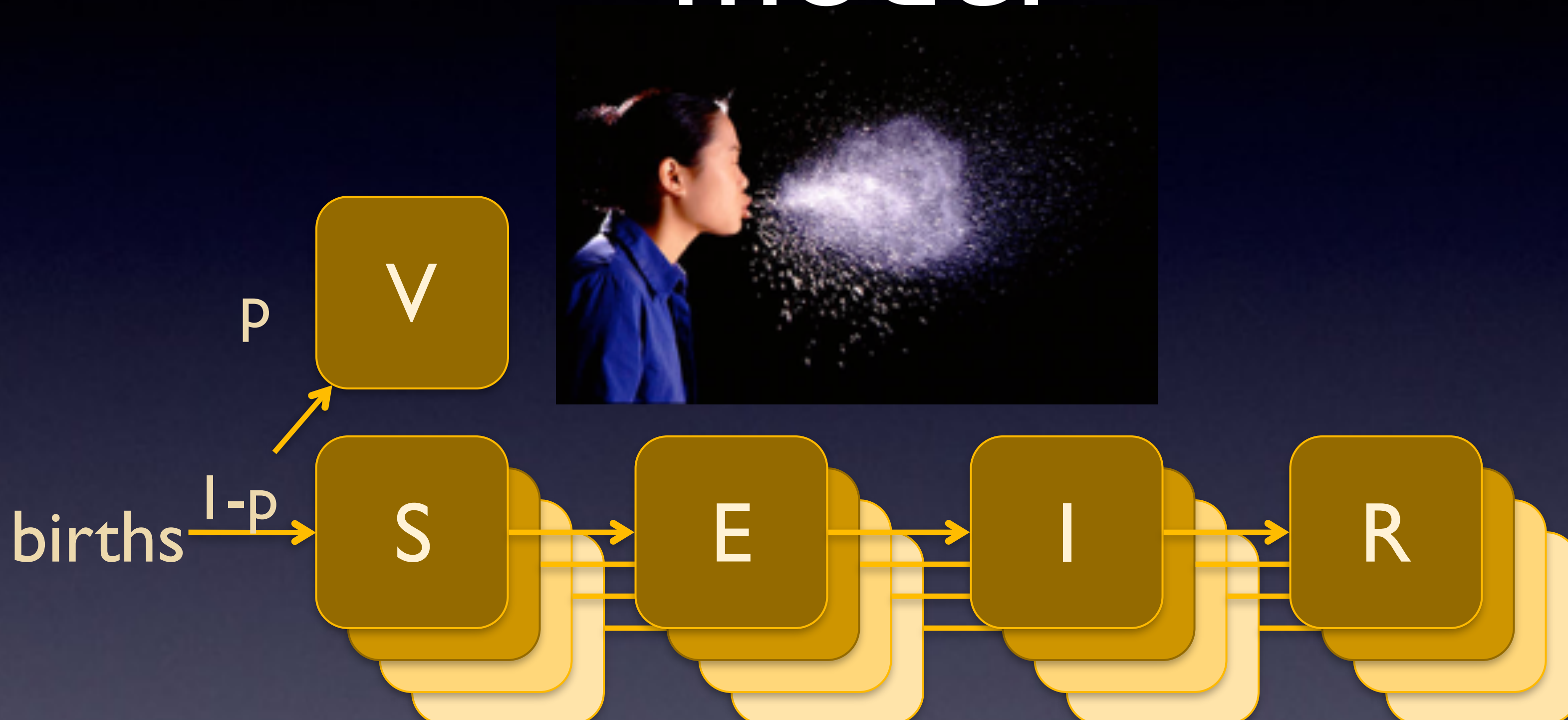



# Age Structured Dynamics




Rohani, Zhong & King (2010) *Science*

# Age-structured SEIR model




Model, simulated as time varying Markov Chain
Updating of age-classes occurs annually
0-19 one-year classes, and 20+

# Age-specific transmission rate

Force of infection determine by:

- Contact structure ($c_{i\,j}$) -- from Mossong study
- Probability that contact is with infectious -- $I_j/N_j$
- Transmission probability, given contact -- $q_i$

$$\lambda_i = q_i \sum_j c_{ij} \frac{I_j}{N_j}$$

Can use data to

- determine transmission probability, given contact -- $q_i$
- validate model

# Model-data comparison