Sexually Transmitted Infections

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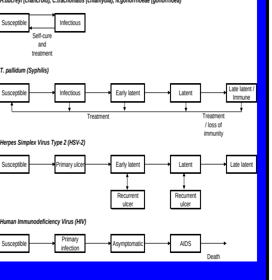
Objectives

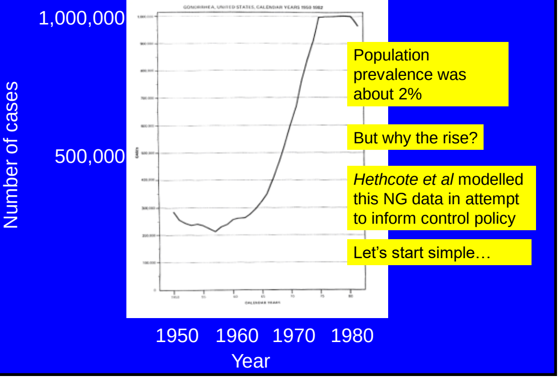
- Understand the important characteristics of sexually transmitted infections and how they differ from the infections modelled so far
- Use simple deterministic compartmental models to explore the transmission dynamics of short-duration curable STIs such as gonorrhoea to,
  - Explore the importance of heterogeneity in sexual activity for STI invasion and endemic prevalence
  - Appreciate the importance of mixing patterns on R_0, the rate of STI spread, the equilibrium STI prevalence and the utility of 'Q', a summary measure of mixing
- Explore the importance of heterogeneity in sexual activity and mixing patterns for STI control
- Appreciate the similarity between a heterosexual STI model and a host-vector infection model

STI characteristics

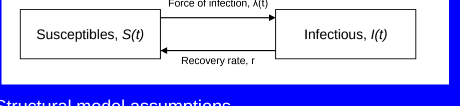
- Transmission requires intimate contact
- Population at risk subset of the pop.
- Force of infection not related to population density
- Natural history varies markedly between STIs, eg
  - Asymptomatic infection particularly in women
  - No effective immune response
  - No recovery from infection
  - Some STIs enhance the probability of the transmission of other STI
  - Some STIs kill
- Great heterogeneity in sexual behaviour and transmission rates within and between populations



Gonorrhoea Cases- US data (1950-82)

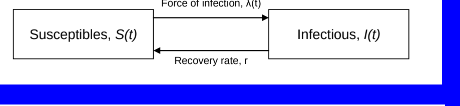


Gonorrhoea - SIS model



- Structural model assumptions
  - Negligible incubation period
  - No immunity from infection
  - Individuals are not differentiated by age or sex...
  - Individuals can be either susceptible or infected and infectious

Gonorrhoea - SIS model



$$\frac{dS(t)}{dt} = -\lambda(t)S(t) + rI(t)$$
$$\frac{dI(t)}{dt} = +\lambda(t)S(t) - rI(t)$$

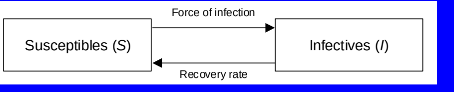
- $\lambda(t)$, the force of infection at time t,
- r , the recovery rate per year

Also assume
- c, effective rate of partner change per year
- β_p, probability of transmission of the STI during a sexual partnership

$\beta \rightarrow c\ \beta_p$

- Note we separate the two implicit components of β used in early sessions
  - a *behavioural* component
    - *c,* the effective rate of partner change/ year
  - An *biological* component
    - β_p , probability of transmission of the STI during a sexual partnership

Force of infection for randomly mixing SIS model of STI transmission



- Assume sexual partners are chosen randomly
  => Probability partners are infectious equals the prevalence at time *t* = I(t)/N.
  (ie 'Frequency dependence' or 'True mass-action')
- Force of infection = $\lambda(t) = c\ \beta_p \dfrac{I(t)}{N}$ Eqn 1.5
- Assume parameter values and make predictions …

Parameters

Assume parameter values:

c = 2 partners each year

Ok?

β = 0.75 per partenrship

D = 2 months (with some treatment)

What is going to happen?

Gonorrhoea - SIS model

The reproduction number

$R_0 = c * \beta_{ptr} * D$
$= 2 * 0.75 * 0.167$
$= ??$

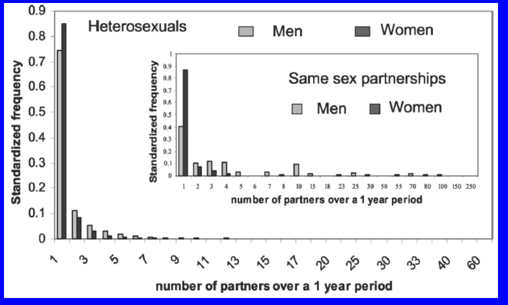
For $R_0 > 1$ we would need

- average annual partner change rate in the whole sexually active population of > 8, or
- duration of infection of 8 months,
- or combination of both higher…

Gonorrhoea in the US

- Why did Gonorrhoea *not* fade out of the US population, but *did* fade out of our model?
- It may not be a parameterisation problem, but a structural problem with our model

Reported annual number of partners for heterosexual and homosexual men and women in Britain (zeros omitted)

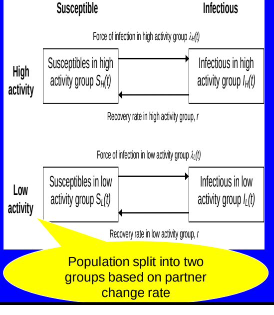


National Survey of Sexual Attitudes and Lifestyles, 2000 ; *Schneeberger, Mercer et al, 2004*

Gonorrhoea in the US

- Why did Gonorrhoea *not* fade out of the US population, but *did* fade out of our model?
- It may not be a parameterisation problem, but a structural problem with our model
- Let's explore the impact of splitting the population into a high and a low activity group
- …while keeping the total number of partnerships per unit time constant, in the population

2 activity-group model of Gonorrhoea transmission



$$\frac{dS_j(t)}{dt} = -\lambda_j(t)S_j(t) + rI_j(t)$$

$$\frac{dI_j(t)}{dt} = +\lambda_j(t)S_j(t) - rI_j(t)$$

Where j indicates high or low activity group

Let's assume:
- Proportionate mixing (partnerships chosen at random => more active people more likely to be chosen)
- Keep mean ptr change rate = 2/yr
- High activity is 2% of population
- 1.4/y in low activity
  => ~ 31/y in high activity

Force of infection for 2 activity-group model of gonorrhoea transmission

From before, the force of infection is:

$$\lambda(t) = c\,\beta_p\,i(t)$$

Why can't we use this formula directly to determine the force of infection *on a high or low activity group member?*

Force of infection for 2 group model of gonorrhoea transmission

Two reasons:

1) ______________________

2) ______________________

Force of infection for 2 group model of gonorrhoea transmission

FOI is partner change rate in that group times β_p times some average of the prevalence in the 2 groups, *p(t)*:

$$\lambda_j(t) = c_j \beta_p p(t) \quad \text{(Eq 1.9)}$$

Where 'some average' *p(t)* is

$$p(t) = g_H \times i_H(t) + g_L \times i_L(t) \quad \text{(Eq 1.10)}$$

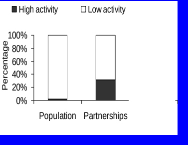
where g_H and g_L are the probabilities that a partner, selected according to proportionate mixing, will be a member of the high or low-activity group; and $i_H(t)$ and $i_L(t)$ are the prevalences in the groups

Prob partner will be a member of high activity group (panel 1-4)

$$g_H = \frac{c_H n_H}{c_H n_H + c_L n_L}$$

$$g_H = \frac{31.4 \times 0.02}{31.4 \times 0.02 + 1.4 \times 0.98}$$

$$g_H = 0.31$$



Here 31% of partnerships
from 2% population in high activity group

Calculating R_0 in a population with heterogeneity in sexual activity

- So if c_H=31.4 per year, c_L=1.4 per year, *D=2 months* and β = 0.75
- # secondary infections from high or low activity individual in a susceptible population:

R_H	$= c_H \beta D$	= 31.4	* 0.75 * 0.167 =	3.93
R_L	$= c_L \beta D$	= 1.4	* 0.75 * 0.167 =	0.18

- At invasion, 22x more infections due to each infected high-activity group member than low
- So will the STI invade?

R_0 for 2-activity group, proportionate mixing model of NG transmission

R_0 is the weighted average of R_H and R_L

(Proof in Panel 1-5)

For proportionate mixing g_H = 0.31 & g_L = 0.69

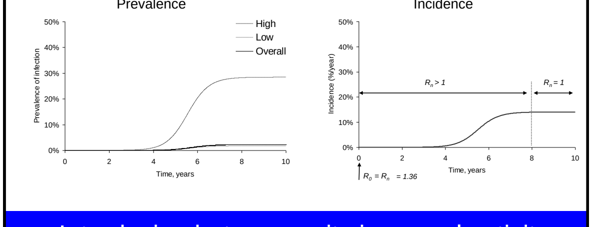
$R_0 = g_H R_H + g_L R_L$

$R_0 = 0.31 * 3.93 + 0.69 * 0.18 =$ 1.36

> 1 and therefore gonorrhoea endemic

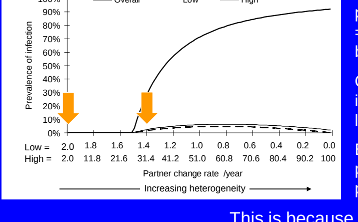
(Formula and proof for any mixing pattern in Panel 1-8)

Predicted prevalence and overall incidence of gonorrhoea in a model with heterogeneity in activity



- Introducing heterogeneity in sexual activity has also enabled us to predict a low overall infection prevalence of 2.3%
  ~ 2% estimate in US

Effect of increasing heterogeneity in activity on equilibrium STI prevalence



Increasing hetero. with p'ships chosen proportion'ly => more active more likely to be chosen

Once heterogeneity increases above a critical level, R_0 > 1

But, if we continue, NG prevalence in the overall population first ↑ and then ↓

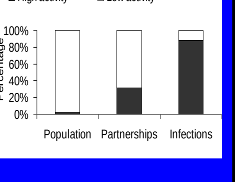
This is because

The impact of ↑ heterogeneity on ↑ the prevalence of infection in the high-activity group (saturation)	Out-weighed by	The impact of ↑ heterogeneity on ↓ the partner change rate in low-activity group

In the extreme, when c_L = 0, gonorrohoea goes extinct in low risk group

Summary

- By adding heterogeneity in risk behaviour (whilst keeping total number of partnerships constant)
- We have
  - been able to predict a low endemic prevalence ~ Data
  - Shown in the vast majority of the population the number of secondary infections << 1
  - Shown high-activity individuals are likely to generate many more secondary infections than low activity, because
    - they are more sexually active, &
    - they are more likely to be infected



- This modelling helped alter Gonorrhoea control policy in the US

Mixing by sexual activity

- Up until now we have assumed *proportionate mixing* i.e. random mixing by proportion of partnerships generated by each group.
- This is likely to be incorrect
- Much social and epidemiological research show people mix with people more like themselves than random
- Other mixing patterns:
  - With-like mixing (also called assortative)
  - With-unlike mixing (disassortative)
- Note, can model mixing by <u>any</u> characteristic
  - e.g. age, gender, activity…

Mixing matrices

- Can summarise mixing patterns in similar way as for respiratory infections
- Use a matrix
- Differ from earlier sessions because elements only measure contact probabilities, not contact and transmission probabilities combined

Mixing matrices

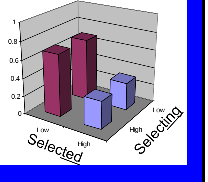
For proportionate mixing:

Probability that someone in the high-activity group forms a partnership with someone in the high-activity group, g_{HH}

=

Probability that someone in the low-activity group forms a partnership with someone in the high-activity group, g_{HL}

$$\text{Partner } j \quad \begin{array}{c|cc} & \multicolumn{2}{c}{\text{Partner } k} \\ & H & L \\ \hline H & g_{HH} & g_{HL} \\ L & g_{LH} & g_{LL} \end{array} \qquad = \quad \begin{array}{c|cc} & H & L \\ \hline H & 0.31 & 0.31 \\ L & 0.69 & 0.69 \end{array}$$

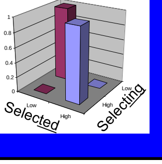


(See Panel 1-4 in notes for calculation of probabilities)

Mixing matrices

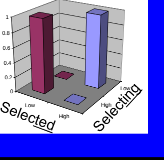
Purely *with-like*

$$\begin{array}{c|cc} & H & L \\ \hline H & 1 & 0 \\ L & 0 & 1 \end{array}$$



Purely *with-unlike*

$$\begin{array}{c|cc} & H & L \\ \hline H & 0 & 1 \\ L & 1 & 0 \end{array}$$



Summary measure of mixing, *Q*

- Useful to have a summary measure
- Sum the values along the diagonal of the matrix
- Adjust it so
  - Q = 1 when purely *with-like*
  - Q = 0 when *proportionate*
  - Q = -1 when purely *with-unlike*

$$Q = \frac{\left(\sum_{j=k} g_{jk} - 1\right)}{b - 1}$$

b is the number of groups

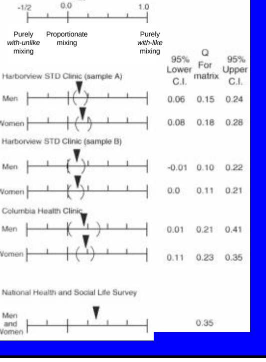
- Eg, for proportionate should = 0

$$\begin{array}{c|cc} & H & L \\ \hline H & 0.31 & 0.31 \\ L & 0.69 & 0.69 \end{array}$$

- $Q = \dfrac{0.31 + 0.69 - 1}{2 - 1}$
- $= \dfrac{1 - 1}{1}$
- $= 0$

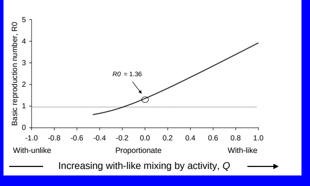
Gupta, AIDS '89

The value of the measure Q for mixing between sexual activity groups in four studies of sexual behaviour in the US



Garnett, 96

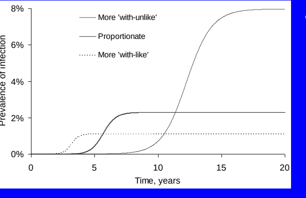
Effects of mixing on R_0



- Keep c, D and β_p constant
- R_0 increases as the mixing pattern becomes more *with-like*

- Higher-activity individuals tend to contact other higher activity individuals more frequently
- Higher-activity individuals have a higher partner change rate and therefore generate more secondary infections
- R_0 ↑

Effects of mixing on rate of STI spread

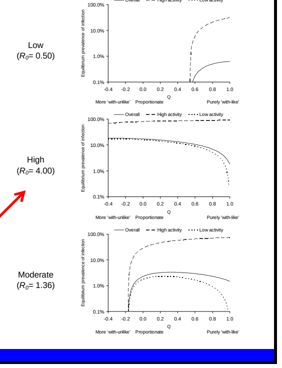


- For a given R_0, increasing *with-like* mixing means infection
  - invades more rapidly
    - BUT
  - results in lower equilibrium prevalence (!)

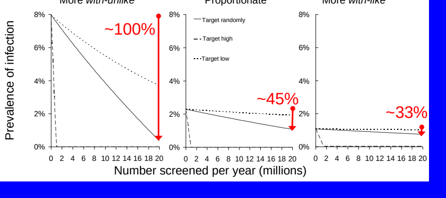
- Quicker rise: Higher-activity individuals are more likely to transmit infection to other higher-activity individuals, who generate new infections more quickly than lower activity individuals
- Lower equilibrium prevalence: Prevalence rises more quickly in high-activity group and more contacts are 'wasted' on infected's earlier than in scenarios with more mixing with lower-activity group, but same R_0

Effects of mixing on equilibrium STI prevalence

- Population level impact of changes not always intuitive
- Eg Behavioural message to general population (ie low risk) women: '*don't partner with men who you think have other partners*'
  - ie ↑ '*with-like*' mixing
- If all else equal, increasing *with-like* mixing may not lead to a reduction equilibrium prevalence in overall pop.
- It depends on R_0
  - At high R_0 , prev may ↓
  - At low R_0 , prev may ↑
  - At moderate R_0, prev ↑ or ↓



Implications of heterogeneity in sexual activity and mixing on STI control (R_0=1.36)



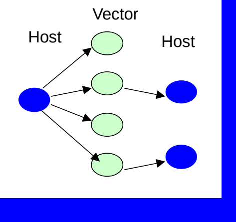
- Prioritising higher-risk members is more effective per-person-screened than at random or low-activity
- Increased *with-like* mixing tends to make STIs more difficult to control (~100% → ~45% → ~33%)
  - Fewer infections 'wasted' on low-activity group

Two gender STI model

- If we are modelling heterosexual mixing between the genders. Which of these three types of mixing between the genders are we modelling?
  - *With-like* mixing
  - *With-unlike* mixing
  - *Proportionate* mixing

'

Transmission between genders



Transmission from males to females to males…

Looks a bit like host vector-borne modelling in which the infection is transmitted from host to vector to host…
But here the 'vector' is the other gender.
Ross noticed this in 1911, and Hethcote based his STI modelling equations on those used by Ross to describe malaria transmission

Summary

- Understand the important characteristics of sexually transmitted infections and how they differ from the infections modelled so far
- Use simple deterministic compartmental models to explore the transmission dynamics of short-duration curable STIs such as gonorrhoea to,
  - Explore the importance of heterogeneity in sexual activity for STI invasion and endemic prevalence
  - Appreciate the importance of mixing patterns on R_0, the rate of STI spread, the equilibrium STI prevalence and the utility of 'Q', a summary measure of mixing
- Explore the importance of heterogeneity in sexual activity and mixing patterns for STI control
- Appreciate the similarity between a heterosexual STI model and a host-vector infection model

Key references

- *Hethcote, H. and J. Yorke* (1984). Lecture notes in biomathematics: Gonorrhea transmission and control (vol 56). S. Levin. **56**. Download from http://www.math.uiowa.edu/~hethcote/
- *Gupta, S., R. M. Anderson and R. M. May (1989).* "Networks of sexual contacts: implications for the pattern of spread of HIV." AIDS **3**(12): 807-17.

Sexually Transmitted Infections

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Be a virus, see the world.

Per act and per partnership transmission probability

We assumed $\beta_{ptr} = 1$.

This is an approximation of the cumulative probability of transmission for a number of sexual contacts.

If the per sex act probability of transmission is β_{act} the per partnership transmission probability is:

$$\beta_{ptr} = 1 - (1 - \beta_{act})^{acts}$$

$1 - \beta_{act}$ — Probability of **not** getting infected in one act

$(1 - \beta_{act})^{acts}$ — Probability of **not** getting infected in 'acts' sex acts

$1 - (1 - \beta_{act})^{acts}$ — Probability of **getting** infected in 'acts' sex acts

Calculating the per partnership transmission probability

If $\beta_{act} = 25\%$

For one sex act:

$$\beta_{ptr} = 1 - (1 - 0.25)^1 = 1 - 0.75 = 25\ \%$$

Calculating the per partnership transmission probability

For two sex acts:

$$\beta_{ptr} = 1 - (1 - 0.25)^2$$
$$= 1 - (1 - 0.25)(1 - 0.25)$$
$$= 1 - 0.75 * 0.75$$
$$= 1 - 0.56$$
$$\mathbf{= 44\ \%}$$

Calculating the per partnership transmission probability

Similarly:

*For **10** acts:*

$\beta_{ptr} = 1 - (1 - 0.25)^{10} = 1 - 0.06 = \mathbf{94\ \%}$

*For **15** acts:*

$\beta_{ptr} = 1 - (1 - 0.25)^{15} = 1 - 0.01 = \mathbf{99\ \%}$

So our assumption that β_{ptr} =1 is ok for 15 or more sex acts per partnership

β_{ptr} and β_{act}