Host Heterogeneity

Amy Greer, BSc MSc PhD
Canada Research Chair in Population Disease Modeling and Associate Professor

Ontario Veterinary College

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FOI

- Force of Infection (FOI) is typically denoted by λ
- Defined as the rate at which susceptible individuals acquire an infectious disease
- Directly proportional to beta (β) which is transmissibility

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Review: Calculating β for a randomly mixing population

β = the probability of an effective contact/unit time between 2 specific individuals

$\beta = R_0 / (D*N)$

or

$\beta I(t) = \lambda(t)$ (e.g. from seroprevalence data)

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Review: Calculating β for a randomly mixing population

$\beta S(t)I(t) = \lambda(t)S(t)$

We can cancel out the # of susceptibles S(t) from each side:

$\beta I(t) = \lambda(t)$

If we rearrange the equation, we can isolate β:

$\beta = \lambda(t)/I(t)$

Note: For a given value for the (equilibrium) force of infection, it is possible to estimate both the number of susceptible and infectious individuals and this will allow you to estimate β using the expression above.

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Age-specific differences in FOI

Observation: For some infections, the force of infection appears to be higher for children than for adults

What are some possible reasons for this observation?

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Possible explanations

1. Age-dependent mixing patterns
   – children most likely to mix with other children (rather than adults), who are also most likely to be infectious, at least for measles, rubella etc.
2. Age-dependent difference in susceptibility
   – children are more likely to be susceptible to infection than adults
3. Genetic or other differences in susceptibility or exposure
   – those most susceptible to infection are infected at a young age

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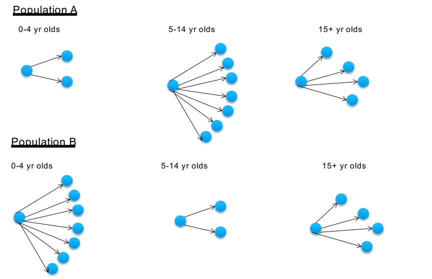
In which population will it be easier to control transmission using infant vaccination?



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Methods for incorporating heterogeneous mixing

Consider a population in which mixing patterns differ for children and adults.

The overall FOI experienced by children (the "young") at a given time t ($\lambda_y(t)$) is given by the sum of the FOI attributable to contact with other children ($\lambda_{yy}(t)$) and that attributable to contact with adults (the "old") ($\lambda_{yo}(t)$).

Given the information above, write out the equations for:
1) the FOI in the young $\lambda_y(t)$ = ?
2) The FOI in the old $\lambda_o(t)$ = ?

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Answer

$$\lambda_y(t) = \lambda_{yy}(t) + \lambda_{yo}(t)$$

$$\lambda_o(t) = \lambda_{oy}(t) + \lambda_{oo}(t)$$

Each of these components $\lambda_{yy}(t)$, $\lambda_{yo}(t)$, $\lambda_{oy}(t)$, $\lambda_{oo}(t)$ can be expressed in terms of the product of the probability of a specific child effectively contacting another specific child per unit time and the # of infectious children as follows:

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Deriving the expression for the FOI in children due to contact with other children ($\lambda_{yy}(t)$)

The number of new infections among children which are attributable to contact with other children is given by the expressions.

$$\lambda_{yy}(t)S_y(t) \text{ AND } \beta_{yy}S_y(t)\, I_y(t)$$

$$\lambda_{yy}(t)\cancel{S_y(t)} = \beta_{yy}\cancel{S_y(t)}\, I_y(t)$$

$$\lambda_{yy}(t) = \beta_{yy}\, I_y(t)$$

FOI experienced by children which is attributable to contact with other children is given by the expression above.

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Deriving the expression for the FOI in children due to contact with adults($\lambda_{y0}(t)$)

The number of new infections among children which are attributable to contact with adults is given by the expressions.

$$\lambda_{yo}(t)S_y(t) \text{ AND } \beta_{yo}S_y(t)\, I_o(t)$$

$$\lambda_{yo}(t)\cancel{S_y(t)} = \beta_{yo}\cancel{S_y(t)}\, I_o(t)$$

$$\lambda_{yo}(t) = \beta_{yo}\, I_o(t)$$

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Substitute to find the total FOI among children

$\lambda_y(t) = \lambda_{yy}(t) + \lambda_{yo}(t)$ (A)

$\lambda_{yy}(t) = \beta_{yy}\, I_y(t)$ (B)

$\lambda_{yo}(t) = \beta_{yo}\, I_o(t)$ (C)

$$\lambda_y(t) = \beta_{yy}\, I_y(t) + \beta_{yo}\, I_o(t)$$

Use the same logic to derive the expression for the FOI among adults

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Substitute to find the total FOI among adults

$\lambda_o(t) = \lambda_{oo}(t) + \lambda_{oy}(t)$ (A)

$\lambda_{oo}(t) = \beta_{oo} I_o(t)$ (B)

$\lambda_{oy}(t) = \beta_{oy} I_y(t)$ (C)

$$\lambda_o(t) = \beta_{oy} I_y(t) + \beta_{oo} I_o(t)$$

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Review of Matrices (it's not that bad!)

Matrices provide a convenient means of summarizing sets of equations which need to be satisfied simultaneously. For example:

5x+3y=6

3x+4y=3

$$\begin{pmatrix} 5 & 3 \\ 3 & 4 \end{pmatrix}\begin{pmatrix} x \\ y \end{pmatrix}=\begin{pmatrix} 6 \\ 3 \end{pmatrix}$$

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Review of Matrices (it's not that bad!)

4x + 8y + 3z = 18

2x + y + 5z = 12

X + 3y + 8z = 4

$$\begin{pmatrix} 4 & 8 & 3 \\ 2 & 1 & 5 \\ 1 & 3 & 8 \end{pmatrix}\begin{pmatrix} x \\ y \\ z \end{pmatrix}=\begin{pmatrix} 18 \\ 12 \\ 4 \end{pmatrix}$$

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Extend the logic to FOI equations

$\lambda_y(t) = \beta_{yy} I_y(t) + \beta_{yo} I_o(t)$
$\lambda_o(t) = \beta_{oy} I_y(t) + \beta_{oo} I_o(t)$

$$\begin{pmatrix} \lambda_y(t) \\ \lambda_o(t) \end{pmatrix} = \begin{pmatrix} \beta_{yy} & \beta_{yo} \\ \beta_{oy} & \beta_{oo} \end{pmatrix} \begin{pmatrix} I_y(t) \\ I_o(t) \end{pmatrix}$$

This is known as the "beta" matrix and is most commonly called the "WAIFW" matrix (Anderson and May, 1991). Be aware that there are sometimes other notations used in the literature.

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Possible structures for the WAIFW matrices

$$\begin{pmatrix} \lambda_y(t) \\ \lambda_o(t) \end{pmatrix} = \begin{pmatrix} \beta_{yy} & \beta_{yo} \\ \beta_{oy} & \beta_{oo} \end{pmatrix} \begin{pmatrix} I_y(t) \\ I_o(t) \end{pmatrix}$$

Values for the "betas" can be calculated if we know age-specific force of infections (e.g. from age-specific seroprevalence data) and the number of infectious individuals in each age group. BUT, there is a problem....

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The most common (and realistic) constraint

1. Assume that the probability that a child contacts and transmits to an adult is the same as the probability that an adult contacts and transmits to a child

$\beta_{oy} = \beta_{yo} = \beta_1$

$$\begin{pmatrix} \lambda_y(t) \\ \lambda_o(t) \end{pmatrix} = \begin{pmatrix} \beta_{yy} & \beta_1 \\ \beta_1 & \beta_{oo} \end{pmatrix} \begin{pmatrix} I_y(t) \\ I_o(t) \end{pmatrix}$$

This reduces the matrix equation to 2 equations and 3 unknowns so a further constraint is required. What are our options?

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Other possible constraints

$$\begin{pmatrix} \beta_{yy} & \beta_{yo} \\ \beta_{oy} & \beta_{oo} \end{pmatrix}$$

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

$\beta_{oy} = \beta_{yo} = \beta_{oo} = \beta_2$

Probability that an adult contacts and infects a child is the same as the probability that an adult contacts and infects and adult

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

$\beta_{oy} = \beta_{yo} = \beta_{yy} = \beta_1$

Children are equally likely to contact and infect another child or adult and adults have unique mixing patterns with other adults.

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An Example of a WAIFW calculation

Suppose that in your population, the equilibrium FOI for rubella is 0.12 and 0.05 per year for individuals under and over 15 years. Also assume that within this population, these age-specific FOI values result in 29 and 6 infectious cases among children and adults.

Write out the equations for the equilibrium FOI in relation to the equilibrium # of infectious individuals

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$$\begin{pmatrix} 0.12 \\ 0.05 \end{pmatrix} = \begin{pmatrix} \beta_{yy} & \beta_{yo} \\ \beta_{oy} & \beta_{oo} \end{pmatrix} \begin{pmatrix} 29 \\ 6 \end{pmatrix}$$

Lets assume a totally unrealistic WAIFW matrix for a start (because it's easy). What does this structure imply?

$$\begin{pmatrix} 0.12 \\ 0.05 \end{pmatrix} = \begin{pmatrix} \beta_1 & 0 \\ 0 & \beta_2 \end{pmatrix} \begin{pmatrix} 29 \\ 6 \end{pmatrix}$$

Solve for the Beta terms:

$0.12 = 29\ \beta_1$
$0.05 = 6\ \beta_2$

$\beta_1 = 0.00413$ per year
$\beta_2 = 0.008$ per year

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$$\begin{pmatrix} 0.12 \\ 0.05 \end{pmatrix} = \begin{pmatrix} \beta_{yy} & \beta_{yo} \\ \beta_{oy} & \beta_{oo} \end{pmatrix} \begin{pmatrix} 29 \\ 6 \end{pmatrix}$$

Lets assume a more realistic WAIFW matrix. What does this structure imply?

$$\begin{pmatrix} 0.12 \\ 0.05 \end{pmatrix} = \begin{pmatrix} \beta_1 & \beta_2 \\ \beta_2 & \beta_2 \end{pmatrix} \begin{pmatrix} 29 \\ 6 \end{pmatrix}$$

Solve for the Beta terms:

$0.12 = 29\beta_1 + 6\beta_2$

$0.05 = (29+6)\beta_2$

What do we do now? How do we solve this?

$0.05 = (29+6)\beta_2$

$\beta_2 = 0.0014$ per year

Substitute β_2 into the other equation and solve for β_1

$0.12 = 29\beta_1 + 6(0.0014)$

$\beta_1 = 0.0038$ per year

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Methods for calculating the number of S and I individuals

Review: In a randomly mixing population

The expected proportion of susceptibles in different age groups (assuming the FOI is not age-dependent)

$$s(a) = e^{-\lambda a}$$

The overall # of S individuals can be found by summing up the avg. # of S in each age group

$$\sum_a = s(a)N(a)$$

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Methods for calculating the number of S and I individuals

The average # of infectious individuals in the population is given by the expression:

Number of individuals newly infected (λS) * Duration of infectiousness (D)

The avg. # of infectious individuals in the population is given by:

$=\lambda SD$ **OR** $\lambda S/r$ (if $D = 1/r$)

D = average duration of infection and r = 1/D = rate at which individuals recover

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Methods for calculating the number of S and I individuals

In a non-randomly mixing population

Extend the logic from the randomly mixed example. In this case we need estimates of the average # of young and old infectious individuals.

Avg. # of young infectious individuals:

$\lambda_y S_y D$ or $\lambda_y S_y / r$

Avg. # of old infectious individuals:

$\lambda_o S_o D$ or $\lambda_o S_o / r$

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Estimating the reproductive number for heterogeneously mixing populations

REMINDER of what we know for a homogenously mixed population:

$R_e = R_0 * S$

If the infection is at equilibrium, then $R_e = 1$

Therefore, $R_0 = 1/S^*$

(where S* = proportion of population Susceptible at equilibrium)

Herd immunity threshold:

$H = 1\text{-}S^* = 1\text{-}(1/R_0)$ This relationship is no longer applicable if assumption of random mixing is not met!

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Estimating the reproductive number for heterogeneously mixing populations

1. Measure prevalence of infection in the population, using a serosurvey
2. Estimate the forces of infection
3. Choose the structure of the WAIFW matrix
4. Calculate the transmission coefficients (betas)
5. Formulate the "next generation matrix" (NGM)
6. Calculate R0 from the NGM

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Calculating the NGM

In a population with heterogeneous mixing, the number of secondary cases resulting from an infected case is going to depend on which sub-group the infected individual belongs to.

Each of these "reproduction numbers" can be expressed in terms of the coefficients from the WAIFW matrix.

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Reproductive Numbers

Homogeneously mixed population:

$R_0 = \beta * N * D$

Heterogeneously mixed population:

$R_{yy} = \beta_{yy} * N_y * D$

$R_{oy} = \beta_{oy} * N_o * D$

$R_{yo} = \beta_{yo} * N_y * D$

$R_{oo} = \beta_{oo} * N_o * D$

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The Next Generation Matrix

$$\begin{pmatrix} R_{yy} & R_{yo} \\ R_{oy} & R_{oo} \end{pmatrix} = \begin{pmatrix} \beta_{yy} N_y D & \beta_{yo} N_y D \\ \beta_{oy} N_o D & \beta_{oo} N_o D \end{pmatrix}$$

The number of secondary cases resulting from the introduction of an infected case into a totally susceptible population will be some average of each of these R_0 values (Diekmann et al, 1990)

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$$\begin{pmatrix} R_{yy} & R_{yo} \\ R_{oy} & R_{oo} \end{pmatrix}$$

Example 1

1. In a population with the following NGM

$$\begin{pmatrix} 1 & 1 \\ 1 & 1 \end{pmatrix}$$

An infectious case in either of the sub-groups causes 1 secondary infectious case in its own sub-group and one secondary infectious case in the other subgroup and therefore leads to 2 secondary cases. The basic reproductive number in this population is therefore 2.

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$$\begin{pmatrix} R_{yy} & R_{yo} \\ R_{oy} & R_{oo} \end{pmatrix}$$

Example 2

1. In a population with the following NGM

$$\begin{pmatrix} 2 & 1 \\ 1 & 2 \end{pmatrix}$$

One infectious case in either of the subgroups causes 2 infectious cases in its own subgroup and 1 in the other subgroup and therefore causes 3 infections total. The R_0 in this population is therefore 3.

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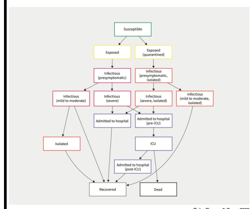
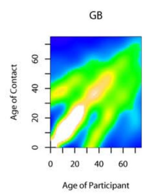


Tuite, Fisman, & Greer, 2020
Cited > 400 times



Mossong et al. 2008

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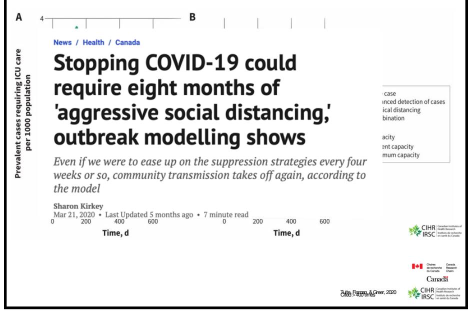
News / Health / Canada

Stopping COVID-19 could require eight months of 'aggressive social distancing,' outbreak modelling shows

Even if we were to ease up on the suppression strategies every four weeks or so, community transmission takes off again, according to the model

Sharon Kirkey
Mar 21, 2020 • Last Updated 5 months ago • 7 minute read

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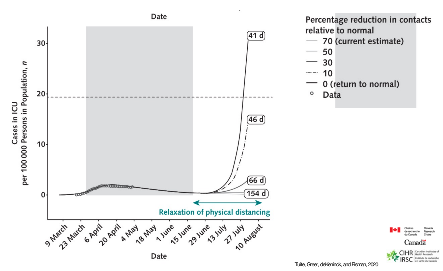

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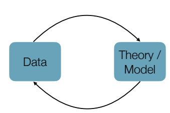
- Cross-sectional surveys (May, July, Sept, Dec 2020)
  - Perceived effectiveness and confidence in the abil… …iety of Canadi… …res
  - 24-hour…
  - Child-re… …nd Dec, 2020)



- Longitudinal survey (monthly between July – Nov 2020)
  - Changes over time in avoidance behaviours

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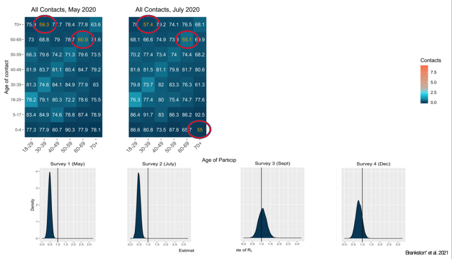
All Contacts, May 2020
All Contacts, July 2020
Age of contact
Contacts
7.5
5.0
2.5
0.0
18-29
30-39
40-49
50-59
60-69
70+
Age of Particip
Survey 1 (May)
Survey 2 (July)
Survey 3 (Sept)
Survey 4 (Dec)
Density
Estimat
ate of R_t
Brankston* et al. 2021

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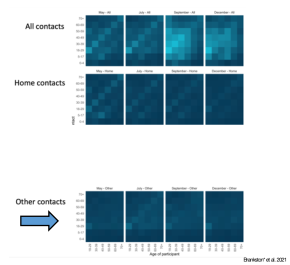
All contacts
Home contacts
Other contacts
Brankston* et al. 2021

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