

**Potential Population Health Outcomes and Expenditures of HIV
Vaccination Strategies in the United States**

APPENDIX

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HIV Transmission

We developed a dynamic compartmental model that includes HIV transmission via heterosexual and homosexual contact, and from needle-sharing. Table A-1 shows the variable names and descriptions used in the compartmental model.

The sufficient contact rate between uninfected and infected individuals is represented as a matrix, $\lambda = [\lambda_{i,j}]$, where $\lambda_{i,j}$ represents the sufficient contact rate between members of (uninfected) compartment i and members of (infected) compartment j . To calculate the total contact rate, $\lambda_{i,j}$, we first converted the annual transmission probability to a continuous rate, according to the formula $rate = -\ln(1 - p)/t$. We then summed over the three modes of transmission: needle-sharing ($\gamma_{i,j}$), opposite-sex (heterosexual) contact ($\beta_{i,j}^o$), and same-sex (homosexual) contact ($\beta_{i,j}^s$). For small probability values, we used the approximation $p \approx -\ln(1 - p)$. The total contact rate, $\lambda_{i,j}$, is:

$$\begin{aligned}\lambda_{i,j} &= -\ln(1 - \gamma_{i,j}) + -\ln(1 - \beta_{i,j}^o) + -\ln(1 - \beta_{i,j}^s) \\ &\approx \gamma_{i,j} + \beta_{i,j}^o + \beta_{i,j}^s\end{aligned}\tag{A.1}$$

The transmission probabilities via needle-sharing, opposite-sex, and same-sex contact were modeled as binomial processes, where a “success” is defined as infection transmission. Uninfected individuals randomly select a partner n times; the probability of “success” is the probability of transmission per partnership.

An important aspect of modeling HIV prevention and treatment programs is including their effects on transmission probabilities. By stratifying the population into multiple com-

partments, we grouped individuals with similar characteristics together. We accounted for differences between compartments by adjusting the transmission probabilities appropriately.

For example, the annual probability of transmission, $\sigma_{i,j}$, via heterosexual contact between an uninfected, circumcised male in compartment i and a female with AIDS in compartment j was calculated as:

$$\sigma_{i,j} = \pi_{mf}^{aids} (1 - \epsilon_c) \quad (\text{A.2})$$

where π_{mf}^{aids} is the annual probability of infection transmission from a female with AIDS to an uncircumcised, uninfected male, and ϵ_c is the reduction in heterosexual HIV acquisition in uninfected males due to circumcision.

The transmission probability, $\sigma_{i,j}$, can be further modified by the presence of a preventive vaccine or HAART. For example, if the uninfected male receives a preventive vaccine, and the infected female receives HAART, the above transmission probability becomes:

$$\sigma_{i,j} = \pi_{mf}^{aids} (1 - \epsilon_c)(1 - \epsilon_{pv})(1 - \delta_h^s) \quad (\text{A.3})$$

where ϵ_{pv} is the reduction in HIV acquisition in uninfected individuals due to preventive vaccination, and δ_h^s is the reduction in sexual infectivity in infected individuals due to HAART.

We calculated the probability of infection transmission per risky shared needle (i.e., a needle shared between an uninfected IDU and infected IDU), $\tau_{i,j}$, in manner similar to that for sexual transmission. For example, the probability of infection transmission between an uninfected IDU who receives a preventive vaccine and an infected IDU with symptomatic

HIV who receives HAART is:

$$\tau_{i,j} = \pi^{sym}(1 - \epsilon_{pv})(1 - \delta_h^d) \quad (\text{A.4})$$

where π^{sym} is the per shared-needle probability of infection transmission from a symptomatic HIV-infected IDU to an uninfected IDU, and δ_h^d is the reduction in drug injection (needle-sharing) infectivity in infected individuals due to HAART.

The sufficient contact rates due to needle-sharing ($\gamma_{i,j}$), opposite-sex sexual contact ($\beta_{i,j}^o$), and same-sex sexual contact ($\beta_{i,j}^s$) are modeled as follows:

$$\begin{aligned} P\{T\} &= 1 - P\{\text{no T}\} \\ &= 1 - (P\{\text{no T per trial}\})^{\# \text{ trials}} \\ &= 1 - (1 - P\{T \text{ per trial}\})^{\# \text{ trials}} \\ &= 1 - (1 - P\{\text{select person in } j\} P\{T \text{ per trial} \mid \text{select person in } j\})^{\# \text{ trials}} \end{aligned}$$

where T refers to disease transmission and a trial is either a sexual partnership or shared needle.

The needle-sharing sufficient contact rate between uninfected individuals in compartment i and infected individuals in compartment j is:

$$\gamma_{i,j}(t) = 1 - \left(1 - \left[\frac{X_j(t)d_j s_j}{\sum_k X_k(t)d_k s_k}\right] \tau_{i,j}\right)^{d_i s_i} \quad (\text{A.5})$$

where i, j, k correspond to compartments of IDUs. The term in brackets, $\left[\frac{X_j(t)d_j s_j}{\sum_k X_k(t)d_k s_k}\right]$,

corresponds to the probability of selecting a needle-sharing partner in compartment j , based on a proportional mixing assumption (i.e., individuals with many partners are more likely to select a partner who also has many partners).

The opposite-sex (heterosexual) sufficient contact rate between uninfected individuals in compartment i and infected individuals in compartment j is:

$$\beta_{i,j}^o(t) = 1 - \left(1 - \left[\frac{X_j(t)n_j^o(1-u_j^o\kappa)}{\sum_k X_k(t)n_k^o(1-u_k^o\kappa)} \right] \sigma_{i,j} \right)^{n_i^o(1-u_i^o\kappa)} \quad (\text{A.6})$$

where i is male and j, k are female, or i is female and j, k are male. The term in brackets, $\left[\frac{X_j(t)n_j^o(1-u_j^o\kappa)}{\sum_k X_k(t)n_k^o(1-u_k^o\kappa)} \right]$, corresponds to the probability of selecting a sexual partner in compartment j .

The same-sex (homosexual) sufficient contact rate between uninfected individuals in compartment i and infected individuals in compartment j is:

$$\beta_{i,j}^s(t) = 1 - \left(1 - \left[\frac{X_j(t)n_j^s(1-u_j^s\kappa)}{\sum_k X_k(t)n_k^s(1-u_k^s\kappa)} \right] \sigma_{i,j} \right)^{n_i^s(1-u_i^s\kappa)} \quad (\text{A.7})$$

where i, j, k correspond to compartments of MSM. The term in brackets, $\left[\frac{X_j(t)n_j^s(1-u_j^s\kappa)}{\sum_k X_k(t)n_k^s(1-u_k^s\kappa)} \right]$, again corresponds to the probability of selecting a sexual partner in compartment j .

The overall sufficient contact rate between uninfected individuals in compartment i and infected individuals in compartment j is:

$$\lambda_{i,j}(t) \approx \gamma_{i,j}(t) + \beta_{i,j}^o(t) + \beta_{i,j}^s(t) \quad (\text{A.8})$$

where i and j correspond to any compartments.

System of Nonlinear Differential Equations

We created the following set of 24 differential equations for each of the six risk groups (male IDU, male MSM, male IDU/MSM, male other, female IDU, female other). For compactness, we only show the equations for one risk group. The remaining five risk groups utilize similar equations, with modified indices. For ease of notation, we let X_i denote $X_i(t)$.

A schematic representation of the model is shown in Figure A-1. In the diagram, boxes represent cohorts of individuals, stratified by HIV status, treatment status if infected, preventive vaccine status, and circumcision status. Arrows represent transitions between compartments. Although not shown, individuals may also leave each compartment according to the mortality or maturation rate. A description of all model parameters is given in Table A-1.

$$\frac{dX_1}{dt} = \rho_1 \sum_{\forall i} X_i + \omega_{pv} X_2 - pv_1 X_1 - \left(\sum_{j \geq 11} \lambda_{1,j}(t) \right) X_1 - \mu_1 X_1 \quad (\text{A.9})$$

$$\frac{dX_2}{dt} = -\omega_{pv} X_2 + pv_1 X_1 - \left(\sum_{j \geq 11} \lambda_{2,j}(t) \right) X_2 - \mu_2 X_2 \quad (\text{A.10})$$

$$\frac{dX_3}{dt} = \rho_3 \sum_{\forall i} X_i + \omega_{pv} X_4 - pv_3 X_3 - \left(\sum_{j \geq 11} \lambda_{3,j}(t) \right) X_3 - \mu_3 X_3 \quad (\text{A.11})$$

$$\frac{dX_4}{dt} = -\omega_{pv} X_4 + pv_3 X_3 - \left(\sum_{j \geq 11} \lambda_{4,j}(t) \right) X_4 - \mu_4 X_4 \quad (\text{A.12})$$

$$\frac{dX_{11}}{dt} = \left(\sum_{j \geq 11} \lambda_{1,j}(t) \right) X_1 + \omega_{pv} X_{12} - pv_{11} X_{11} - \theta_{11} X_{11} - \mu_{11} X_{11} \quad (\text{A.13})$$

$$\frac{dX_{12}}{dt} = \left(\sum_{j \geq 11} \lambda_{2,j}(t) \right) X_2 - \omega_{pv} X_{12} + pv_{11} X_{11} - \theta_{12} X_{12} - \mu_{12} X_{12} \quad (\text{A.14})$$

$$\frac{dX_{13}}{dt} = \left(\sum_{j \geq 11} \lambda_{3,j}(t) \right) X_3 + \omega_{pv} X_{14} - pv_{13} X_{13} - \theta_{13} X_{13} - \mu_{13} X_{13} \quad (\text{A.15})$$

$$\frac{dX_{14}}{dt} = \left(\sum_{j \geq 11} \lambda_{4,j}(t) \right) X_4 - \omega_{pv} X_{14} + pv_{13} X_{13} - \theta_{14} X_{14} - \mu_{14} X_{14} \quad (\text{A.16})$$

$$\frac{dX_{21}}{dt} = \omega_{pv} X_{22} - pv_{21} X_{21} + (1 - \phi_{11}) \theta_{11} X_{11} - \theta_{21} X_{21} - \hat{\phi}_{21} X_{21} - \mu_{21} X_{21} \quad (\text{A.17})$$

$$\frac{dX_{22}}{dt} = -\omega_{pv} X_{22} + pv_{21} X_{21} + (1 - \phi_{12}) \theta_{12} X_{12} - \theta_{22} X_{22} - \hat{\phi}_{22} X_{22} - \mu_{22} X_{22} \quad (\text{A.18})$$

$$\frac{dX_{23}}{dt} = \omega_{pv} X_{24} - pv_{23} X_{23} + (1 - \phi_{13}) \theta_{13} X_{13} - \theta_{23} X_{23} - \hat{\phi}_{23} X_{23} - \mu_{23} X_{23} \quad (\text{A.19})$$

$$\frac{dX_{24}}{dt} = -\omega_{pv} X_{24} + pv_{23} X_{23} + (1 - \phi_{14}) \theta_{14} X_{14} - \theta_{24} X_{24} - \hat{\phi}_{24} X_{24} - \mu_{24} X_{24} \quad (\text{A.20})$$

$$\frac{dX_{31}}{dt} = \omega_{pv} X_{32} - pv_{31} X_{31} + \phi_{11} \theta_{11} X_{11} + \hat{\phi}_{21} X_{21} - \theta_{31} X_{31} - \mu_{31} X_{31} \quad (\text{A.21})$$

$$\frac{dX_{32}}{dt} = -\omega_{pv} X_{32} + pv_{31} X_{31} + \phi_{12} \theta_{12} X_{12} + \hat{\phi}_{22} X_{22} - \theta_{32} X_{32} - \mu_{32} X_{32} \quad (\text{A.22})$$

$$\frac{dX_{33}}{dt} = \omega_{pv} X_{34} - pv_{33} X_{33} + \phi_{13} \theta_{13} X_{13} + \hat{\phi}_{23} X_{23} - \theta_{33} X_{33} - \mu_{33} X_{33} \quad (\text{A.23})$$

$$\frac{dX_{34}}{dt} = -\omega_{pv} X_{34} + pv_{33} X_{33} + \phi_{14} \theta_{14} X_{14} + \hat{\phi}_{24} X_{24} - \theta_{34} X_{34} - \mu_{34} X_{34} \quad (\text{A.24})$$

$$\frac{dX_{41}}{dt} = \omega_{pv} X_{42} - pv_{41} X_{41} + \theta_{21} X_{21} - \hat{\phi}_{41} X_{41} - \mu_{41} X_{41} \quad (\text{A.25})$$

$$\frac{dX_{42}}{dt} = -\omega_{pv} X_{42} + pv_{41} X_{41} + \theta_{22} X_{22} - \hat{\phi}_{42} X_{42} - \mu_{42} X_{42} \quad (\text{A.26})$$

$$\frac{dX_{43}}{dt} = \omega_{pv} X_{43} - pv_{43} X_{43} + \theta_{23} X_{23} - \hat{\phi}_{43} X_{43} - \mu_{43} X_{43} \quad (\text{A.27})$$

$$\frac{dX_{44}}{dt} = -\omega_{pv} X_{44} + pv_{43} X_{43} + \theta_{24} X_{24} - \hat{\phi}_{44} X_{44} - \mu_{44} X_{44} \quad (\text{A.28})$$

$$\frac{dX_{51}}{dt} = \omega_{pv} X_{52} - pv_{51} X_{51} + \theta_{31} X_{31} + \hat{\phi}_{41} X_{41} - \mu_{51} X_{51} \quad (\text{A.29})$$

$$\frac{dX_{52}}{dt} = -\omega_{pv} X_{52} + pv_{51} X_{51} + \theta_{32} X_{32} + \hat{\phi}_{42} X_{42} - \mu_{52} X_{52} \quad (\text{A.30})$$

$$\frac{dX_{53}}{dt} = \omega_{pv} X_{54} - pv_{53} X_{53} + \theta_{33} X_{33} + \hat{\phi}_{43} X_{43} - \mu_{53} X_{53} \quad (\text{A.31})$$

$$\frac{dX_{54}}{dt} = -\omega_{pv} X_{54} + pv_{53} X_{53} + \theta_{34} X_{34} + \hat{\phi}_{44} X_{44} - \mu_{54} X_{54} \quad (\text{A.32})$$

Model Instantiation

We instantiated the system of nonlinear differential equations (A.9-A.32) with initial conditions using 2007 data on population sizes and HIV prevalence levels among each risk group. We divided the HIV-infected population into the three health states (asymptomatic HIV, symptomatic HIV, AIDS) in proportion to the average time spent in each state. We then adjusted the fraction of individuals in each state to account for the increase in life expectancy among individuals with symptomatic HIV and AIDS who are receiving antiretroviral therapy. We also estimated the fraction of men who are circumcised and we assumed this remained constant over the duration of the model's time horizon. For the preventive vaccination scenarios, we assumed some fraction of the population is initially vaccinated (i.e., the vaccination coverage).

Model Outcomes

We numerically solved the system of nonlinear differential equations to calculate the number of individuals in each compartment over time. We then calculated the following outcome measures: HIV prevalence, new HIV infections, discounted costs and health benefits (quality-adjusted life years experienced), and incremental cost-effectiveness ratios.

We calculated HIV prevalence for each of the six risk groups (male IDU, male MSM, male IDU/MSM, male other, female IDU, female other) as follows:

$$\text{HIV prevalence at time } t = \frac{\sum_{i \geq 11} X_i(t)}{\sum_{\forall i} X_i(t)} \quad (\text{A.33})$$

We calculated the (undiscounted) number of new HIV infections that occur in the entire population over the time horizon, T .

$$\text{New HIV infections} = \int_0^T \sum_{i \leq 4} \sum_{j \geq 11} \lambda_{i,j}(t) X_i(t) dt \quad (\text{A.34})$$

Total health benefits for the entire population were measured in discounted quality-adjusted life years (QALYs). We assumed an infinite time horizon to account for health benefits occurring after the intervention duration.

$$\text{QALYs} = \int_0^\infty e^{-rt} \sum_{\forall i} q_i X_i(t) dt \quad (\text{A.35})$$

Total discounted costs for the entire population were calculated as the sum of annual healthcare costs for all individuals, and total vaccination costs over the intervention's duration.

$$\text{Costs} = \int_0^\infty e^{-rt} \sum_{\forall i} c_i X_i(t) dt + \int_0^T e^{-rt} \sum_{i \leq 4} c_{pv} p v_i X_i(t) dt \quad (\text{A.36})$$

Finally, we calculated the incremental cost-effectiveness ratio (ICER) of all vaccination strategies, relative to the status quo (where no one is vaccinated).

$$\text{ICER} = \frac{\text{Costs}_{VaccineStrategy} - \text{Costs}_{StatusQuo}}{\text{QALY}_{VaccineStrategy} - \text{QALY}_{StatusQuo}} \quad (\text{A.37})$$

In some cases, we also calculated the ICER of one vaccination strategy relative to another (e.g., universal vaccination relative to targeted vaccination of high-risk groups).

Figure A-1: Schematic diagram of compartmental model

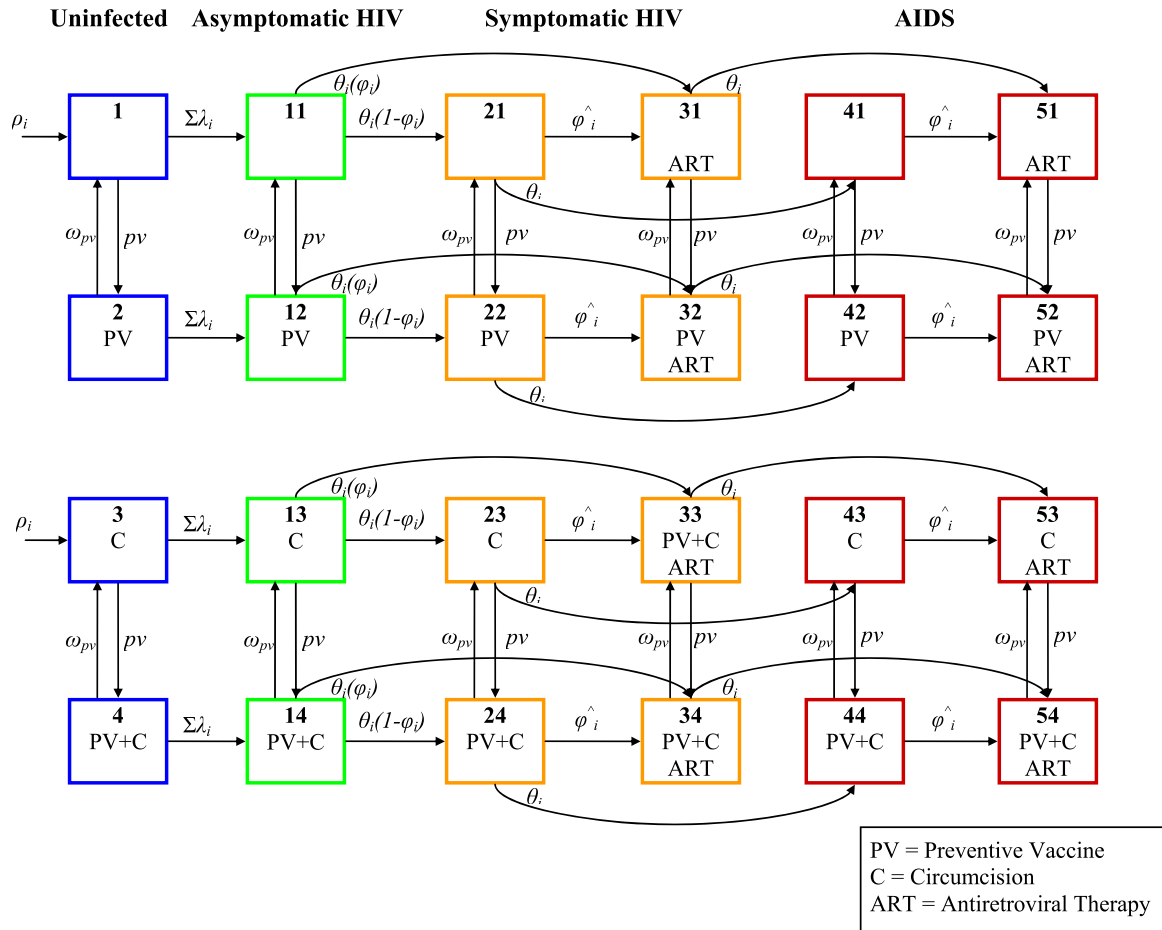


Table A-1: Dynamic compartmental model variables

Variable	Description
Population Variables	
$X_i(t)$	Number of people in compartment i at time t
Demographic Parameters	
ρ_i	Entry rate of individuals into compartment i
μ_i	Mortality and maturation rate for individuals in compartment i
r	Annual discount rate
Disease Parameters	
θ_i	HIV disease progression rate for individuals in compartment i
c_i	Annual healthcare cost for individuals in compartment i
q_i	Quality-of-life adjustment for individuals in compartment i
Preventive Vaccine Parameters	
pv_i	Preventive vaccination rate for individuals in compartment i
$1/\omega_{pv}$	Average duration of preventive vaccine
ϵ_{pv}	Preventive vaccine efficacy in reducing HIV acquisition in uninfected individuals
δ_{pv}^s	Preventive vaccine efficacy in reducing sexual infectivity in infected individuals
δ_{pv}^d	Preventive vaccine efficacy in reducing drug injection infectivity in infected individuals
p_{pv}	Change in number of sexual partners due to preventive vaccination
c_{pv}	Cost of preventive vaccine
Circumcision Parameters	
ϵ_c	Circumcision efficacy in reducing HIV acquisition in uninfected individuals
δ_c^s	Circumcision efficacy in reducing sexual infectivity in infected individuals
Treatment Parameters	
ϕ_i	Fraction of individuals from compartment i who begin HAART at CD4=350 cells/mm ³

Variable	Description
$\hat{\phi}_i$	Rate of individuals from compartment i who begin HAART at $CD4 < 350$ cells/mm ³
δ_h^s	HAART efficacy in reducing sexual infectivity in infected individuals
δ_h^d	HAART efficacy in reducing drug injection infectivity in infected individuals

Injection Drug Use Parameters

d_i	Average number of drug injections per year by individuals in compartment i
s_i	Fraction of shared drug injections by individuals in compartment i
$\tau_{i,j}$	Probability of infection transmission per shared injection between an uninfected individual in compartment i and an infected individual in compartment j
π^k	Probability of infection transmission per shared injection between an uninfected individual and an individual with HIV status k , where $k = asym$ (asymptomatic HIV), sym (symptomatic HIV), $aids$ (AIDS)

Sexual Behavior Parameters

n_i^s	Average number of same-sex sexual partners per year by individuals in compartment i
n_i^o	Average number of opposite-sex sexual partners per year by individuals in compartment i
u_i^s	Condom usage among same-sex sexual partnerships by individuals in compartment i
u_i^o	Condom usage among opposite-sex sexual partnerships by individuals in compartment i
κ	Condom effectiveness in reducing HIV transmission
$\sigma_{i,j}$	Annual probability of infection transmission per unprotected sexual partnership between an uninfected individual in compartment i and an infected individual in compartment j
π_{mf}^k	Annual probability of infection transmission per unprotected sexual partnership between an uninfected male and a female with HIV status k , where $k = asym$ (asymptomatic HIV), sym (symptomatic HIV), $aids$ (AIDS)
π_{fm}^k	Annual probability of infection transmission per unprotected sexual partnership between an uninfected female and a male with HIV status k , where $k = asym$ (asymptomatic HIV), sym (symptomatic HIV), $aids$ (AIDS)
π_{mm}^k	Annual probability of infection transmission per unprotected sexual partnership between an uninfected male and a male with HIV status k , where $k = asym$ (asymptomatic HIV), sym (symptomatic HIV), $aids$ (AIDS)

Variable	Description
Transmission Variables	
$\lambda_{i,j}(t)$	Total sufficient contact rate at time t between uninfected members of compartment i and infected members of compartment j
$\gamma_{i,j}(t)$	Sufficient contact rate at time t between uninfected members of compartment i and infected members of compartment j due to drug injection (needle-sharing)
$\beta_{i,j}^s(t)$	Sufficient contact rate at time t between uninfected members of compartment i and infected members of compartment j due to same-sex (homosexual) partnerships
$\beta_{i,j}^o(t)$	Sufficient contact rate at time t between uninfected members of compartment i and infected members of compartment j due to opposite-sex (heterosexual) partnerships
