Dynamic pair formation models

Application to sexual networks and STI

Mirjam Kretzschmar

rivm

UMC
University Medical Center
Utrecht

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Models for sexually transmitted infections

Which frameworks?

- HIV/AIDS: SI framework
- chlamydia and gonorrhoea : SIS framework
- hepatitis B: SIR framework

What do we have to consider?

Behaviour and disease specific parameters

Contact patterns:

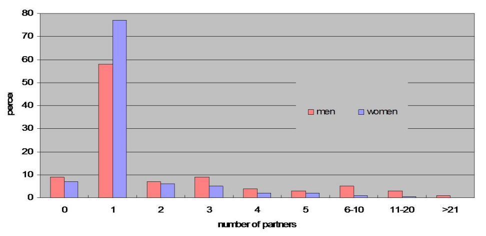
- heterogeneity in number of contacts (core group)
- mixing
- partnership duration
- partnership overlap

Disease specific characteristics:

- Variable infectivity
- symptomatic/asymptomatic infections
- long/short time scales
- immunity
- reinfection

Heterogeneity in contact rates

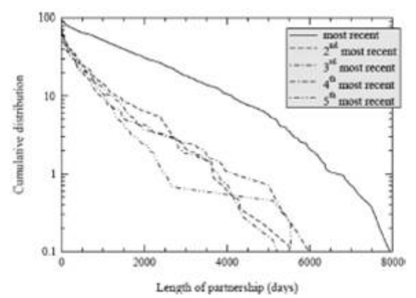
activity levels, core groups



- most people have few partners
- some have many (core group)
- men and women report different numbers of partners

Partnership duration

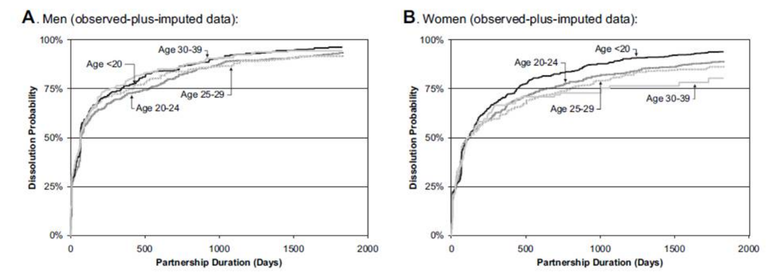
Foxman et al. 2006



- some partnerships dissolve very quickly, others have exponentially distributed duration
- ongoing partnerships censored
- model with instantaneous contacts cannot capture this feature

Partnership duration

Nelson et al. 2010



- age dependence
- 25% partnerships casual
- what is impact of partnership duration on transmission dynamics?

Historical remarks

Historical remarks

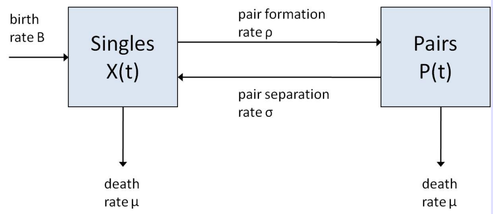
Pair formation models used in mathematical demography (marriage models).

First introduced to epidemiology by Dietz & Hadeler (1988)

They study age dependent pair formation models in a deterministic framework.

Model formulation

Partnership formation and dissolution

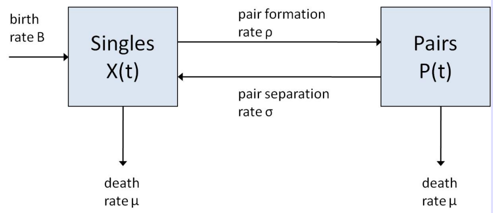


$$\begin{aligned} \frac{dX}{dt} &= B - \mu X - \rho X + 2\sigma P + 2\mu P \\ \frac{dP}{dt} &= \frac{1}{2}\rho X - \sigma P - 2\mu P \end{aligned}$$

Assume pair formation process is at equilibrium.

Model formulation

equilibrium



birth rate B

Singles X(t)

pair formation rate ρ

Pairs P(t)

pair separation rate σ

death rate μ

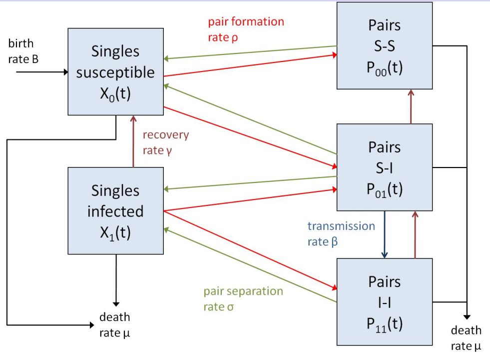
death rate μ

$$
\begin{aligned}
X^{\star} &= \frac{B(\sigma+2\mu)}{\mu(\rho+\sigma+2\mu)} \\
P^{\star} &= \frac{B\rho}{2\mu(\rho+\sigma+2\mu)}
\end{aligned}
$$

So $N = X + 2P = B/\mu$. This means that a fraction $x^{\star} = \frac{\sigma+2\mu}{\rho+\sigma+2\mu}$ is single.

Model formulation

pair formation and SIS infection



Assumptions:

- no distinction between men/women
- individuals are born susceptible
- infection does not increase mortality
- transmission only in pairs of infected and susceptible

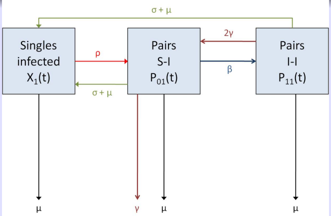
Model formulation

pair formation and SIS infection

$$\begin{aligned}
\frac{dX_0}{dt} &= B - \mu X_0 - \rho X_0 + \sigma(2P_{00} + P_{01}) + \mu(2P_{00} + P_{01}) + \gamma X_1 \\
\frac{dX_1}{dt} &= -\mu X_1 - \rho X_1 + \sigma(2P_{11} + P_{01}) + \mu(2P_{11} + P_{01}) - \gamma X_1 \\
\frac{dP_{00}}{dt} &= \frac{1}{2}\frac{\rho X_0^2}{X_0 + X_1} - \sigma P_{00} - 2\mu P_{00} + \gamma P_{01} \\
\frac{dP_{01}}{dt} &= \frac{\rho X_0 X_1}{X_0 + X_1} - \sigma P_{01} - 2\mu P_{01} - \gamma P_{01} - \beta P_{01} + 2\gamma P_{11} \\
\frac{dP_{11}}{dt} &= \frac{1}{2}\frac{\rho X_1^2}{X_0 + X_1} - \sigma P_{11} - 2\mu P_{11} + \beta P_{01} - 2\gamma P_{11}
\end{aligned}$$

We can simplify this model by assuming that the pair formation process is at equilibrium. Then $X_0 = X^\star - X_1$ and $P_{00} = P^\star - P_{01} - P_{11}$.

Model formulation
reduction to 3 equations



$$\begin{aligned}
\frac{dX_1}{dt} &= -(\mu+\rho+\gamma)X_1 + (\sigma+\mu)(2P_{11}+P_{01}) \\
\frac{dP_{01}}{dt} &= \rho X_1\left(1-\frac{X_1}{X^\star}\right) - (\sigma+2\mu+\beta+\gamma)P_{01} + 2\gamma P_{11} \\
\frac{dP_{11}}{dt} &= \frac{\rho X_1^2}{2X^\star} - (\sigma+2\mu+2\gamma)P_{11} + \beta P_{01}
\end{aligned}$$

We can write the prevalence as $I = X_1 + P_{01} + 2P_{11}$.

Model formulation

basic reproduction number

The basic reproduction number can be computed as the product of

- the probability of moving into the single state after being infected
- the number of partners in the remaining life time *M*
- the probability of infecting a susceptible partner *b*

Let us first assume that there is no recovery, i.e. $\gamma = 0$. Then

$$R_0 = \frac{\beta\rho(\sigma+\mu)}{\mu(\rho+\sigma+2\mu)(\sigma+2\mu+\beta)}$$

Model formulation
basic reproduction number

If there is recovery, we also have to take reinfection into account. An individuals partner can recover and get reinfected, so that the index case moves back and forth between P_{11} and P_{01} before the pair separates.
The probability of moving from P_{11} to X_1 either directly or via recovery of the partner, but without reinfecting the partner is

$$q_0 = \frac{\sigma + \mu}{\sigma + 2\mu + 2\gamma} \left(1 + \frac{\gamma}{\sigma + 2\mu + \beta + \gamma} \right)$$

The probability of reinfecting the partner $i > 0$ times before separation is

$$p^i = \left(\frac{\gamma}{(\sigma + 2\mu + 2\gamma)} \frac{\beta}{(\sigma + 2\mu + \beta + \gamma)} \right)^i$$

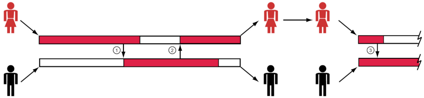
We have to sum the p^i over all $i = 1, 2, ...$ to get the probability that any number of reinfections occur before separation. Because $p < 1$ the sum over all p_i converges to

$$\sum_{i=0}^{\infty} p^i = \frac{1}{(1-p)} = \frac{(\sigma + 2\mu + 2\gamma)(\sigma + 2\mu + \beta + \gamma}{(\sigma + 2\mu)(\sigma + 2\mu + \beta + 2\gamma) + \gamma\beta}$$

Model formulation

basic reproduction number with reinfection

Partner can also reinfect the original index case. In effect reinfection is a prolongation of the infectious period.



First transmission (①), this is counted in the R₀ with and without re-infection within partnerships.

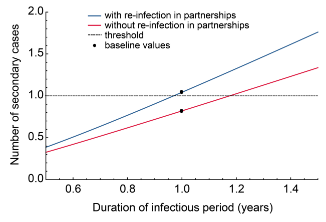
Re-infection (②) prolongs the infectious period, enabling more transmissions in future partners (③).

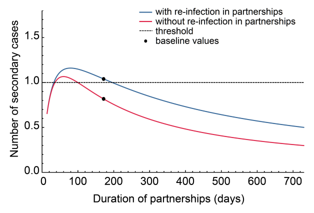
$$R_0 = b\sum_{i=1}^{\infty}(dq)^i = b\frac{dq}{1-dq}$$

b	Probability that the woman transmits her infection to her susceptible partner
q	Probability of a woman getting out off a partnership and still being infected after n number of re-infections (this is mainly dependent on the infection process)
d	Probability of an infected woman getting into a partnership before death or recovery (this is mainly dependent on the pair formation process)

Model formulation

basic reproduction number



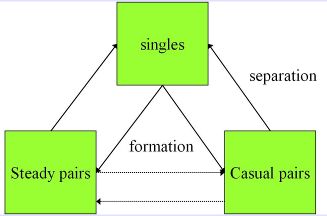


The basic reproduction number depends on the average duration of partnerships. For very short or very long partnership durations the infection cannot establish itself in the population.
Contribution of reinfection to Chlamydia transmission and effects of screening and partner notification

joint work with Janneke Heijne, Sereina Herzog, and Nicola Low (University of Bern).

Different types of partnerships

Steady and casual



Model can reproduce observed distributions of partnership durations.

Variable infectivity

Two stages of infection

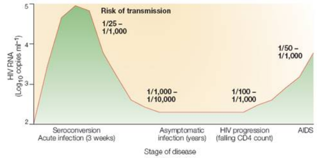
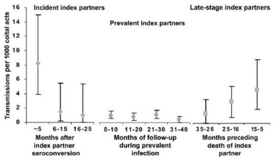
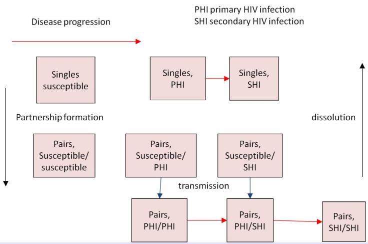


Figure 1 | **The changing viral load during the different stages of disease and the effects of viral load on the probability of sexual transmission of HIV.**



Question: how do partnership duration and variable infectivity interact?

Modelling HIV in MSM
Variable infectivity



Disease progression

PHI primary HIV infection
SHI secondary HIV infection

Singles susceptible

Singles, PHI

Singles, SHI

Partnership formation

dissolution

Pairs, Susceptible/ susceptible

Pairs, Susceptible/ PHI

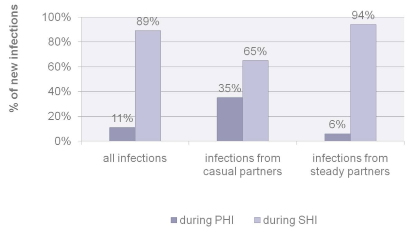
Pairs, Susceptible/ SHI

transmission

Pairs, PHI/PHI

Pairs, PHI/SHI

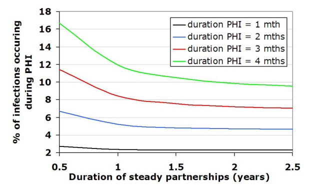
Pairs, SHI/SHI

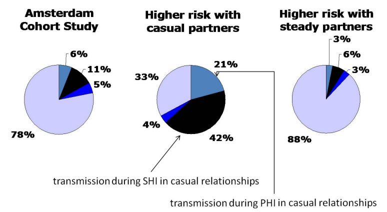


Pair formation model with instantaneous contacts added (casual partnerships).
Xiridou et al AIDS 2003; AIDS 2004

Fraction of transmissions from primary HIV infection

Variable infectivity





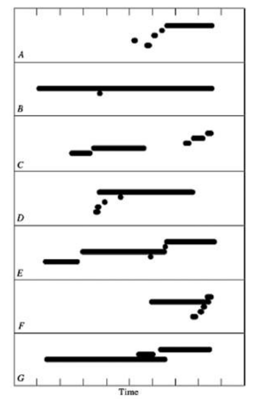
Conclusions:

- Primary HIV infection: important in transmission from casual partners, but not in transmission from steady partners
- Advanced epidemic: contribution of PHI to HIV incidence is small, if steady partners are the major source of infection

Other issues ...

other models?

- age dependene, age mixing
- differences men - women
- hetero- and homosexual populations
- heterogeneity in partner change rates
- overlap in partnerships, concurrent partnerships



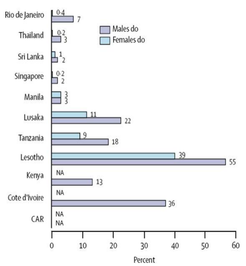
⟶ Networks

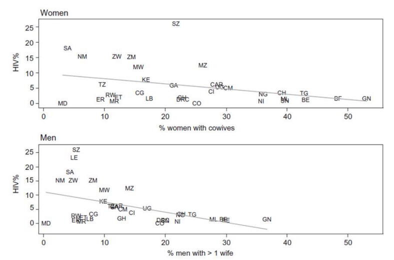
One option: use individual based simulations to model overlapping partnerships.

Model with star shaped components

The concurrency debate

Is concurrency driving the HIV epidemic in Sub Saharan Africa?



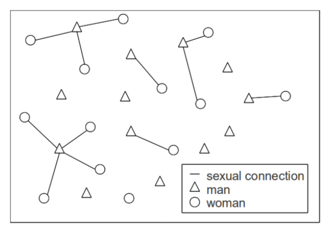


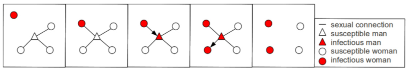
Halperin & Epstein Lancet 2004

Reniers & Watkins AIDS 2010

Modelling polygyny

Project KaYin Leung, joint work with Odo Diekmann.





Modelling polygyny

Equations for pair formation process

$$\begin{aligned} x: &= \text{the fraction of single women,} \\ p_j: &= \text{the fraction of men with } j \text{ partners, } j \geq 0. \end{aligned}$$

The set of ODEs describing the partnership dynamics is:

$$\begin{aligned} \frac{dx}{dt} &= \frac{\mu}{2} - \frac{2B\rho}{\mu} x \sum_{k=0}^{\infty} p_k + (\sigma + \mu) \sum_{k=1} k p_k - \mu x, \\ \frac{dp_0}{dt} &= \frac{\mu}{2} - \frac{2B\rho}{\mu} x p_0 + (\sigma + \mu) p_1 - \mu p_0, \\ \frac{dp_j}{dt} &= \frac{2B\rho}{\mu} x p_{j-1} - \left(\frac{2B\rho}{\mu} x + (\sigma + \mu) j \right) p_j \\ &\quad + (\sigma + \mu)(j+1) p_{j+1} - \mu p_j, \end{aligned} \tag{1}$$

for $j \geq 1$.

Modelling polygyny

Equations for infection dynamics:

- x_0, x_1, denote the fractions of susceptible and infected women
- $p_{n,k}$, and $q_{n,k}$ denote the fractions of men with n partners of which k are infected

We assume that the pair formation process is at equilibrium, then the susceptible fractions can be eliminated from the system.
The fraction of infected men is given by

$$i_m = \sum_{n=0}^{\infty} \sum_{k=0}^{n} q_{n,k},$$

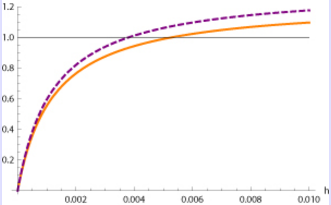
and the fraction of infected women by

$$i_f = x_1 + \sum_{n=1}^{\infty} \sum_{k=1}^{n} k(p_{n,k} + q_{n,k}).$$

First results

R_0 can be computed from R_f (number of infected men by one infected woman) and R_m (number of infected women by one infected man) as

$$R_0 = \sqrt{R_f R_m}. \tag{2}$$



Comparison of R_0 for monogamous (orange) and polygamous (purple) populations.

$$R_0 = \sqrt{R_m R_f} > R_f = R_0^M,$$

i.e. the basic reproduction number is always larger in the polygynous population than in the monogamous population.

Oongoing work

Polygyny model (with KaYin Leung and Odo Diekmann):

- can we compute endemic equilibrium explicitly?
- Relaxing the assumptions: dependency between partners
- Adding instantaneous contacts between men and women
- Dependence of R_0 on parameters in more complex situations
- Relationship with data

Reinfection in partnerships (with Janneke Heijne, Sereina Herzog, Nicola Low):

- take short term immunity into account
- effectiveness of screening and partner notification
- distinguish risk levels (core group)
- Estimate contribution of reinfections in partnerships to prevalence

Open question:
Are other analytically tractable variants of the pair formation framework possible?

Acknowledgements

Modelling reinfection in SIS pair formation models:
Janneke Heijne, Sereina Herzog, Nicola Low (University of Bern, Switzerland)

Modelling polygynous populations:
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Modelling chlamydia infections in heterosexual populations:
Boris Schmid (RIVM)