Community viral load

We explore how sexual behaviour and STI co-infection (HSV2, HCV) dynamics jointly influence the evolution of HIV viral load, and subsequently the rate of new HIV infections.

1. Implement HIV-HSV2 (resp. HCV) co-infection in SIMPACT
2. Simulate

   ~ 10,000 scenarios in a homosexual population of 10,000 men:

   - introducing ART in 1994 (simulate as an intervention event, adapt every 1-2 year, vary monitoring.cd4.threshold);
   - and varying the following parameters:
     1) parameters related to sexual behavior (agegap formation hazard, MSM version):
        - $\alpha_{numrel,sum}$: penalty per ongoing relationship
        - $\alpha_{numrel,diff}$: penalty for differing degrees (very negative value results in more assortative mixing w.r.t. degree)
        - $\alpha_{eagerness,diff}$: penalty for differing intrinsic sexual drive (very negative value results in more assortative mixing w.r.t. intrinsic sexual drive)
        - scale parameters of the distribution from which individuals draw intrinsic sexual drive value (E_{man1} and E_{man2}). This scale parameters influences the amount of heterogeneity in intrinsic sexual drive levels in the population. Simulate different types of distributions.
     2) parameters related to intra-couple HIV transmission
        - rho: correlation between SPVLs of infector and newly infected individual (to study SPVL heritability)
        - d: penalty on transmission hazard per ongoing relationship
        - mean and stdev of the distribution from which SPVL values are drawn for individuals who acquire infection in the course of a simulation run
        - mean and stdev from which SPVL values are drawn (investigate role of founder effects).

   We can sample using Latin Hypercube Sampling. Software: R – lhs package, function randomLHS.

   Key assumptions:

   - heritability of set point viral load
   - agegap formation hazard

3. For each of the 10,000 scenarios, we calculate the following summary statistics:
   1) To characterize sexual network connectivity
      - point prevalence of concurrency at t15 (and other time points)
      - summary statistics of network connectivity:

        - degree distribution:

          For a sexual network, vertices represent persons and edges sexual

relationships between them. The degree d of a vertex represents the number of sexual partners of a person, and the degree distribution is the distribution of d.

- conditional distribution: relative frequencies of the form $f_{d'|d}$ with which edges from a vertex of degree d are connected to another vertex of degree d'. Means of these conditional distributions as a function of d summarize associations between persons with a high number of sexual partners and persons with a low number of partners.

- degree likelihood: measure proportional to the sum, over all edges, of the products $d(v_1)d(v_2)$ of the degrees of the vertices v_1, v_2 defining the edges $e = (v_1, v_2)$

- closeness centrality: high closeness centrality vertices correspond to highly influential individuals. People with high closeness centrality in a sexual network are highly responsible for the spread of HIV.

- betweenness centrality: indicates the extent to which individuals transmit HIV to others within the sexual network.

- average distances between distinct vertices: can be used to describe geographical distances between persons.

- summary statistics of network assortativity:

  - assortativity coefficient: minimum (between -1 and 1) = perfectly dissortative, every edge connects vertices (individuals) of two different categories; 1 = perfectly assortitative, edges connect only vertices (individuals) from the same category; 0 = random.

  - for continuous characteristics (e.g. age): Pearson correlation coefficient.

- summary statistics of network heterogeneity:

  - degree distribution

2) To characterize time-trend in viral load distribution
   - mean and median log10 SPVL of seed HIV infections
   - difference t0 – t15 in mean, median, stdev and IQR log10 viral load
   - difference t0 – t15 in mean, median, stdev and IQR log10 SPVL
   - also other time points than t15
3) To characterize the course of the HIV epidemic
   - HIV prevalence at t15

Commented [DH1]: Is dus iets anders dan dat we dachten tijdens onze meeting op 9 nov. Is dit wel zinvol om dit te berekenen?

Commented [DH2]: Heeft volgens mij niet echt veel te betekenen in termen van sexual networks. Weglaten?

- Cumulative HIV incidence
- Average age among HIV infected people at t15
- Also other time points than t15

4) To characterize transmission dynamics
   - Average number of new infections over the complete infectious period
   - Average number of new infections over the complete infectious period, per log10 SPVL bin
5) To characterize HIV-HSV2 (resp. HIV-HCV) co-infection
   - HSV2 (resp. HCV) prevalence at t 15
   - HIV-HSV2 (resp. HIV-HCV) prevalence at t15
   - Cumulative HSV2 (resp. HCV) incidence
   - Cumulative HIV-HSV2 (resp. HIV-HCV) incidence
   - Average age among HSV2 (resp. HCV) infected people
   - Average age among HIV-HSV2 (resp. HIV-HCV) infected people
   - Also other time points than t15

4. Symbolic regression models (surrogate models) will be fitted to evaluate links between the summary statistics above. Software: Java, UA (code developed by Lander Willem & Sean Stijven); R: rgp package + eventually multivator package (R).
5. Sensitivity analysis:
   - examine the role of founder effects (extremely high / low VL in seeding HIV infections) in driving the time-trend in community VL distribution;
   - study the effect of relaxing the assumption that intra-couple transmission rate is independent of the number of ongoing relationships individuals have. Therefore, consider the following two models
     1) intra-couple transmission is a function of the viral load
        h = exp(a + b*V^(-c)) where V is the viral load.
     2) Sexual activity within relationships may decrease with growing numbers of concurrent relationships that man 1 (P_i) and man 2 (P_j) have.
        h = exp(a + b*V^(-c) + d*(P_i + P_j)