Mathematical and Statistical Insights in Evaluating State Dependent Effectiveness of HIV Prevention Interventions

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Pre-exposure prophylaxis (PrEP) is any medical or public health procedure used before exposure to the disease causing agent, its purpose is to prevent, rather than treat or cure a disease (such as malaria, and HIV). PrEP can also refer to the aggressive use of vaccination (such as for rabies).

Most commonly, PrEP refers to an experimental HIV-prevention strategy that would use antiretrovirals to protect HIV-negative people from HIV infection.

According to ‘UNAIDS report on the global AIDS epidemic 2013’, as of 2012, there were **35.3 million** people living with HIV worldwide and **2.3 million** people became newly infected with HIV by estimation, and many people are at risk for HIV infection through sexual transmission. Therefore preemptive measures must be taken to prevent further dissemination. PrEP provides a promising prevention strategy for further HIV transmission.
In 2010, evidence from two different randomized clinical trials (Grant et al. (2010); Karim et al. (2010)) suggested that PrEP products based on antiretroviral drug Tenofovir taken orally as a pill (oral PrEP) or applied topically in the form of gel (vaginal microbicides (VMB)) can help prevent HIV.

First in South Africa, the CAPRISA 004 trial demonstrated a 39% (95%CI, 6% to 60%) overall decrease in HIV incidence among women in the VMB (gel) arm of the trial who were advised to use the product before and after each sex act (Karim et al. (2010)).

Later, the Global iPrEx trial of a daily use of a combination of two oral antiretroviral drugs, emtricitabine and tenofovir disoproxil fumarate, demonstrated a 44% efficacy (95%CI, 15% to 63%) reduction in the incidence of HIV, among men-who-have sex with men (MSM) (Grant et al. (2010)).

In 2012, one product (oral Truvada) was approved for PrEP use by FDA in United States, and recommended for use in South Africa. And there has been a broad discussion on what will be population-level benefits from wide-scale PrEP use in high prevalence settings.
Mathematical models have been used to simulate HIV transmission among MSM, and HIV heterosexual transmission stratified by gender (Abbas et al. (2007); Dimitrov et al. (2010, 2011); Pretorius et al. (2010); Vissers et al. (2008); Wilson et al. (2008)). Often a single intervention outcome based on

- cumulative number of infections prevented
- fractions of infections prevented
- reduction in HIV prevalence
- reduction in HIV incidence

has been used to evaluate the effectiveness of PrEP interventions.

These indicators express a wide variation over time and often disagree in their forecast on the success of the intervention (Dimitrov et al. (2010); Pretorius et al. (2010)). Therefore, the conclusions of many modeling studies are significantly influenced by the choice of the evaluation method and the period of evaluation (Dimitrov et al. (2011)).

In this work, we develop a deterministic mathematical model of HIV transmission to evaluate the public-health impact of oral PrEP interventions, compare PrEP effectiveness with respect to different evaluation methods, and analyze its dynamics over time.
Figure 1: Flow diagram of a PrEP intervention for the model (1) formulation.

$S^p$: Susceptible using PrEP; $S$: Susceptible not using PrEP;
$A$: AIDS (non-sexually active).

$N = S^p + S + I^p + I$: Total sexually active population.
"dual-protection" Model

\[
\begin{align*}
\frac{dS^p}{dt} &= k\Lambda - (1 - \alpha_s)\beta \frac{S^p I}{N} - (1 - \alpha_s)(1 - \alpha_i)\beta \frac{I^p S^p}{N} - \mu S^p \\
\frac{dS}{dt} &= (1 - k)\Lambda - \beta \frac{IS}{N} - (1 - \alpha_i)\beta \frac{I^p S}{N} - \mu S \\
\frac{dI^p}{dt} &= (1 - \alpha_s)\beta \frac{IS^p}{N} + (1 - \alpha_s)(1 - \alpha_i)\beta \frac{I^p S^p}{N} - (\mu + d)I^p \\
\frac{dI}{dt} &= \beta \frac{IS}{N} + (1 - \alpha_i)\beta \frac{I^p S}{N} - (\mu + d)I.
\end{align*}
\]

with initial conditions:

\[
\begin{align*}
S^p(0) &= k_1(1 - P)N(0) \\
S(0) &= (1 - k_1)(1 - P)N(0) \\
I^p(0) &= (1 - \theta)k_1 PN(0) \\
I(0) &= (1 - (1 - \theta)k_1)PN(0),
\end{align*}
\]

and that \(N = S^p + S + I^p + I\).
### Table 1: Parameter description and baseline values

<table>
<thead>
<tr>
<th>Par.</th>
<th>Description</th>
<th>Value</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>$d$</td>
<td>HIV carrier’s annual rate of progression to AIDS</td>
<td>0.1302</td>
<td>fitted (sta (2012))</td>
</tr>
<tr>
<td>$\Lambda$</td>
<td>Annual rate at which individuals become sexually active</td>
<td>38094</td>
<td>calc. (sta (2012))</td>
</tr>
<tr>
<td>$\frac{1}{\mu}$</td>
<td>Time (in years) to remain sexually active</td>
<td>( \frac{1}{0.0250} )</td>
<td>fitted (sta (2012))</td>
</tr>
<tr>
<td>$b_a$</td>
<td>HIV acquisition risk per act</td>
<td>0.0030</td>
<td>fitted (sta (2012))</td>
</tr>
<tr>
<td>$n$</td>
<td>Number of sexual acts per year per individual</td>
<td>65.8494</td>
<td>fitted (sta (2012))</td>
</tr>
<tr>
<td>$\beta$</td>
<td>Cumulative HIV-acquisition risk</td>
<td>$\beta(n, b_a)$</td>
<td>calc.</td>
</tr>
<tr>
<td>$N(0)$</td>
<td>Initial sexually active population</td>
<td>$10^6$</td>
<td>assumed</td>
</tr>
<tr>
<td>$P$</td>
<td>Initial HIV prevalence</td>
<td>0.166</td>
<td>(sta (2012))</td>
</tr>
<tr>
<td>$k_1$</td>
<td>Initial PrEP coverage</td>
<td>0.2</td>
<td>assumed</td>
</tr>
<tr>
<td>$\theta$</td>
<td>Reduction in the initial fraction of HIV positive</td>
<td>0.5</td>
<td>assumed</td>
</tr>
<tr>
<td>$k$</td>
<td>Proportion of the new recruits that start using PrEP</td>
<td>$k = k_1$</td>
<td>assumed</td>
</tr>
<tr>
<td>$\alpha_s$</td>
<td>Efficacy of PrEP in reducing susceptibility of PrEP users</td>
<td>0.5</td>
<td>assumed</td>
</tr>
<tr>
<td>$\alpha_i$</td>
<td>Efficacy of PrEP in reducing infectiousness of PrEP users</td>
<td>0.5</td>
<td>assumed</td>
</tr>
</tbody>
</table>

\[
\beta = 1 - (1 - b_a)^n.
\]
If assume using PrEP has no effect on the infectiousness \( (\alpha_i = 0) \) or that infected individuals do not take PrEP anymore, then the model becomes:

\[
\begin{align*}
\frac{dS^p}{dt} &= k\Lambda - (1 - \alpha_s)\beta \frac{S^p I}{N} - \mu S^p \\
\frac{dS}{dt} &= (1 - k)\Lambda - \beta \frac{SI}{N} - \mu S \\
\frac{dI}{dt} &= \beta \frac{SI}{N} + (1 - \alpha_s)\beta \frac{S^p I}{N} - (\mu + d)I
\end{align*}
\]

with initial conditions:

\[
\begin{align*}
S^p(0) &= k_1(1 - P)N(0) \\
S(0) &= (1 - k_1)(1 - P)N(0) \\
I(0) &= PN(0),
\end{align*}
\]

and that \( N = S^p + S + I \). The model without intervention:

\[
\begin{align*}
\frac{dS}{dt} &= \Lambda - \beta \frac{SI}{N} - \mu S \\
\frac{dI}{dt} &= \beta \frac{SI}{N} - (\mu + d)I
\end{align*}
\]

with initial conditions:

\[
\begin{align*}
S(0) &= (1 - P)N(0) \\
I(0) &= PN(0),
\end{align*}
\]

and that \( N = S + I \).
Modeling Assumptions

- The HIV prevalence in the whole population is representative for the HIV prevalence among each gender, i.e., the chance to have a HIV-positive partner is proportional to the total HIV prevalence.
- Individuals are assumed to have a fixed number of sex acts per year.
- Sexual behavior of an individual does not change if he/she starts using PrEP but sexual activity stops once AIDS is developed.
- The use of PrEP reduces both HIV susceptibility and infectiousness and by this reduces the HIV acquisition risk per sex act.
- We assume perfect adherence to PrEP: individuals who start using PrEP continue to follow the prescribed regimen indefinitely. However, the scenario with no reduction of infectiousness due to PrEP ($\alpha_i = 0$) is equivalent to immediate withdrawal from PrEP after HIV acquisition.
- The use of other HIV prevention measures including condom use, male circumcision, and ARV treatments are not considered.
We used demographic and HIV prevalence data representative for the sexually active population (15-49 years old) in South Africa for the period between 2001 and 2011 (sta (2012)) to parameterize our models in the scenario without PrEP.

- Start with initial parameter values borrowed from published studies: 
  \[ b_a = 0.0038 \text{(Boily et al. (2009))}, \ n = 80 \text{(Kalichman et al. (2009); Wawer et al. (2005))}, \ \mu = 1/35 \text{(UNAIDS (2009))}, \text{ and } \ d = 1/10 \text{(Morgan et al. (2002); Porter and Zaba (2004))}. \n\]

- We minimize the error measurement \[ \sum_{i=1}^{n} \left| ps_i - p_i \right| / n, \] where \(ps_i\) represents the HIV prevalence from model simulation, \(p_i\) represents the HIV prevalence from data, and \(n\) represents the number of data points.

- We obtain the following parameter set which fits best the prevalence data from year 2001 to year 2011: \(b_a = 0.0030, \ n = 65.8494, \ \mu = 0.0250, \text{ and } \ d = 0.1302.\)
Figure 2: (a) HIV prevalence among sexually active population in South Africa for the period 2001-2011 from data and fitted with the “no intervention” model; (b) Long-term projections of the HIV prevalence based on fitted “no intervention” model.
### Table 2: Indicator description

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_i(T)$</td>
<td>Cumulative indicator</td>
<td>Cumulative number of infections prevented over the period $[0, T]$ due to the usage of PrEP</td>
</tr>
<tr>
<td>$F_i(T)$</td>
<td>Fractional indicator</td>
<td>Fraction of infections prevented over the period $[0, T]$ due to the usage of PrEP</td>
</tr>
<tr>
<td>$P_i(T)$</td>
<td>Prevalence indicator</td>
<td>Reduction in HIV-prevalence at time $t = T$ due to the usage of PrEP</td>
</tr>
<tr>
<td>$aI_i(T)$</td>
<td>Incidence indicator</td>
<td>Reduction in the annual HIV incidence at time $t = T$ due to the usage of PrEP</td>
</tr>
<tr>
<td>$\hat{C}_i(T)$</td>
<td>Reduction indicator</td>
<td>Reduction in the projected number of infections at time $t = T$ due to the usage of PrEP</td>
</tr>
<tr>
<td>$\hat{F}_i(T)$</td>
<td>Fractional reduction indicator</td>
<td>Fraction of the projected number of infections at time $t = T$ reduced due to the usage of PrEP</td>
</tr>
</tbody>
</table>
Figure 3: Comparison of the indicators ($a_I$, $P_I$, and $F_I$) projections for two PrEP interventions over 50-year period. Intervention 1 assumes that $\theta = 0$ and $\alpha_s = \alpha_i = 0.5$. Intervention 2 assumes that $\theta = 1$, $\alpha_s = 0.5$ and $\alpha_i = 0.9$. All other parameters are fixed on their baseline parameter values from Table 1.

- Each of the incidence, prevalence and fractional indicators shows increasing effectiveness of both interventions over 50 years after initiation of PrEP (Fig. 3) with more benefits attributed to Intervention 1 initially but higher impact of Intervention 2 in a long-term.

- However, they disagree on the timing when the advantage of the Intervention 1 ends. Therefore, if PrEP is evaluated over periods between 17 and 32 years the choice of quantitative indicator is critical. We take a closer look at the key drivers of those discrepancies in the indicators’ dynamics.
To utilize the calculation of the cumulative indicators, we need to keep track of the cumulative number of new infections:

\[
\begin{align*}
\frac{dS^p}{dt} &= k\Lambda - (1 - \alpha_s)(1 - \alpha_i)\beta \frac{S^p I}{N} - \mu S^p \\
\frac{dS}{dt} &= (1 - k)\Lambda - \beta \frac{SI}{N} - (1 - \alpha_i)\beta \frac{IS^p}{N} - \mu S \\
\frac{dI^p}{dt} &= (1 - \alpha_s)\beta \frac{IS^p}{N} + (1 - \alpha_s)(1 - \alpha_i)\beta \frac{IS^p}{N} - (\mu + d)I^p \\
\frac{dl}{dt} &= \beta \frac{IS}{N} + (1 - \alpha_i)\beta \frac{IS^p}{N} - (\mu + d)l. \\
\frac{d(I^p_{New})}{dt} &= (1 - \alpha_s)\beta \frac{S^p I}{N} + (1 - \alpha_s)(1 - \alpha_i)\beta \frac{S^p I^p}{N} \\
\frac{d(I_{New})}{dt} &= \beta \frac{SI}{N} + (1 - \alpha_i)\beta \frac{SI^p}{N},
\end{align*}
\]

(4)

with \( I_{New}(0) = I^p_{New}(0) = 0 \).

\[
\begin{align*}
\frac{dS}{dt} &= \Lambda - \beta \frac{SI}{N} - \mu S \\
\frac{dl}{dt} &= \beta \frac{SI}{N} - (\mu + d)l \\
\frac{d(I_{New})}{dt} &= \beta \frac{SI}{N}
\end{align*}
\]

(5)

with \( I_{New}(0) = 0 \).

we use \([\ ]\) to denote variables from the model without PrEP (5) and \([\ ]_{DP}\) for variables from the “dual-protection” model with PrEP (4).
Using these notations, the qualitative indicators have the following expressions:

\[ C_i(T) = \int_0^T \left( [\frac{d}{dt} I_{New}(t)] - \left[ \frac{d}{dt} I^p_{New}(t) + \frac{d}{dt} I_{New}(t) \right] \right) dt \]

\[ F_i(T) = \frac{\int_0^T \left( [\frac{d}{dt} I_{New}(t)] \right) - \left[ \frac{d}{dt} I^p_{New}(t) + \frac{d}{dt} I_{New}(t) \right] dt}{\int_0^T [\frac{d}{dt} I_{New}(t)] dt} \]

\[ P_i(T) = 1 - \frac{\left[ \frac{I^p(T) + I(T)}{SP(T)+S(T)+[I^p(T)+I(T)]} \right]_{DP}}{\left[ \frac{I(T)}{S(T)+I(T)} \right]} \]

\[ aI_i(T) = 1 - \frac{\left[ \int_T^{T+1} \left[ \frac{d}{dt} I^p_{New}(t) \right] dt \right]_{DP}}{\left[ \frac{S^p(T)+S(T)}{S(T)} \right]} \]

\[ \hat{C}_i(T) = [I(T)] - [I^p(T) + I(T)]_{DP} \]

\[ \hat{F}_i(T) = \frac{[I(T)] - [I^p(T) + I(T)]_{DP}}{[I(T)]} = 1 - \left[ \frac{I^p(T) + I(T)}{I(T)} \right]_{DP} \].
Integral evaluated on derivative function can be simplified:

\[ C_I(T) = [I_{New}(T)] - [I^p_{New}(T) + I_{New}(T)]_{DP} \]

\[ F_I(T) = \frac{[I_{New}(T)] - [I^p_{New}(T) + I_{New}(T)]_{DP}}{[I_{New}(T)]} = 1 - \frac{[I^p_{New}(T) + I_{New}(T)]_{DP}}{[I_{New}(T)]} \]

\[ P_I(T) = 1 - \left[ \frac{I^p(T) + I(T)}{S^p(T) + S(T) + I^p(T) + I(T)} \right]_{DP} \]

\[ aI_I(T) = 1 - \left[ \frac{I^p_{New}(T+1) + I_{New}(T+1) - (I^p_{New}(T) + I_{New}(T))}{S^p(T) + S(T)} \right]_{DP} \]

\[ \hat{C}_I(T) = [I(T)] - [I^p(T) + I(T)]_{DP} \]

\[ \hat{F}_I(T) = \frac{[I(T)] - [I^p(T) + I(T)]_{DP}}{[I(T)]} = 1 - \frac{[I^p(T) + I(T)]_{DP}}{[I(T)]} \]

The indicators \( F_I, P_I, aI_I, \) and \( \hat{F}_I \) are dimensionless. The other two indicators \( C_I \) and \( \hat{C}_I \) measure changes in population group sizes, and are not dimensionless.
Initial Dynamics of the Indicators

Using the initial conditions of the two models and the definitions of the indicators, then apply Taylor approximation, we obtain that shortly after the start of intervention:

\[ C_l \approx \left[ \alpha_s + (1 - \theta)\alpha_i(1 - \alpha_s k_1) \right] k_1 \beta P(1 - P) N(0) dt \]

\[ F_l \approx \left[ \alpha_s + (1 - \theta)\alpha_i(1 - \alpha_s k_1) \right] k_1 \]

\[ P_l \approx \left[ \alpha_s + (1 - \theta)\alpha_i(1 - \alpha_s k_1) \right] k_1 \beta (1 - P) dt \]

\[ a_l I \approx (1 - \alpha_s k_1)[1 - (1 - \theta)\alpha_i k_1] \{1 - (1 - \alpha_s k_1)k_1[1 - (1 - \theta)\alpha_i k_1]\} k_1 \beta P dt \]

\[ \hat{C}_l \approx \left[ \alpha_s + (1 - \theta)\alpha_i(1 - \alpha_s k_1) \right] k_1 \beta P(1 - P) N(0) dt \]

\[ \hat{F}_l \approx \left[ \alpha_s + (1 - \theta)\alpha_i(1 - \alpha_s k_1) \right] k_1 \beta (1 - P) dt. \]

Here we assume \( dt = 1 \) for the approximation for \( a_l I \) because the definition of the incidence indicator is on annual basis.
Fractional indicator($F_i$) represents a metric of the “immediate impact of PrEP” on the HIV epidemic, which is independent of the specific population and the status of the HIV epidemic in it.

The initial behavior of all other indicators depend on the HIV prevalence ($P$) at the time of PrEP introduction as well as on the cumulative HIV-acquisition risk ($\beta$).

The cumulative ($C_i$) and reduction ($\hat{C}_i$) indicators also depend on the initial population size ($N(0)$), which is consistent with the fact that only indicators $C_i$ and $\hat{C}_i$ measure changes on population group sizes, and are not dimensionless.
\[ C'_i \approx [\alpha_s + (1 - \theta)\alpha_i(1 - \alpha_s k_1)]k_1 \beta P(1 - P)N(0) \]
\[ P'_i \approx [\alpha_s + (1 - \theta)\alpha_i(1 - \alpha_s k_1)]k_1 \beta (1 - P) \]
\[ aI'_i \approx (1 - \alpha_s k_1)[1 - (1 - \theta)\alpha_i k_1] \{1 - (1 - \alpha_s k_1)k_1[1 - (1 - \theta)\alpha_i k_1]\}k_1 \beta P \]
\[ \hat{C}'_i \approx [\alpha_s + (1 - \theta)\alpha_i(1 - \alpha_s k_1)]k_1 \beta P(1 - P)N(0) \]
\[ \hat{F}'_i \approx [\alpha_s + (1 - \theta)\alpha_i(1 - \alpha_s k_1)]k_1 \beta (1 - P). \]

Notice that initially \( C'_i \approx \hat{C}'_i \) and \( P'_i \approx \hat{F}'_i \).

We study the sensitivity of the initial rate of change of the reduction indicators (\( \hat{C}_i \) and \( \hat{F}_i \)) to some of the intervention (\( \theta, k_1 \)) and epidemic (\( P \)) parameters by simulations (Fig. 4), since these parameters are easier to evaluate at community levels.
Figure 4: Initial growth rate of reduction ($\hat{C}_I$) and fractional reduction ($\hat{F}_I$) indicators with respect to (a) $\theta$, (b) $k_1$ and (c) $P$. $\hat{C}_I$ is denoted by green solid line, while $\hat{F}_I$ is denoted by blue dashed line. All other parameters are fixed on their baseline parameter values from Table 1.
• The initial rate of change is more sensitive to $k_1$ than to $\theta$ and $P$.

• The growth rate of both indicators expresses qualitatively similar behavior with respect to the intervention parameters ($\theta$, $k_1$).

• In contrast, the dependence on the initial HIV prevalence ($P$) show serious discrepancies (Fig. 4(c)).
  • The initial growth rate of the reduction indicator ($\hat{C}_I$) increases when the HIV prevalence ($P$) ranges from 0 to 50% which includes all realistic values observed so far, particularly in Sub-Saharan Africa (Fig. 4(c)).

  • In comparison, the increase in HIV prevalence ($P$) within the same range implies smaller growth rate of the fractional reduction indicator $\hat{F}_I$. 
In resource-constrained settings, it is unrealistic to expect the HIV epidemic will die out without additional intervention. Therefore, we assume that the basic reproduction number of the “no intervention” model is \( R_0 = \frac{\beta}{\mu + d} > 1 \). The asymptotic HIV prevalence in this case is given by:

\[
\left[ \frac{I}{S+I} \right] = 1 - \frac{\mu + d}{\beta} = 1 - \frac{1}{R_0}.
\]

If the PrEP intervention is strong enough to cause the eradication of HIV in the population, i.e., the HIV epidemic approaches the disease-free equilibrium with the “dual-protection” model, then the asymptotic behavior of all indicators is well determined:

- the cumulative indicator \((C_I)\) will grow to \( \infty \);
- the reduction indicator \((\hat{C}_I)\) will stabilize at \( \frac{R_0 - 1}{\beta - d} \Lambda \);
- all other indicators will approach 1.
Unfortunately, PrEP intervention alone is unlikely to be sufficient to eradicate HIV. In that case we show that the asymptotic behavior of the indicators can be expressed in terms of the asymptotic proportion ($p$) of the HIV-positive subpopulation which have been infected while using PrEP

$$p = \left[ \frac{I^p}{I^p + I} \right]_{DP}.$$

Expressions for the asymptotic values of four of the indicators:

$$P_I = 1 - \frac{R_0 - \frac{1 - \alpha_s(1 - p)}{(1 - \alpha_s)(1 - \alpha_{ip})}}{R_0 - 1},$$

$$aI = 1 - \frac{R_0 \frac{(1 - \alpha_s)(1 - \alpha_{ip})}{1 - \alpha_s(1 - p)} - 1}{R_0 - 1},$$

$$\hat{C}_I = \left[ \frac{R_0 - 1}{\beta - d} - \frac{R_0 (1 - \alpha_{ip})(1 - \alpha_s k) - 1}{\beta (1 - \alpha_{ip})(1 - \alpha_s p) - d} \right] \Lambda,$$

$$\hat{F}_I = 1 - \frac{R_0 (1 - \alpha_{ip})(1 - \alpha_s k) - 1}{R_0 - 1} \frac{\beta - d}{\beta (1 - \alpha_{ip})(1 - \alpha_s p) - d} \Lambda$$

and the asymptotic rate of growth of the cumulative indicator:

$$C_i' = (\mu + d) \hat{C}_i.$$
They are independent of the initial HIV prevalence ($P$) and the control on the PrEP use by HIV-positive individuals ($\theta$) which have been of critical importance for the initial dynamics of the indicators.

Cumulative indicators ($\hat{C}_i$ and $C_i$) depend indirectly on the population size ($N$) which determines the entry rate in the population ($\Lambda$).

The reduction indicator is proportional to the annual number of new infections prevented due to PrEP use in a long term.

Although recruitment parameters such as $k$ and $\Lambda$ are not explicitly present in some of the expressions above they may affect the asymptotic proportion of PrEP users among infected subpopulation ($p$).
The indicators reach a specific threshold of 20% at times varying from 3 to 11 years after the introduction of PrEP.

The times needed to report 50% effectiveness are farther apart. It takes 24 years and 33 years to reduce in half the expected HIV incidence and HIV prevalence, respectively. However, almost 90 years are necessary to reduce the cumulative number of new infections by 50%.

Figure 5: Long term dynamics of the quantitative indicators based on simulations with “dual-protection” and “no intervention” models using parameters from Table 1.
Sensitivity Analysis

- Using the algorithm presented in Blower and Dowlatabadi (1994) we calculate the **Partial Rank Correlation Coefficients (PRCC)** which evaluate the monotonicity of the model outcomes (indicators) in terms of the model parameters.

- Values of $PRCC$ closer to $\pm 1$, imply stronger correlation between the output indicator and the input parameter while the sign of the coefficients determines if the outcomes grow or decrease with an increase of the input parameters.

- We choose 1000 random parameters combinations of those input parameters sampled uniformly from $[0.5, 1.5]$ *(baseline parameter value in Table 1)*. The rest of the parameters are fixed on their baseline values in Table 1.
Figure 6: Partial rank correlation coefficients (PRCC) between model parameters and the quantitative indicators over 10 and 100 years.
Correlations for 10-year intervention suggest that from the fitted parameters the indicators are most sensitive to the factors \((b_a \text{ and } n)\) which determine the transmission rate \(\beta\). However, their influence over time decreases.

The intervention outcomes are split into two groups with respect to their correlation with the AIDS progression rate \((d)\): the cumulative indicators being negatively correlated while the rest being positively correlated with \(d\).

Although \(P\) appears in the initial conditions only, it continues to have strong influence on all the cumulative and reduction indicators for more than 10 years while its impact on the fraction of prevented infection gets even stronger over time.

In contrast, the influence of the initial control on the PrEP use by HIV-positive individuals \((\theta)\) reduces substantially in time.
Among the intervention parameters, PrEP coverage \((k)\) and PrEP efficacies per act \((\alpha_s \text{ and } \alpha_i)\) express strong positive correlation with all the indicators in a short term. It remains significant in a long term for all outcomes.

This confirms that PrEP coverage and protection level are critical to the intervention success regardless which qualitative metric is used.

The prevalence \((P_I)\) and the annual incidence \((aI_I)\) indicators express almost the same sensitivity to all parameters. Therefore they should have consistent projections when evaluating the impact of the intervention.
The most often mathematically modeled prevention interventions for HIV are male circumcision, ART (test and treat strategy as prevention), microbicides, and PrEP. Using related key words, we collected and screened papers from ‘Web of Knowledge’ database and ‘PubMed’ database. For each related paper, we collect the information about the population being modeled, recruitment mechanism, mechanisms of departures from the population, and assumptions regarding migration.
Models without Intervention: Different Entrance Rates

\[ \frac{dS}{dt} = f(N) - \beta \frac{SI}{N} - \mu S \triangleq P(S, I) \]

\[ \frac{dI}{dt} = \beta \frac{SI}{N} - (\mu + d)I \triangleq Q(S, I). \]

with

\[ f(N) = \Lambda, \ rN, \text{ or } rN(1 - \frac{N}{K}). \]
Table 3: Stability conditions for the models in absence of PrEP. Extinction steady state is globally stable when $r < \mu$, so in the table it is assumed that $r > \mu$ and further assumed that $\beta > d$ and $\mu + d > r$ for linear and logistic entrance rates.

<table>
<thead>
<tr>
<th>Recruitment type</th>
<th>Parameter conditions</th>
<th>Outcomes</th>
<th>HIV prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>$\beta &lt; \mu + d$</td>
<td>disease free state</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$\beta &gt; \mu + d$</td>
<td>endemic state</td>
<td>$1 - \frac{\mu + d}{\beta}$</td>
</tr>
<tr>
<td>Linear</td>
<td>$\beta &lt; \mu + d$</td>
<td>disease free state</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$\mu + d &lt; \beta &lt; \frac{(\mu + d)d}{\mu + d - r}$</td>
<td>endemic state</td>
<td>0 or $1 - \frac{r}{\beta - d}$</td>
</tr>
<tr>
<td></td>
<td>$\beta &gt; \frac{(\mu + d)d}{\mu + d - r}$</td>
<td>extinction</td>
<td>1 $- \frac{r}{\beta - d}$</td>
</tr>
<tr>
<td>Logistic</td>
<td>$\beta &lt; \mu + d$</td>
<td>disease free state</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$\mu + d &lt; \beta &lt; \frac{(\mu + d)d}{\mu + d - r}$</td>
<td>endemic state</td>
<td>$1 - \frac{\mu + d}{\beta}$</td>
</tr>
<tr>
<td></td>
<td>$\beta &gt; \frac{(\mu + d)d}{\mu + d - r}$</td>
<td>extinction</td>
<td>$1 - \frac{r}{\beta - d}$</td>
</tr>
</tbody>
</table>
Models with PrEP Intervention: Constant Entrance Rate

\[
\begin{align*}
\frac{dS^p}{dt} &= k\Lambda - (1 - \alpha_s)\beta \frac{S^pI}{N} - \mu S^p \\
\frac{dS}{dt} &= (1 - k)f(N) - \beta \frac{SI}{N} - \mu S \\
\frac{dI}{dt} &= \beta \frac{SI}{N} + (1 - \alpha_s)\beta \frac{S^pI}{N} - (\mu + d)I
\end{align*}
\] (7)

**Proposition 1**

With nonnegative initial conditions, solutions for (7) are nonnegative and bounded with \(N(t) = \max\{N(0), \frac{\Lambda}{\mu}\}\). Now assume \(\beta > d\).

- When \(R_0 < 1\) the model (7) has an unique (disease-free) equilibrium \(E_0 = (\frac{k}{\mu}\Lambda, \frac{1-k}{\mu}\Lambda, 0)\) which is stable. Global stability of \(E_0\) has been proved given extra condition \(R_0 < \frac{\mu}{\mu+d}\).

- When \(R_0 > 1\) the disease-free equilibrium \(E_0\) is unstable. The system has a unique endemic equilibrium \(E^* = (S^{p*}, S^*, I^*)\). The endemic equilibrium \(E^*\) is stable when \(\frac{\mu+d}{d}[\beta(1 - \alpha_s) - d] + \alpha_s(1 - k)d > 0\). \((E^* \text{ may be stable whenever exists, can be further studied in future.})\)
Models with PrEP Intervention: Linear Entrance Rate

\[
\frac{dS^p}{dt} = krN - (1 - \alpha_s)\beta \frac{S^pI}{N} - \mu S^p \triangleq P(S^p, S, I) \\
\frac{dS}{dt} = (1 - k)rN - \beta \frac{SI}{N} - \mu S \triangleq Q(S^p, S, I) \\
\frac{dI}{dt} = \beta \frac{SI}{N} + (1 - \alpha_s)\beta \frac{S^pI}{N} - (\mu + d)I \triangleq R(S^p, S, I)
\]

with \( \lim_{(S^p, S, I) \to (0, 0, 0)} \frac{S^pI}{N} = 0 \) and \( \lim_{(S^p, S, I) \to (0, 0, 0)} \frac{SI}{N} = 0 \). Thus we define \( P(0, 0, 0) = Q(0, 0, 0) = R(0, 0, 0) = 0 \).

To further study stability of \( E = (0, 0, 0) \), we need to rewrite the system by defining \( p = \frac{S^p}{N} \), \( s = \frac{S}{N} \), then \( i = \frac{I}{N} = 1 - p - s \), and

\[
\frac{dp}{dt} = kr - rp - [(1 - \alpha_s)\beta - d]pi \triangleq X(p, i) \\
\frac{di}{dt} = [\beta - (d + r) - \alpha_s\beta p - (\beta - d)i]i \triangleq Y(p, i) \\
\frac{dN}{dt} = [r - \mu - di]N \\
\frac{dl}{dt} = [\beta(1 - p - i) + (1 - \alpha_s)\beta p - (\mu + d)]l.
\]
Proposition 2

All solutions of (8) with nonnegative initial conditions remain nonnegative.
Periodic solutions for (8) do not exist when \( \beta - d > 0 \).
The unique steady state \( E = (0, 0, 0) \) implies population extinction. It is globally stable if \( r < \mu \).
Assume \( r > \mu \) and \( \beta > d \),

- **when** \( (1 - k)\beta + k(1 - \alpha_s)\beta < d + r \), \( E_1 = (p^* = k, i^* = 0) \) is globally stable, with \( \lim_{t \to \infty} N(t) = \infty \) and
  - \( \lim_{t \to \infty} I(t) = 0 \) if \( R_0 < 1 \),
  - \( \lim_{t \to \infty} I(t) = \infty \) if \( R_0 > 1 \);

- **when** \( (1 - k)\beta + k(1 - \alpha_s)\beta > d + r \), \( E_2 = (p^* > 0, i^* > 0) \) is globally stable,
  - \( \lim_{t \to \infty} N(t) = 0 \) if \( i^* > \frac{r - \mu}{d} \), and \( \lim_{t \to \infty} I(t) = 0 \),
  - \( \lim_{t \to \infty} N(t) = \infty \) if \( i^* < \frac{r - \mu}{d} \), and \( \lim_{t \to \infty} I(t) = \infty \).
Models with PrEP Intervention: Logistic Entrance Rate

\[
\begin{align*}
\frac{dS^p}{dt} &= krN(1 - \frac{N}{K}) - (1 - \alpha_s)\beta \frac{S^p I}{N} - \mu S^p \\
\frac{dS}{dt} &= (1 - k)rN(1 - \frac{N}{K}) - \beta \frac{SI}{N} - \mu S \\
\frac{di}{dt} &= \beta \frac{SI}{N} + (1 - \alpha_s)\beta \frac{S^p I}{N} - (\mu + d)i
\end{align*}
\] (13)

with \(\lim_{(S^p, S, I) \to (0,0,0)} \frac{S^p I}{N} = 0\) and \(\lim_{(S^p, S, I) \to (0,0,0)} \frac{SI}{N} = 0\). Thus we define \(P(0,0,0) = Q(0,0,0) = R(0,0,0) = 0\).

To further study the stability of \(E_{00} = (0,0,0)\), we need to rewrite the system by defining \(p = \frac{S^p}{N}\), \(s = \frac{S}{N}\), then \(i = \frac{I}{N} = 1 - p - s\), and

\[
\begin{align*}
\frac{dp}{dt} &= kr(1 - \frac{N}{K}) - r(1 - \frac{N}{K})p - [(1 - \alpha_s)\beta - d]pi \\
\frac{di}{dt} &= [\beta - d - r(1 - \frac{N}{K}) - \alpha_s \beta p - (\beta - d)i]i \\
\frac{dN}{dt} &= [r(1 - \frac{N}{K}) - \mu - di]N
\end{align*}
\] (14)
Proposition 3

The biologically relevant region
\[ \{(S_p(t), S(t), I(t))| S_p(t) \geq 0, S(t) \geq 0, I(t) \geq 0, S_p(t) + S(t) + I(t) \leq K\} \] is positively invariant with respect to (13).

The model has three possible steady states: population extinction \( E_{00} = (0, 0, 0) \),
disease-free \( E_{01} = (k \frac{r-\mu}{r} K, (1 - k) \frac{r-\mu}{r} K, 0) \) and endemic \( E^* = (S_p^*, S^*, I^*) \).
The extinction steady state is globally stable if \( r < \mu \).
Assume \( r > \mu \),
- the infection free steady state \( E_{01} \) is stable when \( R_0 < 1 \) and unstable when \( R_0 > 1 \);
- the extinction steady state \( E_{00} \) is stable when \( (1 - k) \beta + k (1 - \alpha_s) \beta > d + r \) and unstable when \( (1 - k) \beta + k (1 - \alpha_s) \beta < d + r \);
- further assume \( \beta > \mu + d \), then the positive steady state \( E^* \) exists when \( R_0 > 1 \) and \( i^* = \frac{I^*}{N^*} < \frac{r-\mu}{d} \) and does not exist when \( R_0 < 1 \) or \( i^* = \frac{I^*}{N^*} > \frac{r-\mu}{d} \).

Positive steady states are too complicated to be expressed explicitly.
Table 4: Models with intervention, assume $r > \mu$ and $\beta > d$. Notice that $\beta = \tilde{\beta}$ when $i^* = \frac{r - \mu}{d}$ (See Proposition 2 and 3).

<table>
<thead>
<tr>
<th>Recruitment type</th>
<th>Parameter conditions</th>
<th>Outcomes</th>
<th>HIV prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>$\beta &lt; \frac{\mu + d}{1 - \alpha s k}$</td>
<td>disease free state</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$\beta &gt; \frac{\mu + d}{1 - \alpha s k}$</td>
<td>endemic state</td>
<td>$\frac{\mu I^<em>}{\Lambda - d I^</em>}$</td>
</tr>
<tr>
<td>Linear</td>
<td>$\beta &lt; \frac{\mu + d}{1 - \alpha s k}$</td>
<td>disease free state</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$\frac{\mu + d}{1 - \alpha s k} &lt; \beta &lt; \max{\frac{r + d}{1 - \alpha s k}, \tilde{\beta}}$</td>
<td>endemic state</td>
<td>0 or $i_{lin}^*\left(\frac{r - \mu}{d}\right)$</td>
</tr>
<tr>
<td></td>
<td>$\beta &gt; \tilde{\beta}$</td>
<td>extinction</td>
<td>$i_{lin}^*(&gt; \frac{r - \mu}{d})$</td>
</tr>
<tr>
<td>Logistic</td>
<td>$\beta &lt; \frac{\mu + d}{1 - \alpha s k}$</td>
<td>disease free state</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$\frac{\mu + d}{1 - \alpha s k} &lt; \beta &lt; \max{\frac{r + d}{1 - \alpha s k}, \tilde{\beta}}$</td>
<td>endemic state</td>
<td>$i_{log}^*\left(\frac{r - \mu}{d}\right)$</td>
</tr>
<tr>
<td></td>
<td>$\beta &gt; \tilde{\beta}$</td>
<td>extinction</td>
<td>$i_{log}^*(&gt; \frac{r - \mu}{d})$</td>
</tr>
</tbody>
</table>
Figure 7: Epidemic parameter values (except $\beta$) are chosen by fitting HIV prevalence data from South Africa (see Table 5). PrEP coverage ($k = 0.2$) and PrEP efficacy ($\alpha_s = 0.5$) are assumed. Initial conditions are adapted from year 2011.
Table 5: Baseline parameter values generated from data fitting.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Constant entrance</th>
<th>Linear entrance</th>
<th>Logistic entrance</th>
<th>Initial guess</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta$</td>
<td>0.196924711</td>
<td>0.196935536</td>
<td>0.196924711</td>
<td>$1 - (1 - 0.0038)^{80} \approx 0.26256628106$</td>
</tr>
<tr>
<td>$\mu$</td>
<td>0.029793556</td>
<td>2.93E-02</td>
<td>0.02438153</td>
<td>$1/35 \approx 0.028571428571429$</td>
</tr>
<tr>
<td>$d$</td>
<td>0.119146121</td>
<td>0.11955454</td>
<td>0.125</td>
<td>$1/10 = 0.1$</td>
</tr>
<tr>
<td>$\Lambda$</td>
<td>996344</td>
<td></td>
<td></td>
<td>fixed value calculated from data</td>
</tr>
<tr>
<td>$r$</td>
<td>0.04095</td>
<td>0.0511875</td>
<td></td>
<td>fixed value or initial guess 0.04095</td>
</tr>
<tr>
<td>$K$</td>
<td>1.13E+08</td>
<td></td>
<td>9.00E+07(Figure (22))</td>
<td></td>
</tr>
<tr>
<td>$err$</td>
<td>0.044056109</td>
<td>0.044755966</td>
<td>0.043080597</td>
<td></td>
</tr>
</tbody>
</table>

Here I constrain the parameter values to be within initial guess $\ast (1 \pm 25\%)$, so that the parameter values are always within certain biologically reasonable range.

From the age structured population data of year 2001 in South Africa(Table 14), we estimate population entrance $\Lambda \approx \frac{4981721}{5} \approx 996344$ and the population growth rate $r \approx \frac{996344}{24330699} \approx 0.04095$.

We approximate the initial guess for population carrying capacity $K$ in the model with logistic entrance rate from South Africa Population data(Figure 22).
Figure 8: Population dynamics for models with different recruitment rates: constant (blue), linear (red), and logistic (black). Initial recruitment and parameter values unrelated to recruitment are kept the same across the models (see Table 5).
Figure 9: Dynamics of PrEP effectiveness for models with different recruitment rates: constant (blue), linear (red), and logistic (black). Initial recruitment and parameter values unrelated to recruitment are kept the same across the models (see Table 5). Some indicators take negative values for models with linear entrance rate and logistic entrance rate (not shown).
Bayesian Parameter Estimation

Bayesian inference computes the posterior distributions according to the Bayes’ formula:

\[ p(\theta|D) = p(\theta) \frac{p(D|\theta)}{p(D)} , \]

where

- \( p(\theta) \) represents the prior density, the probability of \( \theta \) before \( D \) is observed;
- \( p(\theta|D) \) represents the posterior probability, the probability of \( \theta \) after \( D \) is observed;
- \( p(D|\theta) \) is the likelihood (or sampling probability for \( D \)), the probability of observing \( D \) given \( \theta \);
- \( p(D) \) is the marginal likelihood, all possible hypotheses being considered:

\[ p(D) = \int_{\theta} p(\theta)p(D|\theta) \, d\theta . \]
\[
\frac{dS}{dt} = \Lambda - \beta \frac{SI}{N} - \mu S
\]
\[
\frac{dI}{dt} = \beta \frac{SI}{N} - (\mu + d)I
\]  \hspace{1cm} (15)

- \(z_i\): the \(i\)th year HIV infected population since 2001 from data.
- \(x_i\): the \(i\)th year HIV infected population predicted by the model.
- \(\sigma\): the observation error in \(z_0\). \(T\) is assumed to be normally distributed with standard deviation \(\sigma\).
- \(x_0\): the starting point of HIV population in the model depends on both \(z_0\) and \(\sigma\).

The total likelihood function is given by

\[
p(D|\theta) = \prod_{i=1}^{T} N(z_i|x_i; \theta) = \prod_{i=1}^{T} \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(z_i-x_i)^2}{2\sigma^2}}. \hspace{1cm} (16)
\]
### Table 6: Parameter description and values from literature

<table>
<thead>
<tr>
<th>Par.</th>
<th>Description</th>
<th>Mean</th>
<th>95% CI</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Lambda$</td>
<td>Annual rate at which individuals become sexually active</td>
<td>996344</td>
<td>derived from Table 14</td>
<td></td>
</tr>
<tr>
<td>$b_a$</td>
<td>HIV acquisition risk per act</td>
<td>0.0038</td>
<td>0.0013-0.011</td>
<td>Boily et al. (2009)</td>
</tr>
<tr>
<td>$n$</td>
<td>Number of sexual acts per year per individual</td>
<td>120</td>
<td></td>
<td>Wawer et al. (2005), Boily et al. (2009)</td>
</tr>
<tr>
<td>$\beta$</td>
<td>Cumulative HIV-acquisition risk</td>
<td></td>
<td>derived from $b_a$ and $n$</td>
<td></td>
</tr>
<tr>
<td>$\frac{1}{\mu}$</td>
<td>Time (in years) to remain sexually active</td>
<td>35</td>
<td></td>
<td>UNAIDS (2009)</td>
</tr>
<tr>
<td>$d$</td>
<td>HIV carrier’s annual rate of progression to AIDS</td>
<td>1/10.9</td>
<td>1/11.3-1/10.6</td>
<td>Porter and Zaba (2004)</td>
</tr>
</tbody>
</table>
Table 7: Assumptions for parameters. $\hat{d}$ is modified $d$. $\beta = 1 - (1 - b_a)^n$.

<table>
<thead>
<tr>
<th>Par.</th>
<th>Distribution</th>
<th>Log mean</th>
<th>Log standard deviation</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Lambda$</td>
<td>constant</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$b_a$</td>
<td>lognormal</td>
<td>$\ln(0.0038)$</td>
<td>0.542394</td>
<td>0.004402</td>
<td>0.0025746</td>
<td>0.0013126 -0.011001</td>
</tr>
<tr>
<td>$n$</td>
<td>Poisson</td>
<td>120</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\beta$</td>
<td>$\beta = \beta(b_a, n)$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\mu$</td>
<td>lognormal</td>
<td>$\ln(1/35)$</td>
<td>0.15(assumed)</td>
<td>0.028895</td>
<td>0.0043587</td>
<td></td>
</tr>
<tr>
<td>$d$</td>
<td>lognormal</td>
<td>$\ln(1/10.9)$</td>
<td>0.0161875</td>
<td>0.091755</td>
<td>0.0014854</td>
<td>0.088888 -0.09469</td>
</tr>
<tr>
<td>$\hat{d}$</td>
<td>lognormal</td>
<td>$\ln(1/10.9)$</td>
<td>0.25</td>
<td>0.094655</td>
<td>0.024038</td>
<td></td>
</tr>
</tbody>
</table>
Figure 10: Parameter prior distributions. 95% confidence intervals (dashed black) are also included for $d$. Sold black lines indicate values obtained from least square fit. (c) is a modification of (b) with a larger standard deviation.
Figure 11: Parameter prior distributions. 95% confidence intervals (dashed black) are also included for $b_a$. Poisson distribution and approximated normal distribution have both been included for $n$. Calculated distribution (based on $b_a$ and $n$) and approximated lognormal distribution have both been included for $\beta$. Sold black lines indicate values obtained from regularized least square fit.
I did not find a prior distribution for $\sigma$ from literature, therefore I choose a non-informative prior distribution.

I assume a Jeffreys prior for $\sigma$ as

$$p(\sigma) \propto \frac{1}{\sigma} \text{ with } \sigma \in [1, 10^6]$$

or $p(\sigma) = \frac{C_\sigma}{\sigma} \text{ with } \sigma \in [1, 10^6]$ and $C_\sigma = \frac{1}{6 \ln(10)}$.

Then prior for $x_0$ becomes

$$p(x_0|z_0, \sigma) = \int_1^{10^6} p(\sigma)p(x_0|z_0, \sigma) \, d\sigma$$

with $p(\sigma) = \frac{C_\sigma}{\sigma}$.
Figure 12: Figure (a) is the prior distribution for $x_0$ when $\sigma = 6.4 \times 10^4$ is fixed. Figure (c) is the prior distribution for $x_0$ when $\sigma$ has a Jeffreys prior as in figure (b).
\( \sigma \) uncertain:

\[
p(\theta | D) \propto p(\theta) p(D | \theta) \propto e^{G(\theta)}
\]

with

\[
G(\theta) \triangleq - \sum_{j=1}^{3} \ln \theta_j - \sum_{j=1}^{3} \frac{(\ln \theta_j - \mu_j)^2}{2\sigma_j^2} - (T + 1) \ln(\sigma) - \ln(\Delta) - \frac{1}{2\sigma^2} \sum_{i=0}^{T} (x_i(\theta) - z_i)^2
\]

and

\[
\Delta \triangleq \int_{0}^{\infty} \frac{1}{\sqrt{2\pi \sigma^2}} e^{-\frac{(x-z_0)^2}{2\sigma^2}} \, dx.
\]

Denote \((\theta_1, \theta_2, \theta_3) = (\mu, d, \beta)\), then the following marginal distributions as posterior probability are obtained:

\[
p(\theta_1) \propto \int_{0}^{\infty} \int_{1}^{10^6} \int_{0}^{1} \int_{0}^{1} e^{G(\theta)} \, d\theta_2 d\theta_3 d\sigma d\theta_0;
\]

\[
p(\theta_2) \propto \int_{0}^{\infty} \int_{1}^{10^6} \int_{0}^{1} \int_{0}^{1} e^{G(\theta)} \, d\theta_1 d\theta_3 d\sigma d\theta_0;
\]

\[
p(\theta_3) \propto \int_{0}^{\infty} \int_{1}^{10^6} \int_{0}^{1} \int_{0}^{1} e^{G(\theta)} \, d\theta_1 d\theta_2 d\sigma d\theta_0;
\]

\[
p(\sigma) \propto \int_{0}^{\infty} \int_{0}^{1} \int_{0}^{1} \int_{0}^{1} e^{G(\theta)} \, d\theta_1 d\theta_2 d\theta_3 d\sigma;
\]

\[
p(x_0) \propto \int_{1}^{10^6} \int_{0}^{1} \int_{0}^{1} \int_{0}^{1} e^{G(\theta)} \, d\theta_1 d\theta_2 d\theta_3 d\sigma.
\]
$$\sigma = 6.4 \times 10^4 \text{ fixed:}$$

$$p(\theta|D) \propto p(\theta)p(D|\theta) \propto e^{G(\theta)}$$

with

$$G(\theta) \triangleq -\sum_{j=1}^{3} \ln \theta_j - \sum_{j=1}^{3} \frac{(\ln \theta_j - \mu_j)^2}{2\sigma_j^2} - \frac{1}{2\sigma^2} \sum_{i=0}^{T} (x_i(\theta) - z_i)^2.$$ 

Denote $$(\theta_1, \theta_2, \theta_3) = (\mu, d, \beta),$$ then the following marginal distributions as posterior probability are obtained:

$$p(\theta_1) \propto \int_{0}^{\infty} \int_{0}^{1} \int_{0}^{1} e^{G(\theta)} \, d\theta_2 \, d\theta_3 \, dx_0;$$

$$p(\theta_2) \propto \int_{0}^{\infty} \int_{0}^{1} \int_{0}^{1} e^{G(\theta)} \, d\theta_1 \, d\theta_3 \, dx_0;$$

$$p(\theta_3) \propto \int_{0}^{\infty} \int_{0}^{1} \int_{0}^{1} e^{G(\theta)} \, d\theta_1 \, d\theta_2 \, dx_0;$$

$$p(x_0) \propto \int_{0}^{1} \int_{0}^{1} \int_{0}^{1} e^{G(\theta)} \, d\theta_1 \, d\theta_2 \, d\theta_3.$$ 

Did not succeed in numerically calculating these integrals.
Metropolis-Hastings algorithm (MCMC method):

1. Initialize parameters $\theta$.
2. Repeat
   1. Propose new values for $\theta$ as $\theta^*$ by sampling from the proposal density $Q(\theta^*, x_{1:T}^*|\theta, x_{1:T})$, and calculate corresponding $x_{1:T}^*$ from ODE.
   2. With probability
      \[
      \min \left( \frac{\Pr(\theta^*, x_{1:T}^*|z_{1:T})}{\Pr(\theta, x_{1:T}|z_{1:T})} \cdot \frac{Q(\theta, x_{1:T}|\theta^*, x_{1:T}^*)}{Q(\theta^*, x_{1:T}^*|\theta, x_{1:T})}, 1 \right),
      \]
      set $\theta = \theta^*$; otherwise set $\theta = \theta$.  

Yuqin Zhao (ASU)  
Doctoral Thesis Defense  
November 11, 2014  
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Apply Bayes’ formula,

- when $\sigma$ has a Jeffreys prior, the acceptance probability becomes
  \[
  \min \left( e^F, 1 \right)
  \]
  with
  \[
  F = \left( \sum_{j=1}^{3} (\ln(\theta_j) - \ln(\theta_j^*)) \right) + (T + 1)(\ln(\sigma) - \ln(\sigma^*))
  + \sum_{j=1}^{3} \frac{(\ln(\theta_j) - \mu_j)^2 - (\ln(\theta_j^*) - \mu_j)^2}{2\sigma_j^2} + \sum_{i=1}^{T} \left( \frac{(x_i - z_i)^2 - (x_i^* - z_i)^2}{2\sigma^2} \right);
  \]
- when $\sigma$ is a fixed value, the acceptance probability becomes
  \[
  \min \left( e^F, 1 \right)
  \]
  with
  \[
  F = \left( \sum_{j=1}^{3} (\ln(\theta_j) - \ln(\theta_j^*)) \right)
  + \sum_{j=1}^{3} \frac{(\ln(\theta_j) - \mu_j)^2 - (\ln(\theta_j^*) - \mu_j)^2}{2\sigma_j^2} + \sum_{i=1}^{T} \left( \frac{(x_i - z_i)^2 - (x_i^* - z_i)^2}{2\sigma^2} \right).\]
Figure 13: $\sigma$ random. All $3 \times 10^6$ iterations. Burn in period dropped.
Figure 14: Red curves indicate the prior distributions. See Figure 12 for prior distributions for $\sigma$ and $x_0$. 
Figure 15: $\sigma = 6.4 \times 10^4$ fixed. All $3 \times 10^6$ iterations. Burn in period dropped.
Figure 16: Red curves indicate the prior distributions.
The chains for $\beta$ and $d$ are highly correlated to each other (correlation coefficients are 0.9822 and 0.9683 for Figure 13 and 15 respectively).

To get better mixing chains for $d$ and $\beta$, treat $\beta$ and $d$ as a group in the following way.

- When $\sigma$ has a Jeffreys prior:
  - the probability to perturb $\mu$ is $\frac{1}{5}$;
  - the probability to perturb both $d$ and $\beta$ is $\frac{2}{5}$;
  - the probability to perturb $\sigma$ is $\frac{1}{5}$;
  - the probability to perturb $x_0$ is $\frac{1}{5}$.

- When $\sigma = 6.4 \times 10^4$ is fixed:
  - the probability to perturb $\mu$ is $\frac{1}{5}$;
  - the probability to perturb both $d$ and $\beta$ is $\frac{2}{5}$;
  - the probability to perturb $x_0$ is $\frac{2}{5}$.
Figure 17: $\sigma$ is random. All $3 \times 10^6$ iterations. Burn in period dropped. $\beta$ and $d$ grouped.
Figure 18: Red curves indicate the prior distributions.
Figure 19: $\sigma = 6.4 \times 10^4$ fixed. All $3 \times 10^6$ iterations. Burn in period dropped. $\beta$ and $d$ grouped.
Figure 20: Red curves indicate the prior distributions.
Table 8: Posterior distributions of 2 independent chains, corresponding to Figure 14. Total acceptance rate is 18.08% for MCMC 1 and 18.09% for MCMC 2.

<table>
<thead>
<tr>
<th>MCMC 1</th>
<th>$\mu$</th>
<th>$d$</th>
<th>$\beta$</th>
<th>$\sigma$</th>
<th>$x_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>0.0277</td>
<td>0.09193</td>
<td>0.1616</td>
<td>65202.6</td>
<td>$3.8899 \times 10^6$</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>$4.11 \times 10^{-3}$</td>
<td>$25.76 \times 10^{-3}$</td>
<td>$32.43 \times 10^{-3}$</td>
<td>$18.87 \times 10^3$</td>
<td>$45.79 \times 10^3$</td>
</tr>
<tr>
<td>95% Credibility Interval</td>
<td>[0.02018 0.0358]</td>
<td>[0.05527 0.15548]</td>
<td>[0.1146 0.2407]</td>
<td>[37450.7 104879.9]</td>
<td>[3.7909 3.9699 10^6]</td>
</tr>
<tr>
<td>Acceptance Rate</td>
<td>31.78%</td>
<td>12.13%</td>
<td>8.31%</td>
<td>2.92%</td>
<td>35.27%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MCMC 2</th>
<th>$\mu$</th>
<th>$d$</th>
<th>$\beta$</th>
<th>$\sigma$</th>
<th>$x_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>0.02786</td>
<td>0.08886</td>
<td>0.1579</td>
<td>64900.5</td>
<td>$3.8915 \times 10^6$</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>$4.064 \times 10^{-3}$</td>
<td>$16.8 \times 10^{-3}$</td>
<td>$20.97 \times 10^{-3}$</td>
<td>$18.53 \times 10^3$</td>
<td>$44.18 \times 10^3$</td>
</tr>
<tr>
<td>95% Credibility Interval</td>
<td>[0.02066 0.03616]</td>
<td>[0.05983 0.1216]</td>
<td>[0.1209 0.1989]</td>
<td>[41664.3 105424.4]</td>
<td>[3.8058 3.9671 \times 10^6]</td>
</tr>
<tr>
<td>Acceptance Rate</td>
<td>31.56%</td>
<td>12.14%</td>
<td>8.33%</td>
<td>2.94%</td>
<td>35.47%</td>
</tr>
</tbody>
</table>
Table 9: Posterior distributions of 2 independent chains, corresponding to Figure 18. Total acceptance rate is 16.58% for MCMC 1 and 16.6% for MCMC 2.

<table>
<thead>
<tr>
<th></th>
<th>MCMC 1</th>
<th></th>
<th>MCMC 2</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>µ</td>
<td>d</td>
<td>β</td>
<td>σ</td>
</tr>
<tr>
<td>Mean</td>
<td>0.02779</td>
<td>0.09057</td>
<td>0.1599</td>
<td>64786.9</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>4.143 × 10⁻³</td>
<td>19.94 × 10⁻³</td>
<td>25.15 × 10⁻³</td>
<td>18.53 × 10³</td>
</tr>
<tr>
<td>95% Credibility Interval</td>
<td>[0.02062, 0.03609]</td>
<td>[0.05545, 0.13109]</td>
<td>[0.119, 0.2104]</td>
<td>[39298.1, 105758]</td>
</tr>
<tr>
<td>Acceptance Rate</td>
<td>31.45%</td>
<td>6.51%</td>
<td>6.51%</td>
<td>2.94%</td>
</tr>
<tr>
<td></td>
<td>µ</td>
<td>d</td>
<td>β</td>
<td>σ</td>
</tr>
<tr>
<td>Mean</td>
<td>0.02781</td>
<td>0.09077</td>
<td>0.1602</td>
<td>64862.6</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>4.194 × 10⁻³</td>
<td>20.34 × 10⁻³</td>
<td>25.52 × 10⁻³</td>
<td>18.77 × 10³</td>
</tr>
<tr>
<td>95% Credibility Interval</td>
<td>[0.02061, 0.03589]</td>
<td>[0.05783, 0.13135]</td>
<td>[0.1155, 0.2117]</td>
<td>[39039.5, 106115.7]</td>
</tr>
<tr>
<td>Acceptance Rate</td>
<td>31.52%</td>
<td>6.5%</td>
<td>6.5%</td>
<td>2.96%</td>
</tr>
</tbody>
</table>
Table 10: Posterior distributions of 2 independent chains, corresponding to Figure 16. Total acceptance rate is 21.95% for MCMC 1 and 21.73% for MCMC 2.

<table>
<thead>
<tr>
<th>MCMC 1</th>
<th>µ</th>
<th>d</th>
<th>β</th>
<th>$x_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>0.02775</td>
<td>0.0894</td>
<td>0.1584</td>
<td>$3.892 \times 10^6$</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>$4.034 \times 10^{-3}$</td>
<td>$18.82 \times 10^{-3}$</td>
<td>$23.53 \times 10^{-3}$</td>
<td>$41.9 \times 10^3$</td>
</tr>
<tr>
<td>95% Credibility Interval</td>
<td>[0.02072, 0.03574]</td>
<td>[0.05844, 0.12386]</td>
<td>[0.1193, 0.2033]</td>
<td>[3.8068 $\times 10^6$, 3.9655 $\times 10^6$]</td>
</tr>
<tr>
<td>Acceptance Rate</td>
<td>31.83%</td>
<td>12.15%</td>
<td>12.15%</td>
<td>35.55%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MCMC 2</th>
<th>µ</th>
<th>d</th>
<th>β</th>
<th>$x_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>0.02782</td>
<td>0.09601</td>
<td>0.1668</td>
<td>$3.8893 \times 10^6$</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>$4.139 \times 10^{-3}$</td>
<td>$23.59 \times 10^{-3}$</td>
<td>$29.47 \times 10^{-3}$</td>
<td>$41.99 \times 10^3$</td>
</tr>
<tr>
<td>95% Credibility Interval</td>
<td>[0.02057, 0.03577]</td>
<td>[0.05479, 0.15023]</td>
<td>[0.1136, 0.234]</td>
<td>[3.8051 $\times 10^6$, 3.9630 $\times 10^6$]</td>
</tr>
<tr>
<td>Acceptance Rate</td>
<td>31.8%</td>
<td>11.56%</td>
<td>11.56%</td>
<td>35.48%</td>
</tr>
</tbody>
</table>
Table 11: Posterior distributions of 2 independent chains, corresponding to Figure 20. Total acceptance rate is 23.09\% for MCMC 1 and 23.09\% for MCMC 2.

<table>
<thead>
<tr>
<th>MCMC 1</th>
<th>$\mu$</th>
<th>$d$</th>
<th>$\beta$</th>
<th>$x_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>0.02803</td>
<td>0.09066</td>
<td>0.1604</td>
<td>3.8907×10^6</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>4.155×10^{-3}</td>
<td>19.9×10^{-3}</td>
<td>24.78×10^{-3}</td>
<td>41.83×10^3</td>
</tr>
<tr>
<td>95% Credibility Interval</td>
<td>[0.02069, 0.03632]</td>
<td>[0.05747, 0.13002]</td>
<td>[0.119, 0.2126]</td>
<td>[3.8063×10^6, 3.9654×10^6]</td>
</tr>
<tr>
<td>Acceptance Rate</td>
<td>31.56%</td>
<td>6.44%</td>
<td>6.44%</td>
<td>35.51%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MCMC 2</th>
<th>$\mu$</th>
<th>$d$</th>
<th>$\beta$</th>
<th>$x_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>0.02804</td>
<td>0.09134</td>
<td>0.1612</td>
<td>3.8904×10^6</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>4.17×10^{-3}</td>
<td>20.32×10^{-3}</td>
<td>25.39×10^{-3}</td>
<td>41.65×10^3</td>
</tr>
<tr>
<td>95% Credibility Interval</td>
<td>[0.02095, 0.03585]</td>
<td>[0.058, 0.13298]</td>
<td>[0.1166, 0.2119]</td>
<td>[3.8095×10^6, 3.9651×10^6]</td>
</tr>
<tr>
<td>Acceptance Rate</td>
<td>31.49%</td>
<td>6.40%</td>
<td>6.40%</td>
<td>35.54%</td>
</tr>
</tbody>
</table>
Effective Sample Size

Because the consecutive values generated by a MCMC simulation are correlated, they provide less accurate estimates than independent samples.

One measure of the accuracy of the estimate and how well the chain is mixing is the effective sample size (ESS).

The ESS is equal to

\[
ESS = \frac{N}{1 + 2 \sum_{k=1}^{\infty} \rho_k(\theta)},
\]

where \(N\) is the number of posterior samples, \(\rho_k\) is the autocorrelation at lag \(k\). The infinite sum is often truncated when \(\rho_k < 0.05\) (ESS (2014), Kass et al. (1998)).
I will use the sample autocorrelation function to estimate the ESS:

\[
\rho_k(\theta_j) = \frac{\sum_{i=1}^{N-k} [\theta_j(i) - \bar{\theta}] \cdot [\theta_j(i + k) - \bar{\theta}]}{N \sum_{i=1}^{N} [\theta_j(i) - \bar{\theta}]^2}, \quad k = 1 \cdots N - 1.
\]

Here \(\bar{\theta}\) is the sample mean of \(\theta_j\), and \(\sum_{i=1}^{N} [\theta_j(i) - \bar{\theta}]^2\) is the sample variance of \(\theta_j\). The sum will be truncated when \(\rho_k < 0.01\).
Table 12: Effective Sample Size, when $d$ and $\beta$ are not grouped.

<table>
<thead>
<tr>
<th>number of samples</th>
<th>$\mu$</th>
<th>$d$</th>
<th>$\beta$</th>
<th>$\sigma$</th>
<th>$x_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$10^4$</td>
<td>6</td>
<td>5</td>
<td>7</td>
<td>44</td>
<td>75</td>
</tr>
<tr>
<td>$10^5$</td>
<td>48</td>
<td>5</td>
<td>4</td>
<td>252</td>
<td>489</td>
</tr>
<tr>
<td>$10^6 - 10^3$</td>
<td>422</td>
<td>21</td>
<td>22</td>
<td>2610</td>
<td>4282</td>
</tr>
<tr>
<td>$3 \times 10^6 - 10^3$</td>
<td>1431</td>
<td>24</td>
<td>24</td>
<td>2154</td>
<td>624</td>
</tr>
</tbody>
</table>

Table 13: Effective Sample Size, when $d$ and $\beta$ are grouped.

<table>
<thead>
<tr>
<th>number of samples</th>
<th>$\mu$</th>
<th>$d$</th>
<th>$\beta$</th>
<th>$\sigma$</th>
<th>$x_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$10^4$</td>
<td>19</td>
<td>10</td>
<td>10</td>
<td>41</td>
<td>59</td>
</tr>
<tr>
<td>$10^5$</td>
<td>39</td>
<td>131</td>
<td>123</td>
<td>302</td>
<td>388</td>
</tr>
<tr>
<td>$10^6 - 10^3$</td>
<td>404</td>
<td>935</td>
<td>877</td>
<td>3095</td>
<td>3154</td>
</tr>
<tr>
<td>$3 \times 10^6 - 10^3$</td>
<td>1298</td>
<td>2639</td>
<td>2326</td>
<td>7873</td>
<td>9081</td>
</tr>
</tbody>
</table>
Figure 21: From year 2003 to 2011, 1000 samples of simulated HIV population observations are plotted for each year. The mean of the simulated observations is plotted in yellow for each year. The true observation is plotted in red for each year.


Dilys Morgan, Cedric Mahe, Billy Mayanja, J Martin Okongo, Rosemary Lubega, and James AG Whitworth. Hiv-1 infection in rural africa: is there a difference in median time to aids and survival compared with that in industrialized countries? *Aids*, 16(4): 597–603, 2002.


<table>
<thead>
<tr>
<th>Age\Year</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-19</td>
<td>4981721</td>
<td>5263274</td>
<td>4923992</td>
<td>4898100</td>
<td>4938000</td>
<td>4975900</td>
<td>5152700</td>
<td>5214300</td>
<td>5226200</td>
<td>5175448</td>
<td></td>
</tr>
<tr>
<td>20-24</td>
<td>4294523</td>
<td>4392357</td>
<td>4679210</td>
<td>4621200</td>
<td>4653800</td>
<td>4675200</td>
<td>4783700</td>
<td>4920900</td>
<td>5018500</td>
<td>4900375</td>
<td></td>
</tr>
<tr>
<td>25-29</td>
<td>3934939</td>
<td>4100416</td>
<td>4291589</td>
<td>4211100</td>
<td>4271100</td>
<td>4335600</td>
<td>4367400</td>
<td>4423500</td>
<td>4518800</td>
<td>4598176</td>
<td></td>
</tr>
<tr>
<td>30-34</td>
<td>3340901</td>
<td>3422110</td>
<td>3696445</td>
<td>3762000</td>
<td>3841500</td>
<td>3863900</td>
<td>3913500</td>
<td>3888300</td>
<td>4035700</td>
<td>4040751</td>
<td></td>
</tr>
<tr>
<td>35-39</td>
<td>3071770</td>
<td>3216513</td>
<td>2851312</td>
<td>2780200</td>
<td>2842100</td>
<td>2972400</td>
<td>3147200</td>
<td>3282300</td>
<td>3465200</td>
<td>3600167</td>
<td></td>
</tr>
<tr>
<td>40-44</td>
<td>2619465</td>
<td>2794291</td>
<td>2538649</td>
<td>2483200</td>
<td>2482800</td>
<td>2400300</td>
<td>2389900</td>
<td>2443200</td>
<td>2524200</td>
<td>2612932</td>
<td></td>
</tr>
<tr>
<td>45-49</td>
<td>2087380</td>
<td>2241976</td>
<td>2213991</td>
<td>2187200</td>
<td>2215000</td>
<td>2223000</td>
<td>2240500</td>
<td>2260000</td>
<td>2230600</td>
<td>2244582</td>
<td></td>
</tr>
<tr>
<td>Total (15-49)</td>
<td>24330699</td>
<td>0</td>
<td>25430937</td>
<td>25195188</td>
<td>24943000</td>
<td>25189700</td>
<td>25445600</td>
<td>25994900</td>
<td>26432500</td>
<td>27019200</td>
<td>27172431</td>
</tr>
<tr>
<td>Prevalence (15-49)</td>
<td>0.16</td>
<td>0.162</td>
<td>0.162</td>
<td>0.162</td>
<td>0.166</td>
<td>0.165</td>
<td>0.164</td>
<td>0.164</td>
<td>0.165</td>
<td>0.166</td>
<td></td>
</tr>
<tr>
<td>Total HIV (15-49)</td>
<td>3892911.84</td>
<td>0</td>
<td>4119812</td>
<td>4081620</td>
<td>4040766</td>
<td>4181490</td>
<td>4198524</td>
<td>4263164</td>
<td>4334930</td>
<td>4458168</td>
<td>4510624</td>
</tr>
<tr>
<td>Total SUS (15-49)</td>
<td>20437787.2</td>
<td>0</td>
<td>21311125</td>
<td>21113568</td>
<td>20902234</td>
<td>21008210</td>
<td>21247076</td>
<td>21731736</td>
<td>22097570</td>
<td>22661807</td>
<td></td>
</tr>
</tbody>
</table>
Figure 22: Initial guess for capacity $K$ is approximated by $2 \times$ South Africa population at year 2001, because of the turning point observed at year 2001.
### Table 15: Population assumptions on HIV models from literature.

<table>
<thead>
<tr>
<th>Paper</th>
<th>Population</th>
<th>Recruitment</th>
<th>Departure (All Linear)</th>
<th>Migration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baggaley et al. (2006)</td>
<td>Heterosexual (15-49 years)</td>
<td>Constant</td>
<td>Aging; death due to HIV; dropout due to side effects (linear);</td>
<td>No</td>
</tr>
<tr>
<td>Andrews et al. (2012)</td>
<td>Heterosexual (15-49 years)</td>
<td>Linear</td>
<td>Background mortality; death due to HIV;</td>
<td>Immigration (with specific HIV prevalence); Emigration (with specific HIV prevalence);</td>
</tr>
<tr>
<td>Hallett et al. (2009)</td>
<td>Heterosexual (15 years and older) and vertical</td>
<td>Delayed linear</td>
<td>Background mortality; death due to HIV(linear);</td>
<td>No</td>
</tr>
<tr>
<td>Karmon et al. (2003)</td>
<td>Heterosexual (all ages)</td>
<td>Constant</td>
<td>Death due to HIV; emigration;</td>
<td>Immigration as recruitment</td>
</tr>
<tr>
<td>Alsallaq et al. (2009)</td>
<td>Heterosexual (sexually active)</td>
<td>Linear</td>
<td>Aging; death due to HIV;</td>
<td>No</td>
</tr>
<tr>
<td>Alsallaq et al. (2013)</td>
<td>Heterosexual (sexually active)</td>
<td>Linear</td>
<td>Background mortality; death due to HIV;</td>
<td>No</td>
</tr>
<tr>
<td>Andersson et al. (2011)</td>
<td>Heterosexual (17 years and older)</td>
<td>Constant</td>
<td>Background mortality; death due to HIV</td>
<td>No</td>
</tr>
<tr>
<td>Dushoff et al. (2011)</td>
<td>Heterosexual (general)</td>
<td>Linear</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Granich et al. (2009)</td>
<td>Heterosexual (15 years and older)</td>
<td>Linear</td>
<td>Background mortality; death due to HIV</td>
<td>No</td>
</tr>
<tr>
<td>Hallett et al. (2008)</td>
<td>Heterosexual (sexually active)</td>
<td>Linear</td>
<td>Aging; death due to HIV</td>
<td>No</td>
</tr>
<tr>
<td>Nagelkerke et al. (2007)</td>
<td>Heterosexual (general)</td>
<td>Linear</td>
<td>Background mortality; death due to HIV</td>
<td>No</td>
</tr>
<tr>
<td>Podder et al. (2007)</td>
<td>Heterosexual (sexually active)</td>
<td>Constant</td>
<td>Background mortality; death due to HIV</td>
<td>No</td>
</tr>
</tbody>
</table>
Table 16: Continued from Table 15. MSM: men who have sex with men.

<table>
<thead>
<tr>
<th>paper</th>
<th>population</th>
<th>recruitment</th>
<th>departure (all linear)</th>
<th>migration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Li et al. (2009)</td>
<td>general</td>
<td>constant</td>
<td>background mortality; death due to HIV;</td>
<td>immigration(linear); emigration(linear);</td>
</tr>
<tr>
<td>Sorensen et al. (2012)</td>
<td>MSM(sexually active)</td>
<td>constant</td>
<td>aging; background mortality; death due to HIV; drop out of care;</td>
<td>immigration as recruitment</td>
</tr>
<tr>
<td>Wagner and Blower (2012)</td>
<td>heterosexual(sexually active)</td>
<td>constant</td>
<td>background mortality; death due to HIV; drop out of treatment;</td>
<td>No</td>
</tr>
<tr>
<td>Nichols et al. (2013)</td>
<td>heterosexual</td>
<td>constant</td>
<td>background mortality; death due to HIV; drop out of treatment;</td>
<td>No</td>
</tr>
<tr>
<td>Abbas et al. (2007)</td>
<td>heterosexual(sexually active)</td>
<td>linear</td>
<td>aging; background mortality; death due to HIV;</td>
<td>No</td>
</tr>
<tr>
<td>Zhao et al. (2013)</td>
<td>heterosexual(sexually active)</td>
<td>constant</td>
<td>aging</td>
<td>No</td>
</tr>
<tr>
<td>Breban et al. (2006)</td>
<td>MSM(general)</td>
<td>constant</td>
<td>bathroom visit</td>
<td>No</td>
</tr>
<tr>
<td>Cox et al. (2011)</td>
<td>heterosexual(general)</td>
<td>constant</td>
<td>death, aging, emigration all in one</td>
<td>emigration(all in one, linear)</td>
</tr>
<tr>
<td>Cremin et al. (2013)</td>
<td>heterosexual(sexually active)</td>
<td>linear</td>
<td>death due to HIV; background mortality</td>
<td>No</td>
</tr>
<tr>
<td>Desai et al. (2008)</td>
<td>MSM(13 years and older)</td>
<td>constant</td>
<td>background mortality; death due to HIV;</td>
<td>No</td>
</tr>
<tr>
<td>Juusola et al. (2012)</td>
<td>MSM(13-64 years)</td>
<td>linear</td>
<td>aging; background mortality; death due to HIV;</td>
<td>No</td>
</tr>
<tr>
<td>Dimitrov et al. (2010)</td>
<td>heterosexual(sexually active)</td>
<td>constant</td>
<td>aging</td>
<td>No</td>
</tr>
</tbody>
</table>
Table 17: Continued from Table. 16. IDU: injection drug users.

<table>
<thead>
<tr>
<th>paper</th>
<th>population</th>
<th>recruitment</th>
<th>departure (all linear)</th>
<th>migration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimitrov et al. (2011)</td>
<td>heterosexual (sexually active)</td>
<td>constant</td>
<td>aging; death due to HIV;</td>
<td>No</td>
</tr>
<tr>
<td>Dimitrov et al. (2012)</td>
<td>heterosexual (sexually active)</td>
<td>constant</td>
<td>aging</td>
<td>No</td>
</tr>
<tr>
<td>Supervie et al. (2010)</td>
<td>MSM (sexually active)</td>
<td>constant</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Supervie et al. (2011)</td>
<td>heterosexual (sexually active)</td>
<td>constant</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Vickerman et al. (2006)</td>
<td>heterosexual (sex workers)</td>
<td>constant</td>
<td>move away</td>
<td>No</td>
</tr>
<tr>
<td>Williams et al. (2006)</td>
<td>heterosexual (sexually active)</td>
<td>linear (fixed total)</td>
<td>death rate due to HIV</td>
<td>No</td>
</tr>
<tr>
<td>Wilson et al. (2008)</td>
<td>heterosexual (sexually active)</td>
<td>constant</td>
<td>background departure; death due to HIV;</td>
<td>No</td>
</tr>
<tr>
<td>Long et al. (2009)</td>
<td>heterosexual and homosexual (sexually active)</td>
<td>linear</td>
<td>mortality and maturation rate;</td>
<td>No</td>
</tr>
<tr>
<td>Londish et al. (2010)</td>
<td>MSM (sexually active)</td>
<td>constant</td>
<td>combined death and exit rates</td>
<td>emigration as exit rate</td>
</tr>
<tr>
<td>Lima et al. (2008)</td>
<td>MSM (and IDU)</td>
<td>constant</td>
<td>mortality rate (not) due to HIV</td>
<td>No</td>
</tr>
<tr>
<td>Law et al. (2001)</td>
<td>MSM (sexually active)</td>
<td>constant</td>
<td>aging; death rate due to HIV;</td>
<td>No</td>
</tr>
</tbody>
</table>