

Abstract

This document contains the details of the model used in the main paper.

Contents	
1 Introduction	1
2 Model without ART	2
3 Model with ART	2
4 Equilibria	3
5 Mixing	3
6 Infection profiles and the effect of treatment	6

Introduction

Throughout, we consider an entirely heterosexual population with a mixing matrix of the form:

$$K = \begin{pmatrix} 0 & M \\ W & 0 \end{pmatrix} \quad (1)$$

where M and W are 2×2 matrices referring to high- and low-sexual activity men and women.

In each case, the stable endemic equilibria of the models were obtained directly by numerically solving algebraic equations derived from setting all t -derivatives equal to zero. The proportion of the population in each activity class at equilibrium was fixed.

In the following two sections we describe the model both with, and without antiretroviral therapy (ART). We then describe how we parametrized the mixing; and finally go on to state our assumptions mortality, infectiousness, and the effect of ART on these.

Note that a simplified notational scheme was used in the main text. The correspondence with the scheme used there is detailed in Table 1.

Model without ART

The model is specified by a set of partial differential equations (PDEs), where τ denotes the time since an individual has been infected. $I_j(t, \tau)$ denotes the density of infectious individuals in class j (the index specifying a gender, and a sexual activity group) who have been infected for a time in the interval $[\tau, \tau + d\tau)$ at time t . An individual at this stage in their infection is assumed to have a relative infectiousness given by a function $\phi(\tau)$ and an excess hazard of death described by a function $\nu(\tau)$. The background mortality rate for disease-free individuals is

denoted μ , and the number of susceptible individuals in a class j is denoted S_j . These quantities obey the dynamics

$$\begin{aligned} \dot{S}_j(t) &= B_j(t) - \sum_k \int K_{jk} S_j(t) \phi(\tau) \frac{I_k(t, \tau)}{N_k(t)} d\tau - \mu S_j(t) \\ (\partial_t + \partial_\tau) I_k(t, \tau) &= -(\nu(\tau) + \mu) I_k(t, \tau) \\ I_j(t, 0) &= \sum_k \int K_{jk} S_j(t) \phi(\tau) \frac{I_k(t, \tau)}{N_k(t)} d\tau \end{aligned}$$

where $B_j(t)$ is the recruitment rate into a given category j , and N_j is the total number of infected and susceptible individuals in category j . The first equation represents the arrival of new susceptibles in category j , and their removal due to infection or death; the second represents the progress of infected individuals through their infection, being removed at an enhanced mortality rate; and the last equation is the boundary condition which accounts for the arrivals of new infections at the point $\tau = 0$.

Model with ART

We will assume that, upon infection, a proportion p_j of the S_j move onto an unbarred I_j time-course corresponding to no treatment, and a proportion $\bar{p}_j = 1 - p_j$ (i.e. the coverage of the intervention) onto the \bar{I}_j time-course (with its treatment-modified $\bar{\phi}$ and $\bar{\nu}$). Thus we have

$$\begin{aligned} \dot{S}_j &= B_j(t) - S_j \sum_k \int \frac{(K_{jk} \phi(\tau) I_k(t, \tau) + K_{jk} \bar{\phi}(\tau) \bar{I}_k(t, \tau))}{N_k(t)} d\tau - \mu S_j(t) \\ (\partial_t + \partial_\tau) I_j(t, \tau) &= -(\mu + \nu(\tau)) I_j(t, \tau) \\ (\partial_t + \partial_\tau) \bar{I}_j(t, \tau) &= -(\mu + \bar{\nu}(\tau)) \bar{I}_j(t, \tau) \\ I_j(t, 0) &= p_j S_j \sum_k \int \frac{(K_{jk} \phi(\tau) I_k(t, \tau) + K_{jk} \bar{\phi}(\tau) \bar{I}_k(t, \tau))}{N_k(t)} d\tau \\ \bar{I}_j(t, 0) &= \bar{p}_j S_j \sum_k \int \frac{(K_{jk} \phi(\tau) I_k(t, \tau) + K_{jk} \bar{\phi}(\tau) \bar{I}_k(t, \tau))}{N_k(t)} d\tau \end{aligned}$$

It is assumed that $\bar{\phi}(\tau)$ and $\bar{\nu}(\tau)$ would only depart from the untreated values, $\phi(\tau)$ and $\nu(\tau)$, once τ reaches the average time at which treatment begins.

Equilibria

Asymptotically, it follows from the continuity equation for I_j above that

$$I_j(\infty, \tau) = I_j(\infty, 0) e^{-H(\tau)} \quad (2)$$

where H is the cumulative hazard $H(\tau) = \int_0^\tau (\nu(\tau) + \mu) d\tau$. Writing the next generation matrix \bar{K}

$$\bar{K} = \int_0^\infty \phi(\tau) e^{-H(\tau)} K d\tau \quad (3)$$

and the equilibrium prevalences in each group as x_j , the boundary condition above yields the algebraic system

$$x_i = (1 - x_i) \sum_k \bar{K}_{ik} x_k \quad (4)$$

which can be solved numerically. The incidences at equilibrium are given by

$$I_i(\infty, 0) x_i / \left(\int e^{-H(\tau)} d\tau \right) \quad (5)$$

Notice that although the asymptotic recruitment rates, B_i , are necessary to determine the sizes of populations, they do not affect the per-capita prevalences. The reproduction number R_0 is defined as the largest eigenvalue of \bar{K} ; the working for the case with ART follows very similarly.

Mixing

Let n_W^j , with $j \in \{H, L\}$, be the number of women in the population who are high- or low-class respectively, and similarly n_M^j , with $j \in \{H, L\}$, for the number of high- and low-class men. Let q_i^j , with $j \in \{H, L\}$ and $i \in \{M, W\}$, be the respective average number of partnerships for a given type of individual during a certain time interval. Let Q be the total number of partnerships owned by men (or equivalently by women), i.e.

$$n_W^H q_W^H + n_W^L q_W^L = Q = n_M^H q_M^H + n_M^L q_M^L \quad (6)$$

Let

$$f_M^j = \frac{n_M^j q_M^j}{Q} \quad (7)$$

be the fraction of all partnerships with j -class men, and similarly. Let

$$\Pi_M = \begin{pmatrix} \Pi_M^{HH} & \Pi_M^{HL} \\ \Pi_M^{LH} & \Pi_M^{LL} \end{pmatrix} \quad (8)$$

be the mixing matrix, comprising of Π_M^{XY} : the proportion of all partnerships which involve an X -class man and an Y -class woman. Similarly, Π_W^{XY} is the proportion of all partnerships which involve an X -class woman and an Y -class man. Because partnerships are symmetrically owned, we have

$$\Pi_M = \Pi_W^T \quad (9)$$

If mixing between the two classes were at random, the mixing would be

$$\Pi_M \begin{pmatrix} f_M^H f_W^H & f_M^H f_W^L \\ f_M^L f_W^H & f_M^L f_W^L \end{pmatrix} \quad (10)$$

If mixing were completely assortative, we would have

$$\Pi_M = \begin{pmatrix} f_M^H & 0 \\ 0 & f_M^L \end{pmatrix} \quad (11)$$

Linearly interpolating between these two extremes so that $\epsilon = 1$ corresponds to completely assortative mixing and $\epsilon = 0$ to completely random, we get

$$\Pi_M(\epsilon) = \begin{pmatrix} f_M^H(\epsilon + (1 - \epsilon)f_W^H) & (1 - \epsilon)f_M^H f_W^L \\ (1 - \epsilon)f_M^L f_W^H & f_M^L(\epsilon + (1 - \epsilon)f_W^L) \end{pmatrix} \quad (12)$$

Note that the transpose condition forces any separate assortativity parameters for men and women to be the same.

The proportion of an X -man's partnerships which are with class- Y women can be calculated as the

$$c_M^{XY}(\epsilon) = \frac{\Pi_M^{XY}(\epsilon)}{(\Pi_M^{XY}(\epsilon) + \Pi_M^{X\bar{Y}}(\epsilon))} \quad (13)$$

where \bar{Y} means “not- Y ”. Thus

$$\begin{aligned} c_M(\epsilon) &= \begin{pmatrix} \frac{f_M^H(\epsilon + (1 - \epsilon)f_W^H)}{f_M^H} & \frac{(1 - \epsilon)f_M^H f_W^L}{f_M^H} \\ \frac{(1 - \epsilon)f_M^L f_W^H}{f_M^L} & \frac{f_M^L(\epsilon + (1 - \epsilon)f_W^L)}{f_M^L} \end{pmatrix} \\ &= \begin{pmatrix} (\epsilon + (1 - \epsilon)f_W^H) & (1 - \epsilon)f_W^L \\ (1 - \epsilon)f_W^H & (\epsilon + (1 - \epsilon)f_W^L) \end{pmatrix} \end{aligned} \quad (14)$$

Thus, for a basis in the order (WH, WL, MH, ML) ,

$$\begin{aligned} M &= \beta \begin{pmatrix} q_M^H(\epsilon + (1 - \epsilon)f_W^H) & q_M^H(1 - \epsilon)f_W^L \\ q_M^L(1 - \epsilon)f_W^H & q_M^L(\epsilon + (1 - \epsilon)f_W^L) \end{pmatrix} \\ W &= \beta \begin{pmatrix} q_W^H(\epsilon + (1 - \epsilon)f_M^H) & q_W^H(1 - \epsilon)f_M^L \\ q_W^L(1 - \epsilon)f_M^H & q_W^L(\epsilon + (1 - \epsilon)f_M^L) \end{pmatrix} \end{aligned} \quad (15)$$

We can therefore determine our choice of next generation by specifying, e.g.

- q_M^H , q_M^L , q_W^H , and q_W^L , with the interpretation of relative partner-change
- rates in each class.
- F_M^H and F_W^H : the fraction of men and women respectively who are in the ‘H’-class.
- R_0^L : the value of R_0 if the whole population consisted of ‘L’-class individuals.
- ϵ : the assortativity.

Other combinations would also be possible. From these we can calculate the β s by, e.g.

$$f_M^H = \frac{F_M^H q_M^H}{F_M^H q_M^H + (1 - F_M^H) q_M^L}, \quad f_M^L = \frac{(1 - F_M^H) q_M^L}{F_M^H q_M^H + (1 - F_M^H) q_M^L} \quad (16)$$

and by using the fact that

$$R_0^L \propto \sqrt{q_M^L q_W^L} \quad (17)$$

with the same constant of proportionality as the next generation matrix.

Table 1. Parameter values for scenarios considered.

Scenario	$q_M^L = q_W^L$	$q_M^H = q_W^H$	R_0^L	$F_M^H = F_W^H$	ϵ
Notation in main text	π	π	R_0^L	$(1-\theta)$	ϵ
A	1	1.613	1.1	0.1	0.5
B	1	4.348	0.7	0.1	0.1
C	1	13.111	0.7	0.1	0.9

In practice we took $F_M^H = F_W^H$ and $q_M^j = q_W^j$ for $j \in \{H, L\}$, and (without loss of generality) $q_M^L = q_W^L = 1$. With these conventions, and with ϕ normalized so that $\int e^{-H} \phi.d\tau = 1$, it is easy to see that $R_0^L = \beta$. We also adjusted the q so as to standardize the equilibrium incidence at 0.015 persons per person per year. The parameters used for the scenarios were therefore those given in Table 1.

Infection profiles and the effect of treatment

Untreated individuals were assumed to live for 11 years after infection (i.e. a step-function survival distribution) and follow the infectious profiles as given in [1] as shown in Fig. 1(a). Individuals started on ART time t after their infection are assumed to live an extra $E(t) = 2.5(11 - t)$ years (step-function survival distribution) : i.e. more than 25 years if treatment is started promptly, with a linearly decreasing return until 11 years when individuals are assumed to have died. The length of the acute and _nal phases are assumed unchanged, and the extra life is achieved by a longer set-point phase. ART introduced at time t is assumed to bring the infectiousness down to $r\%$ of the untreated level, until the last 0.75 years of life when

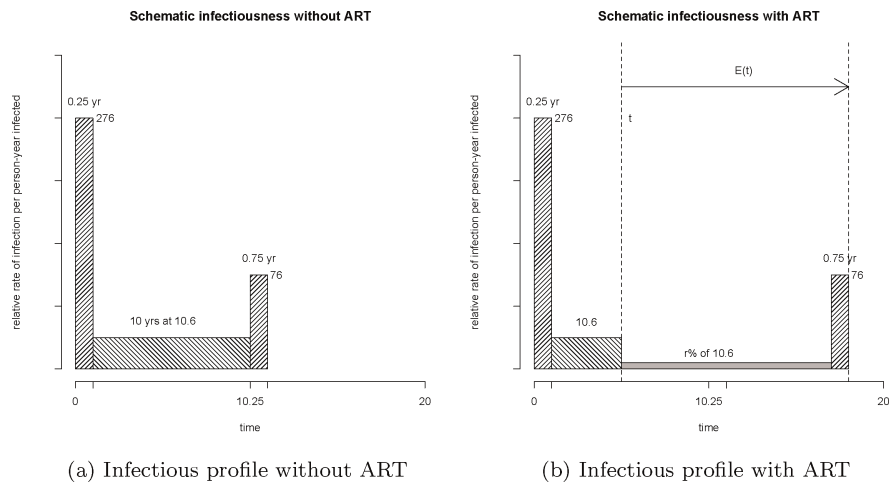


Figure 1. Without ART, individuals are assumed to go through 3 phases of infectiousness before dying after 11 years. If ART is introduced at time t , individuals are assumed to live an extra $E(t) = 2.5 * (11 - t)$ years from then, with an infectiousness of $r\%$ of the untreated set-point level until the last 0.75 years of life.

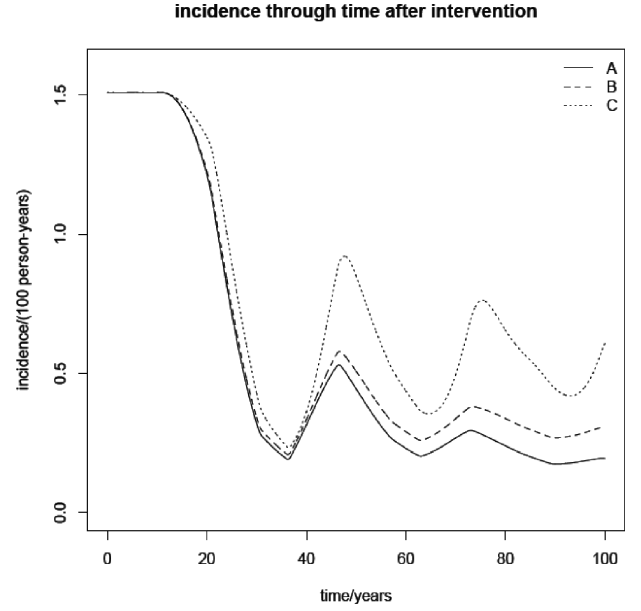


Figure 2. Incidence rate (per 100 person-years at risk) over time following the start of a Test and Treat intervention (ART starting 1 year after infection). The intervention starts in year 10 and reaches 80% coverage by year 20, and the lines show the impact of the intervention on incidence in each of the three scenarios A (solid line), B (dashed line) and C (dotted line). The rebounds in incidence are due to the first cohorts on treatment failing simultaneously, which would be damped in reality by variance in survival times on treatment (although this does not affect the eventual reduction in incidence).

the infectiousness is the same as the last 0.75 years of life without treatment. The choice of value for r is discussed in the main paper. This is shown schematically in Fig. 2(b). In the small region of parameter space where

the extra period of life achieved is less than 0.75 years, the infectiousness in the final stage is assumed to be at a lower, so that it has the same total weight as the same (shorter) stage without treatment.

References

[1] T. Déirdre Hollingsworth, Roy M Anderson, and Christophe Fraser. HIV-1 transmission, by stage of infection. *J INFECT DIS*, 198(5):687–693, Sep 2008.