USC-RAND-UCLA-JH
HIV Model: Development, Calibration, and Validation.

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Abstract

We extended the Sood et al. (2013) and Drabo et al. (2016) models to capture various subgroups of the population, as well as variations in HIV prevalence and transmission across various geographic areas.

1 Introduction

to come

Provide some background information on the HIV epidemic, and on HIV transmission. What are the milestones that have been achieved, and where are the challenges?

The richness of the model allows us to assess the impacts of various interventions on HIV morbidity and mortality as well as on the burden of the disease. We can also study disparities in outcomes.

2 Literature review

to come

Discuss evidence on the efficacy and safety of PrEP, condoms, microbicides, etc, adherence patterns, sexual mixing, drivers of the epidemic, and highlight gaps in the literature

3 Epidemic model of HIV transmission

3.1 Overview of the HIV transmission model

Our extended model follows the basic structure of the Sood et al. (2013) and Drabo et al. (2016) models. Individuals enter the model through birth and immigration at respective annual rates π_X^j and ϕ_X^j. Once in the model, they can transition between health states, which comprise the uninfected (S, SJ, $SPrEP$), primary (P_m, PJ_m, $PPrEP_m$, PT_m), asymptomatic (I_m, IJ_m, $IPrEP_m$, IT_m), symptomatic (E_m, EJ_m, ET_m), and AIDS (A_m, AJ_m, AT_m) stages of HIV infection, where the subscript $m \in \{s,r\}$ denotes the drug-sensitive (s) or drug-resistant (r) strata, corresponding to the virus strain. The compartments S, P, I, E and A denote the populations of individuals unaware of their serostatus; the compartments SJ, PJ, IJ, EJ and AJ denote individuals aware of their serostatus through testing. The compartments PT, IT, ET and AT denote individuals treated with ART in the primary, asymptomatic, symptomatic and AIDS stages, respectively. Finally, $SPrEp$, $PPrEP$, and $IPrEP$ denote individuals using PrEP in the uninfected, primary and symptomatic stages. Depending on their adherence to ART treatment and the efficacy of the treatment, individuals treated with ART (PT, IT, ET and AT) can achieve viral suppression and transit back to healthier states.

At any stage in the model, individuals can exit the model through death at a natural death rate μ, or from HIV/AIDS complications (γ_{A_m}, γ_{AJ_m}, or γ_{AT_m}). The directed arrows denote the transition of men between health states.

We stratify the population by race (White, Black, Hispanic, and Other), age group (0-14, 15-24, 25-34, 35-49, and ≥ 50 years), gender (Female, Male, Transgender Male, and Transgender Female), sexual orientation (Heterosexual and Homosexual/Bisexual), risks group (High- and Low-risk), injection-drug use behavior, and syphilis infection status (No syphilis, Undiagnosed syphilis, Diagnosed untreated syphilis, and Treated syphilis), circumcision status, and homelessness status, given that this population is at increased risk of HIV infection (CITE and make sure this is part of the Literature review section). Hence, at birth, individuals can assume one of 12 demographic characteristics over three demographic groups: They can be White, Black, Hispanic, or Other race/ethnicity, male or female, and males can be circumcised or uncircumcised. Those entering the model through migration can assume one of 48 demographic characteristics.

We assume that individuals become sexually active and discover their sexual orientation between ages 15 and 24 Taylor (2013). Following the evidence reported in Rosario et al. (2006), we assume that sexual orientation remains relatively stable after that age group. [CITE Grov et al. (2017) IF APPROPRIATE]

To capture geographic variations in HIV risk and transmission, we further stratify the population into 26 subareas corresponding to the 26 health districts in Los Angeles County. Our extended model also accounts for migrations between

geographic units, and in and out of the county. This is particularly important to help understand how within and between county population movements affect the dynamics of the epidemic in given geographic unit.

Due to a the lack of reliable data on within county migration patterns, we are unable to estimate with great confidence the changes in different subgroups of the population for different geographic units, owing to these migration patterns.

Table 1: Demographic, geographic, and behavioral characteristics.

Other Characteristics	**Age Group**				
	0-14	**15-24**	**25-34**	**35-49**	**50+**
Race/Ethnicity	White, Black, Hispanic, Asian, Other	White, Black, Hispanic, Asian, Other	White, Black, Hispanic, Asian, Other	White, Black, Hispanic, Asian, Other	White, Black, Hispanic, Asian, Other
Gender	Male, Female	Male, Female, Trans-Male, Trans-Female	Male, Female, Male to Female Trans, Female to Male Trans	Male, Female, Male to Female Trans, Female to Male Trans	Male, Female, Male to Female Trans, Female to Male Trans
Sexual Orientation	Heterosexual, Homosexual, Bisexual	Heterosexual, Homosexual, Bisexual	Heterosexual, Homosexual, Bisexual	Heterosexual, Homosexual, Bisexual	Heterosexual, Homosexual, Bisexual
Sexual Risk	Low-Risk	Low-Risk, High-Risk	Low-Risk, High-Risk	Low-Risk, High-Risk	Low-Risk, High-Risk
Injection Drug Use	Non-IDU	Non-IDU, IDU	Non-IDU, IDU	Non-IDU, IDU	Non-IDU, IDU
Syphilis	No-Syphilis, Syphilis	No-Syphilis, Syphilis	No-Syphilis, Syphilis	No-Syphilis, Syphilis	No-Syphilis, Syphilis
Geography	26 health districts	All 26 Health Districts	All 26 Health Districts	All 26 Health Districts	All 26 Health Districts

In the model, certain socio-demographic (age, gender, sexual orientation), behavioral (sexual risk behavior, injection-drug use), geographic (health district associated with residence), and health (syphilis infection status) characteristics, of the population are allowed to change over time.

Unlike the Sood et al. (2013) and Drabo et al. (2016) models, we allow for individuals treated with antiretroviral therapy (ART) to achieve viral suppression and transition back into compartments with higher CD4 counts and lower viral loads.

3.2 System of ordinary differential equations (ODEs)

The transmission of HIV is captured by a system of ODEs:

$$
\begin{aligned}
dS^j/dt &= \left(\mathbb{1}_{j\in M}(g)\pi_S^g + g^j_{SPrEP} SPrEP^j + \psi^j SJ^j + \phi^j_S + \sum_{i\neq j}\xi^{ij}_S S^i\right) - \left(\sum_l\sum_m \lambda^j_{l,m} + \sum_{i\neq j}\xi^{ji}_S + \omega^j_S + \zeta^j_S + \mu^j_S\right) S^j \\
dSPrEP^j/dt &= \left(\sigma^j_{SP} SJ^j + \phi^j_{SP} + \sum_{i\neq j}\xi^{ij}_{SP} SP^i\right) - \left(\sum_l\sum_m \hat{\lambda}^j_{l,m} + \sum_{i\neq j}\xi^{ji}_{SP} + \omega^j_{SP} + g^j_{SP} + \zeta^j_{SP} + \mu^j_{SP}\right) SP^j \\
dSJ^j/dt &= \left(\omega^j_S S^j + \omega^j_{SP} SP^j + \phi^j_{SJ} + \sum_{i\neq j}\xi^{ij}_{SJ} SJ^i\right) - \left(\sum_l\sum_m \tilde{\lambda}^j_{l,m} + \sum_{i\neq j}\xi^{ji}_{SJ} + \psi^j + \sigma^j_{SP} + \zeta^j_{SJ} + \mu^j_{SJ}\right) SJ^j \\
dP^j_m/dt &= \left(\pi^j_{P_m} + \phi^j_{P_m} + \sum_l\left\{\lambda^j_{l,m} S^j + \tilde{\lambda}^j_{l,m} SJ^j\right\} + g^j_{PP_m} PP^j_m + \sum_{i\neq j}\xi^{ij}_{P_m} P^i_m\right) - \left(\sum_{i\neq j}\xi^{ji}_{P_m} + \omega^j_S + \zeta^j_{P_m} + \mu^j_{P_m}\right) P^j_m \\
dPP^j_m/dt &= \left(\phi^j_{PP_m} + \sum_l \hat{\lambda}^j_{l,m} SP^j + \sigma^j_{PP} P^j_m + \mathbb{1}_s(m) r^j_{PP} PP^j_r + \sum_{i\neq j}\xi^{ij}_{PP_m} PP^i_m\right) - \left(\sum_{i\neq j}\xi^{ji}_{PP_m} + \mathbb{1}_r(m) r^j_{PP} + \omega^j_{PP_m} + g^j_{PP_m} + \rho^j_{PP_m} + \zeta^j_{PI}\right. \\
dPJ^j_m/dt &= \left(\pi^j_{PJ_m} + \omega^j_{P_m} P^j_m + \omega^j_{PP_m} PP^j_m + g^j_{PT_m} TP^j_m + \phi^j_{PJ_m} + \sum_{i\neq j}\xi^{ij}_{PJ_m} PJ^i_m\right) - \left(\sum_{i\neq j}\xi^{ji}_{PJ_m} + \rho^j_{PJ_m} + \sigma^j_{PT_m} + \zeta^j_{PJ_m} + \mu^j_{PJ_m}\right) PJ^j_m \\
dPT^j_m/dt &= \left(\sigma^j_{PT_m} PJ^j_m + \mathbb{1}_s(m) r^j_{PT} TP^j_s + \phi^j_{PT_m} + \sum_{i\neq j}\xi^{ij}_{PT_m} PT^i_m\right) - \left(\sum_{i\neq j}\xi^{ji}_{PT_m} + \mathbb{1}_r(m) r^j_{PT} + \rho^j_{PT_m} + g^j_{PT_m} + \zeta^j_{PT_m} + \mu^j_{PT_m}\right) PT^j_m \\
dI^j_m/dt &= \left(\rho^j_{P_m} P^j_m + g^j_{IP_m} IP^j_m + \phi^j_{I_m} + \sum_{i\neq j}\xi^{ij}_{I_m} I^i_m\right) - \left(\sum_{i\neq j}\xi^{ji}_{I_m} + \omega^j_{I_m} + \sigma^j_{IP_m} + \chi^j_{I_m} + \zeta^j_{I_m} + \mu^j_{I_m}\right) I^j_m \\
dIP^j_m/dt &= \left(\sigma^j_{IP_m} I^j_m + \rho_{IP_m} PP^j_m + \phi^j_{IP_m} + \mathbb{1}_s(m) r^j_{IP} IP^j_r + \sum_{i\neq j}\xi^{ij}_{IP_m} IP^i_m\right) - \left(\sum_{i\neq j}\xi^{ji}_{IP_m} + \mathbb{1}_r(m) r^j_{IP} + \omega^j_{IP_m} + g^j_{IP_m} + \zeta^j_{IP_m} + \mu^j_{IP_m}\right) IP \\
dIJ^j_m/dt &= \left(\omega^j_{I_m} I^j_m + \omega^j_{IP_m} IP^j_m + \rho^j_{PJ_m} PJ^j_m + g^j_{IT_m} IT^j_m + \phi^j_{IJ_m} + \sum_{i\neq j}\xi^{ij}_{IJ_m} IJ^i_m\right) - \left(\sum_{i\neq j}\xi^{ji}_{IJ_m} + \sigma^j_{IT_m} + \chi^j_{IJ_m} + \zeta^j_{IJ_m} + \mu^j_{IJ_m}\right) IJ^j_m \\
dIT^j_m/dt &= \left(\sigma^j_{IT_m} IJ^j_m + \rho_{PT_m} PT^j_m + \phi^j_{IT_m} + \mathbb{1}_s(m) r^j_{IT} IT^j_s + \sum_{i\neq j}\xi^{ij}_{IT_m} IT^i_m\right) - \left(\sum_{i\neq j}\xi^{ji}_{IT_m} + \mathbb{1}_r(m) r^j_{IT} + g^j_{IT_m} + \chi^j_{IT_m} + \zeta^j_{IT_m} + \mu^j_{IT_m}\right) IT \\
dE^j_m/dt &= \left(\chi^j_{I_m} I^j_m + \phi^j_{E_m} + \mathbb{1}_s(m) q^j_E E^j_r + \sum_{i\neq j}\xi^{ij}_{E_m} E^i_m\right) - \left(\sum_{i\neq j}\xi^{ji}_{E_m} + \omega^j_{E_m} + \gamma^j_{E_m} + \mathbb{1}_r(m) q^j_E + \zeta^j_{E_m} + \mu^j_{E_m}\right) E^j_m \\
dEJ^j_m/dt &= \left(\chi^j_{IJ_m} IJ^j_m + \omega^j_{E_m} E^j_m + g^j_{ET_m} ET^j_m + \phi^j_{EJ_m} + \mathbb{1}_s(m) q^j_E EJ^j_r + \sum_{i\neq j}\xi^{ij}_{EJ_m} EJ^i_m\right) - \left(\sum_{i\neq j}\xi^{ji}_{EJ_m} + \sigma^j_{ET_m} + \gamma^j_{EJ_m} + \mathbb{1}_r(m) q^j_E + \zeta^j_{EJ_m}\right. \\
dET^j_m/dt &= \left(\chi_{IT_m} IT^j_m + \sigma^j_{ET_m} EJ^j_m + \phi^j_{ET_m} + \mathbb{1}_r(m) r^j_{ET} ET^j_s + \sum_{i\neq j}\xi^{ij}_{ET_m} ET^i_m\right) - \left(\sum_{i\neq j}\xi^{ji}_{ET_m} + \mathbb{1}_s(m) r^j_{ET} + g^j_{ET_m} + \gamma^j_{ET_m} + \zeta^j_{ET_m} + \mu^j_{ET}\right. \\
dA^j_m/dt &= \left(\mathbb{1}_s(m) q^j_A A^j_r + \gamma^j_{E_m} E^j_m + \phi^j_{A_m} + \sum_{i\neq j}\xi^{ij}_{A_m} A^i_m\right) - \left(\mathbb{1}_r(m) q^j_A + \omega^j_{A_m} + \gamma^j_{A_m} + \zeta^j_{A_m} + \mu^j_{A_m} + \sum_{i\neq j}\xi^{ji}_{A_m}\right) E^j_m \\
dAJ^j_m/dt &= \left(\mathbb{1}_s(m) q^j_A AJ^j_r + \omega^j_{A_m} A^j_m + g^j_{AT_m} AT^j_m + \gamma^j_{EJ_m} EJ^j_m + \phi^j_{AJ_m} + \sum_{i\neq j}\xi^{ij}_{AJ_m} AJ^i_m\right) - \left(\mathbb{1}_r(m) q^j_A + \sigma^j_{AT_m} + \gamma^j_{AJ_m} + \mu^j_{AJ_m} + \zeta^j_{AJ_m} + \right. \\
dAT^j_m/dt &= \left(\mathbb{1}_r(m) r^j_{AT} AT^j_s + \sigma^j_{AT_m} AJ^j_m + \gamma_{ET_m} ET^j_m + \phi^j_{AT_m} + \sum_{i\neq j}\xi^{ij}_{AT_m} AT^i_m\right) - \left(\mathbb{1}_s(m) r^j_{AT} + g^j_{AT_m} + \gamma^j_{AT_m} + \mu^j_{AT_m} + \zeta^j_{AT_m} + \sum_{i\neq j}\xi^{ji}_{AT}\right.
\end{aligned}
$$

where ϕ^j_X and ζ^j_X denote respectively the immigration and emigration rates into and out of profile j for each health state X. The parameter ξ^{ij}_X is defined as $\xi^{ij}_X = r\left(\Gamma^{ij}_X\right)$, and denotes the "demographic profile switching matrix", which captures the transitions of individuals from profile i to profile j in different health states X, due respectively to aging, and changes in sexual risk profile (e.g. from Low-Risk to High-risk), needle-sharing status, syphilis infection status, and geography. The function $r(\cdot)$, defined in Equation (), transforms into a rate its argument, $\Gamma^{ij}_X = \nu^{ij}_X \cdot \theta^{ij}_X \cdot \delta^{ij}_X \cdot \eta^{ij}_X \cdot \iota^{ij}_X$, which represents the product of the annual probabilities of switching from characteristic i to j. It is important to notice

here that ξ_X^{ij} varies by health state; this allows us to capture the potential effects of "risk compensation" as PrEP and ART initiations rates increase in the population.

3.3 Disease transmission

Our model captures three routes of HIV infections, namely (i) the vertical transmission from mother to child, (ii) horizontal transmission via sexual contact, and (iii) horizontal transmission via contaminated blood, the majority of which occurs through shared contaminated injection needles among IDUs. These three types of infection routes will also define three types of force of infections, and their mathematical expressions will depend on how individuals belonging to different population strata give birth, mix sexually, or share needles.

Our extension of the model also captures adaptive risk behaviors by allowing HIV risk perception to affect individual risk behavior, which will in turn affect risk perception after the individual has experienced the consequences of the behavior [CITE 28 FROM PROPOSAL]. For example, the availability of PrEP might decrease individual risk perceptions and induce risky behaviors such as decreased condom use, and non-compliance with treatment, leading to the development of MDR and the loss of drug efficacy [CITE 6, 138-140 FROM PROPOSAL]. Hence, we model the rates of testing, treatment initiation, adherence to treatment, and unprotected sex acts, as well as the number of partners to depend on the elasticities of prevalence which capture the individual's testing, treatment and risk responsiveness to changes in their perceptions of HIV prevalence. Prior studies have shown these statistics to be strongly associated with individual risk perceptions [CITE1 41-143 FROM PROPOSAL].

Risk compensation is modeled as (i) a reduction in the probability of condom and/or clean needle use, (ii) an increase in the number of sexual partner and/or needle sharing partners, and (iii) a change in the sexual and needle-sharing mixing probabilities.

When exposed to ART, wild-type HIV can develop mutations that make the virus resistant to specific HIV drugs. Hence, increased use of ART and PrEP could also lead increased prevalence of mutant strains and MDR.

3.3.1 Vertical (perinatal or mother-to-child) transmission during pregnancy and childbirth

Perinatal transmission of HIV can occur during pregnancy, childbirth (i.e. labor and delivery), or breastfeeding (through breast milk). ART and other HIV-prevention strategies can reduce the risk of vertical transmission to 2% or less. The risk of vertical transmission is especially lowered with early detection of the mother's serostatus before pregnancy or during pregnancy. These women can receive ART during their pregnancy and childbirth and, in some situations, have a scheduled cesarean delivery (i.e. C-section). Babies born to women with HIV receive ART for 4 to 6 weeks after birth and are not breastfed. ART prevents vertical transmission by preventing viral replication, thereby reducing viral load in the body. Reduced viral load protects the mother's health and reduces her risk of transmitting HIV to her child during pregnancy and childbirth. ART regimen can pass from the pregnant woman to her fetus, across the placenta, and hence prophylactically protect the fetus from HIV infection, especially during a vaginal delivery when the baby passes through the birth canal and is exposed to the virus in the mother's blood or other fluids. [CITE]

[See these references for modeling vertical transmission: http://sti.bmj.com/content/sextrans/88/Suppl_2/i44.full.pdf; http://www.epidem.org/sites/default/files/content/resources/attachments/UpdatingMTCTratesReport.pdf]

We model perinatal HIV transmission during pregnancy, childbirth (i.e. labor and delivery) as follows:

$$\pi_{Z_m}^j = r^j \sum_k \sum_{X \in X_Z} \pi^k \hat{\beta}_{X_m}^k X_m^k / F_m^k \tag{18}$$

where $Z \in \{P, PJ\}$ denotes the primary stage of infection, $r^j = r^{d_j}\left(1 - r^{d_j}\right)/(1+r)$ denotes the male to female birth ratio, $d_j = \mathbb{1}_M(j)$ denotes a dummy variable taking the value of one for males ($j = M$) and zero for females ($j = F$), π^k denotes the age-specific annual fertility rate for women in age group k (expressed as a rate per woman), and F_m^k denotes the total number of females in the population, in procreation age group k. The parameter $\hat{\beta}_{X_m}^k$ is the vertical (perinatal) transmission coefficient representing the proportion of children born to infected mothers with strain m in state

X that also become infected, and is defined as:

$$\hat{\beta}^k_{X_m} = \hat{\alpha}_{X_m} = \hat{\alpha}^{\text{base}}_{X_m}(2.45)^{\log_{10}(v_{X_m}/v^{\text{base}}_{X_m})} \tag{19}$$

To capture vertical transmission via breastfeeding, we assume that women aware of their serostatus do not breastfeed, but that a fraction of women unaware of their infection status do breastfeed. The force of infection parameter for breastfeeding is modeled as follows:

$$\overline{\lambda}^j_{Z_m} = p^j_b \sum_k \sum_X (1-e^j_p d_Z)\overline{\beta}^k_{X_m} X^k_m / F^k_m \tag{20}$$

$$\overline{\beta}^k_{X_m} = 1-(1-(1-e_b)\overline{\alpha}_{X_m})^{g^k_b n^k_b}(1-\overline{\alpha}_{X_m})^{(1-g^k_b)n^k_b} \tag{21}$$

3.3.2 Horizontal transmission via sexual contact and contaminated blood

Following our prior approach in modeling HIV/AIDS transmission, we defined the force of infection parameters for the horizontal transmission via sexual contact, and needle sharing as:

$$\lambda^j_{Z_m} = \sum_l \sum_k \sum_{X \in X_Z} (1-e^j_p d_Z)\tilde{C}^{jk}_{X_{lm}} \tilde{\beta}^{kj}_{X_{lm}} X^k_{lm}/N^k_{lm} = \sum_l \sum_k \sum_X (1-e^j_p d_Z) C^j_l P^{jk}_l \beta^{kj}_{X_{lm}} X^k_{lm}/N^k_{lm} \tag{22}$$

$Z \in \{S, SJ, SPrEP\}$ denotes the unaware, aware and PrEP susceptible states, e^j_p denotes the efficacy of PrEP and depends on adherence to PrEP (a^j_p), $d_Z = \mathbb{1}_{SPrEP}(Z)$ is a dummy indicator for whether $Z = SPrEP$, X^k_{lm} denotes the number of infected people from group k and with virus strain m in infected state X who have l-type (sexual or needle-sharing) contacts, N^k_{lm} represents the total population (i.e the sum of the susceptible and all infected individuals in group k), P^{jk}_l denotes the mixing probabilities between individuals in group j and those in group k, and $\beta^{kj}_{X_{lm}}$ denotes the per-partnership probability of HIV transmission from an infected individual in group k and disease state X to a susceptible individual in state Z via l route, and are calculated as:

$$C^{jk}_{X_{lm}} \tilde{\beta}^{kj}_{X_{lm}} = C^j_l P^{jk}_l \beta^{kj}_{X_{lm}} \tag{23}$$

where C^j_l denotes the average number of new l-type partners that individuals in group j acquire each year. The annual probabilities of infection per serodiscordant partnership are defined as

$$\beta^{kj}_{X_{lm}} = 1-(1-(1-e_l)\alpha_{X_{lm}})^{g^{jk}_l n^{jk}_l}(1-\alpha_{X_{lm}})^{(1-g^{jk}_l)n^{jk}_l} \tag{24}$$

where e_l denotes the efficacy of protection (i.e. efficacy of condoms in sexual contacts, and efficacy of clean needle in needle sharing), $\alpha_{X_{lm}}$ represents the per-contact probability of HIV transmission from an infected individual in stage X to a susceptible individual, n^{jk}_l denotes the average numbers of l-type contacts that individuals in group j have per k-type partner per year, and g^{jk}_l represents the proportion of l-type contacts with individuals in group k where protection is used. The per-contact probability of HBV transmission, $\alpha_{X_{lm}}$ are determined by the viral load as follows:

$$\alpha_{X_{lm}} = \alpha^{\text{base}}_{X_{lm}}(2.45)^{\log_{10}(v_X/v^{\text{base}}_X)} \tag{25}$$

where v_X denotes the average viral load in individuals in disease stage X, and $\alpha^{\text{base}}_{X_{lm}}$ denotes the probability of HIV transmission from an infected person in state X with baseline viral load v^{base}_X.

To capture adaptive behavioral responses, we define certain parameters in the model to vary with individual's perceived risk of HIV, as well as their perceptions about the efficacy of preventive technologies such as condoms, PrEP and clean needles. Prior studies have shown the rates of testing, treatment initiation, adherence to treatment, and unprotected sex acts, as well as the sexual mixing matrices that determine how individuals choose sex partners to change over time, and to depend on the individual's perceptions of HIV infection risk, developing MDR, or dying from HIV/AIDS complications

to be strongly associated with individual risk perceptions [CITE1 41-143 FROM PROPOSAL]. Hence we assume that the number of partners (C_l^{jk}) decreases, while the share of contacts that are protected (g_l^{jk}) increases with increased perception of HIV risk, and vice versa. We also assume that C_l^{jk} increases, while g_l^{jk} decreases with PrEP efficacy, because individuals are assumed to prefer unprotected contacts due to the private cost of protection. Furthermore, we assume that risk perception affect mixing probabilities: group j's perception of high disease prevalence in a group k decreases group j's probability of mixing with individuals in k. These result in the following functional forms for key parameters:

$$C_l^j = C_l^j\left(\tilde{R}^j,\tilde{e}_p^j\right) \tag{26}$$

$$P_l^{jk} = P_l^{jk}\left(\tilde{R}^{jk}\right) \tag{27}$$

where $\tilde{R}^j$ and $\tilde{R}^{jk}$ denote the average group-level perceptions of HIV risk, and $\tilde{e}_p^j$ captures the perception of PrEP efficacy among individuals in group j. These perceived risk and efficacy parameters are related to the true disease risk and PrEP efficacy as follow [CITE Tully et al. 2013 in Journal of Theoretical Biology 337:125–132; Tully et al. 2016 in Nature]:

$$\tilde{R}^{jk}(t) = \iota^j\tilde{R}^{jk}(t-1)+(1-\iota^j)R^k(t) \tag{28}$$

$$\tilde{R}^j(t) = \iota^j\tilde{R}(t-1)+(1-\iota^j)R(t) \tag{29}$$

$$\tilde{e}_p^j(t) = \iota^j\tilde{e}_p^j(t-1)+(1-\iota^j)e_p(t), \tag{30}$$

$$\tilde{s}_p^j(t) = \iota^j\tilde{s}_p^j(t-1)+(1-\iota^j)s_p, \tag{31}$$

$$e_p^j(t) = e_p^j\left(a_p^j(t)\right) \tag{32}$$

$$a_p^j(t) = a_p^j\left(\tilde{e}_p^j(t),\tilde{s}_p^j(t)\right) \tag{33}$$

where $R^k=\sum_X X^k/N^k$ and $R=\sum_k\sum_X X^k/N$, with $X\in\{PJ,PT,IJ,IT,EJ,ET,AJ,AT\}$ representing any of the eight infectious compartments where individuals are aware of their serostatus, $\tilde{R}^{jk}(t)$ and $\tilde{R}^{jk}(t-1)$ denote the perceived HIV prevalence in group k by individuals in group j at times t and $t-1$, respectively. The parameters $e_p(t)$ and s_p denote the "real-world" objective efficacy and safety of PrEP. Notice that the objective safety of the PrEP is constant over time, whereas the objective efficacy varies with adherence. The parameter $\iota^j\in[0,1]$ denotes the "local information" parameter characterizing the extent to which the individual's HIV risk perception reflects the accurate information on HIV prevalence, and $\tilde{R}^{jk}(0)=(1-\iota^j)R^k(0)$ denotes the baseline HIV risk perception. Hence, the closer ι^j is to 1 (0), the less (more) accurate the individual's risk perception is. In general, ι^j will be closer to 1 because information about HIV prevalence in a small group of the population will diffuse slowly, whereas the HIV epidemic will change rapidly over the timescale [CITE 144, 145 FROM PROPOSAL; https://www.ncbi.nlm.nih.gov/pubmed/28618981; https://journals.lww.com/lww-medicalcare/Abstract/2012/05000/Adherence_to_and_Effectiveness_of_Highly_Active.9.aspx; https://www.rand.org/pubs/external_publications/EP67214.html; http://aidsinstitute.ucla.edu/workfiles/slides/2017.10.02-Slides.pdf; https://www.enddisparitiesexchange.org/wp-content/uploads/2017/03/CAI-HIV-Presentation-Webinar-2.28.2017.pdf].

3.4 Demographic changes: Birth, aging and mortality rates

Once in the model, individuals transit through the various compartments depending on changes in their perceptions, behaviors, sexual orientation, as well as due to aging.

3.4.1 Inflow of new-borns into the population

We model the inflow of new-borns in the susceptible population as:

$$\pi_S^g = \left(r^g\sum_j\pi^j\right)-\left(\pi_{P_m}^g+\pi_{PJ_m}^g\right) \tag{34}$$

$$d\pi_S^g/dt = -\left(d\pi_{P_m}^g/dt+d\pi_{PJ_m}^g/dt\right) \tag{35}$$

Once in the model, individuals can die with baseline mortality hazard rates xxx and with additional mortality rates from HIV/AIDS complications or complications from other STIs. Each year, individuals who are alive age by one year. We capture this in the aging parameter defined as:

3.5 HIV testing and treatment, and adherence behaviors

3.5.1 HIV testing, PrEP and ART initiation

We assume that HIV risk perception affects HIV testing rates through its effect on the testing probabilities p_ω, and we capture this using the prevalence elasticity of testing as follows:

$$\begin{aligned} \omega_X^j\left(\tilde{n}_X^j,t\right) &= -\ln\left[1-p_\omega\left(\tilde{n}_X^j,t\right)f_X\right]/t & (36)\\ \partial\omega_X^j/\partial\tilde{n}_X^j &= -\left(\partial\ln\left[1-p_\omega\left(\tilde{n}_X^j,t\right)f_X\right]/\partial\tilde{n}_X^j\right)/t & (37)\\ &= e_{\omega_X}^j\left(p_\omega f_X/\tilde{n}_X^j\right)/t(1-p_\omega f_X), & (38)\end{aligned}$$

where $e_{\omega_X}^j=\left(\partial p_\omega/\partial\tilde{n}_X^j\right)\left(\tilde{n}_X^j/p_\omega\right)$ is the prevalence elasticity of testing among individuals in group j and in compartment X, and f_X is the true-positive (for infected) or rue-negative (fo uninfected) pobability among individuals who get tested. This means that for every percent increase (decrease) in HIV prevalence, the probability of testing and thus the testing rate will also increase (decrease) by $e_{\omega_X}^j$ percent. Similarly, we model PrEP initiation and rate to depend on individual's HIV risk perception, as well as their perception about PrEP's efficacy:

$$\begin{aligned} \sigma_X^j &= p_\sigma\left(\tilde{n}_X^j,t\right)f_X & (39)\\ \partial\omega_X^j/\partial\tilde{n}_X^j &= \left(\partial p_\omega/\partial\tilde{n}_X^j\right)f_X = e_{\omega_X}^j\left(p_\omega/\tilde{n}_X^j\right)f_X, & (40)\end{aligned}$$

We model changes in treatment rate to depend of the *ex-ante* perceived efficacy and effectiveness of ART, as measured by the relative mortality rate among treated individuals compared to untreated individuals.

3.5.2 Adherence to treatment

3.5.3 Treatment discontinuation

3.6 Transitions between demographic, behavior, health, and geographic groups

In the model, certain socio-demographic (age, gender, sexual orientation), behavioral (sexual risk behavior, injection-drug use), geographic (health district associated with residence), and health (syphillis infection status) characteristics, of the population are allowed to change over time.

Migration data here: https://www.irs.gov/statistics/soi-tax-stats-county-to-county-migration-data-files

3.7 Disease progression

Once infected, individuals progress through various stages of HIV infection based on their virus strain, disease stage, treatment status, adherence behaviors, and the efficacy of the treatment.

3.8 Estimation of compartment populations

To come: Estimating the populations in each compartment and demographic group

3.9 Estimation of parameters

We assume sexual transmission to only occur among the sexually-active individuals, that is, those 15 years and older. We recognize that this assumption may be invalid, because some teenagers below age 15 may be sexually active.

The mixing matrices are constructed such that both sexual mixing is assumed to be stronger within geographic units than between geographic units. Similarly, needle sharing is assumed to be more likely between individuals in the same geographic unit than people in different geographic units.Jacquez et al. (1988)

Recent data on on sexual mixing: Herbenick et al. (2017)

3.10 Model calibration

We calibrate the model to reproduce the trends in total population, race, age and gender representations, as well as HIV prevalence and incidence in LAC. To do this, we adopt the Latin hypercube sampling approach, and make use of half of the data (the second half of the data is used to validate the model).

3.11 Model validation

To come

3.12 Sensitivity analyses

To come

4 Economic model

To come

4.1 Cost parameters

4.2 Effectiveness parameters

5 Model application: A worked example

To come

6 Future extensions

To come

7 Conclusion

To come

8 References

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