Supplementary Materials

The Necessity of Including Transgender Populations in Mathematical Models for HIV Treatment and Prevention: Current Barriers and Policy Implications

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1. Model Description and Parameterization

Model Description

We developed a deterministic compartmental mathematical model using ordinary differential equations (ODEs) to simulate HIV transmission among TNB people and their sex partners in the US, and assess the benefits of increased HIV prevention utilization. The model structure was developed with input from the Seattle Trans and Non-binary Sexual Health (STARS) Advisory Board, comprised of nine TNB individuals from the Seattle area who met bimonthly between February 2021 and July 2022.

The individuals in the simulated population were divided into seven demographic groups: transgender women, transgender men, non-binary people assigned male at birth (AMAB), non-binary people assigned female at birth (AFAB), sexual minority cisgender men, sexual minority cisgender women, and heterosexual cisgender men. We chose to disaggregate non-binary people by their sex assigned at birth due to prior research demonstrating differences in the epidemiology of HIV/STIs among non-binary people by sex assigned at birth.[1]

The model assumed that sexual partnerships occurred between all demographic groups, except that heterosexual cisgender men only partnered with transgender and cisgender women. To minimize model complexity, we chose to model first degree partnerships (e.g., TNB people and their partners), but not second-degree partnerships (e.g., the partners of the partners of TNB people) with demographic groups not already included in our model. Specifically, the model excludes heterosexual cisgender women since data suggest that >99% of cisgender women who partner with transgender people identity as lesbian, gay, bisexual, pansexual or queer.[2] However, this means our model does not account for HIV transmission patterns between cisgender men and heterosexual cisgender women. In addition to being stratified by gender identity and sexual minority status, the model was further stratified by the likelihood of HIV acquisition (e.g., higher or lower). We assumed assortative mixing among groups defined by higher/lower likelihood of HIV acquisition.

HIV-negative individuals were stratified by current PrEP use. People living with HIV were stratified by HIV stage (acute, chronic, AIDS) and by stage of HIV care engagement (undiagnosed, diagnosed and not on ART, on ART but not virally suppressed, and virally suppressed; Figure 4.1). The rates at which simulated individuals acquire HIV depends on the annual number of partners per person, sex acts per partnership, the fraction of sex acts protected by condoms and PrEP, and the HIV transmission probability per sex act with an HIV-positive partner. Complete model description including model equations is provided in Appendix D.

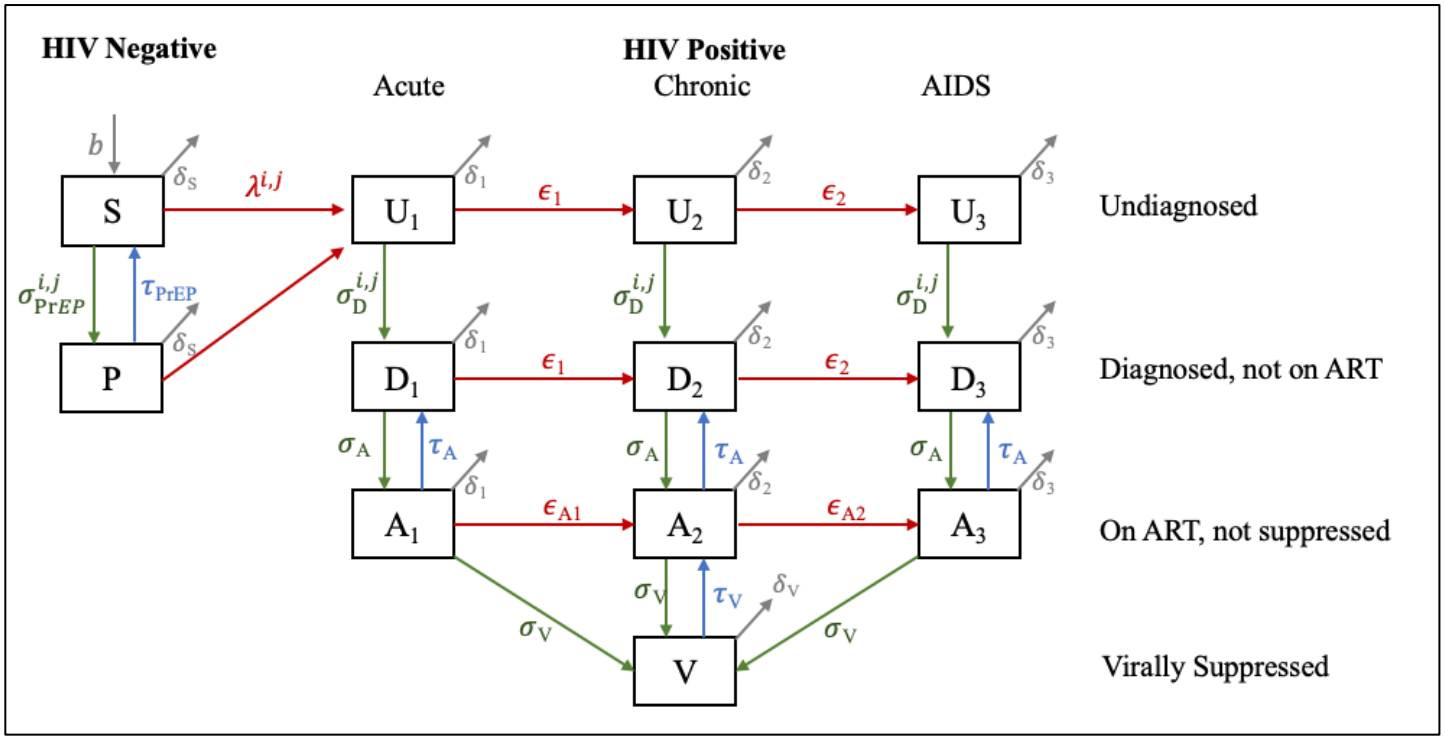

Figure 1. Model Schematic. *Progression along disease stages is indicated with horizontal (red) arrows and progression through HIV care engagement indicated with vertical (green and blue) arrows.*

Mathematical Formulae

Our model is described by a system of 168 ordinary differential equations (12 compartments for disease stage and engagement in care x 7 demographic groups x 2 groups defined by higher/lower likelihood of HIV acquisition).

We used the following indexing to represent:

- Demographic group $i \in$ {1 (trans women), 2 (trans men), 3 (non-binary AMAB), 4 (non-binary AFAB), 5 (sexual minority cis men), 6 (sexual minority cis women), 7 (heterosexual cis men)}
- Higher/lower likelihood of HIV acquisition $j \in$ {1 (lower), 2 (higher)}
- Disease stage $k \in$ {1 (acute), 2 (chronic), 3 (AIDS)}

The simulated population is stratified into the following compartment (see Figure 1):

- $S^{i,j}$: HIV-negative (i.e. susceptible) population not currently using PrEP in demographic group i and strata j
- $P^{i,j}$: HIV-negative (i.e. susceptible) population currently using PrEP in demographic group i and strata j
- $U_k^{i,j}$: Undiagnosed HIV-positive population in demographic group i, strata j, and disease stage k
- $D_k^{i,j}$: Diagnosed HIV-positive population not on ART in demographic group i, strata j, and disease stage k
- $A_k^{i,j}$: HIV-positive population on ART but not virally suppressed in demographic group i, strata j, and disease stage k
- $V^{i,j}$: HIV-positive population who are virally suppressed in demographic group i and strata j
- $N^{i,j}$: Total population in demographic group i and strata j

Model parameters include:

- ϵ: progression along disease stages (horizontal arrows in Figure 1)
  - ϵ_1: acute to chronic among those not on ART
  - ϵ_2: chronic to AIDS among those not on ART
  - ϵ_{A1}: acute to chronic among those on ART
  - ϵ_{A2}: chronic to AIDS among those on ART
- σ: progression through engagement with care (vertical arrows)
  - $\sigma_{\mathrm{PrEP}}^{i,j}$: rate of PrEP initiation in demographic group i and strata j
  - $\sigma_{\mathrm{D}}^{i,j}$: rate of diagnosis via HIV testing in demographic group i and strata j
  - σ_{A}^{i}: rate of ART initiation in demographic group i
  - σ_{V}: rate of viral suppression
- τ: drop rate/discontinuation from engagement with care
  - $\tau_{\mathrm{PrEP}}^{i,j}$: PrEP discontinuation rate in demographic group i and strata j
  - τ_{A}^{i}: ART discontinuation rate in demographic group i
  - τ_{V}: drop from virally suppression
- b: "birth" rate of entering population
- δ: death rates
  - δ_{S}: death rate among HIV-negative population
  - δ_{k}: death rate among HIV-positive population by disease stage k
  - δ_{V}: death rate among virally suppressed HIV-positive population
- α_{PrEP}: PrEP efficacy per sex act
- $\alpha_{condoms}$: condom efficacy per sex act
- α_{ART}: ART efficacy in reducing infectiousness per sex act when not virally suppressed
- $m^{ij,uv}$: probability of demographic group i and strata j partnering with demographic group u and strata v (from mixing matrix)
- $\eta^{i,j}$: average annual number of sex partners for demographic group i and strata j
- n^{ij}: average number of sex acts per partnership per year for demographic group i and strata j
- c^{ij}: proportion of sex acts using a condom for demographic group i and strata j
- β: HIV transmission probability per sex act
- β_k: multiplier for increased per sex act transmission probability by disease stage k
- θ_k: multiplier for reduced sexual activity with AIDS

We define the force of infection, $\lambda^{i,j}$, for demographic group i and strata j as:

$$\lambda^{i,j} = \eta^{i,j}\, n^{ij}\, (1 - c^{ij}\alpha_{condoms}) \sum_{u,v} m^{ij,uv} \times \left(\sum_{k=1,2,3} \theta_k \beta_k \beta \frac{\left(\mathrm{U}_{\mathrm{k}}^{\mathrm{u},v} + \mathrm{D}_{\mathrm{k}}^{\mathrm{u},v}\right)}{N^{u,v}} + (1 - \alpha_{ART})\, \beta_k \beta \frac{\mathrm{A}_{\mathrm{k}}^{\mathrm{u},v}}{N^{u,v}} \right)$$

The model is defined by the following equations:

- HIV Negative:

$$\frac{dS^{i,j}}{dt} = bN^{i,j} + \left(-\sigma_{PrEP}^{i,j} - \lambda^{i,j} - \delta_S\right)S^{i,j} + \tau_{PrEP}P^{i,j}$$

$$\frac{dP^{i,j}}{dt} = \left(-\tau_{PrEP} - (1 - \alpha_{PrEP})\lambda^{i,j} - \delta_S\right)P^{i,j} + \sigma_{PrEP}^{i,j}S^{i,j}$$

- Acute HIV:

$$\frac{dU_1^{i,j}}{dt} = \left(-\sigma_D^{i,j} - \epsilon_1 - \delta_1\right)U_1^{i,j} + \lambda^{i,j}S^{i,j} + (1 - \alpha_{PrEP})\lambda^{i,j}P^{i,j}$$

$$\frac{\mathrm{d}D_1^{\mathrm{i,j}}}{\mathrm{dt}} = \left(-\sigma_{\mathrm{A}}^{i} - \epsilon_1 - \delta_1\right)\mathrm{D}_1^{\mathrm{i,j}} + \sigma_D^{i,j}\mathrm{U}_1^{\mathrm{i,j}} + \tau_{\mathrm{A}}^{i}\mathrm{A}_1^{\mathrm{i,j}}$$

$$\frac{\mathrm{d}A_1^{\mathrm{i,j}}}{\mathrm{dt}} = \left(-\sigma_V - \epsilon_{A1} - \tau_{\mathrm{A}}^{i} - \delta_{A1}\right)\mathrm{A}_1^{\mathrm{i,j}} + \sigma_{\mathrm{A}}^{i}\mathrm{D}_1^{\mathrm{i,j}}$$

- Chronic HIV:

$$\frac{\mathrm{dU}_2^{\mathrm{i,j}}}{\mathrm{dt}} = \left(-\sigma_D^{i,j} - \epsilon_2 - \delta_2\right)\mathrm{U}_2^{\mathrm{i,j}} + \epsilon_1\mathrm{U}_1^{\mathrm{i,j}}$$

$$\frac{\mathrm{d}D_2^{\mathrm{i,j}}}{\mathrm{dt}} = \left(-\sigma_{\mathrm{A}}^{i} - \epsilon_2 - \delta_2\right)\mathrm{D}_2^{\mathrm{i,j}} + \sigma_D^{i,j}\mathrm{U}_2^{\mathrm{i,j}} + \tau_{\mathrm{A}}^{i}\mathrm{A}_2^{\mathrm{i,j}} + \epsilon_1\mathrm{D}_1^{\mathrm{i,j}}$$

$$\frac{\mathrm{d}A_2^{\mathrm{i,j}}}{\mathrm{dt}} = \left(-\sigma_V - \epsilon_{A2} - \tau_{\mathrm{A}}^{i} - \delta_{A2}\right)\mathrm{A}_2^{\mathrm{i,j}} + \sigma_{\mathrm{A}}^{i}\mathrm{D}_2^{\mathrm{i,j}} + \tau_V V^{i,j} + \epsilon_{A1}\mathrm{A}_1^{\mathrm{i,j}}$$

- AIDS:

$$\frac{\mathrm{dU}_3^{\mathrm{i,j}}}{\mathrm{dt}} = \left(-\sigma_D^{i,j} - \delta_3\right)\mathrm{U}_3^{\mathrm{i,j}} + \epsilon_2\mathrm{U}_2^{\mathrm{i,j}}$$

$$\frac{\mathrm{d}D_3^{\mathrm{i,j}}}{\mathrm{dt}} = \left(-\sigma_{\mathrm{A}}^{i} - \delta_3\right)\mathrm{D}_3^{\mathrm{i,j}} + \sigma_D^{i,j}\mathrm{U}_3^{\mathrm{i,j}} + \tau_{\mathrm{A}}^{i}\mathrm{A}_3^{\mathrm{i,j}} + \epsilon_2\mathrm{D}_2^{\mathrm{i,j}}$$

$$\frac{\mathrm{d}A_3^{\mathrm{i,j}}}{\mathrm{dt}} = \left(-\sigma_V - \tau_{\mathrm{A}}^{i} - \delta_{A3}\right)\mathrm{A}_3^{\mathrm{i,j}} + \sigma_{\mathrm{A}}^{i}\mathrm{D}_3^{\mathrm{i,j}} + \epsilon_{A2}\mathrm{A}_2^{\mathrm{i,j}}$$

- Virally Suppressed:

$$\frac{dV^{i,j}}{\mathrm{dt}} = (-\tau_V - \delta_V)V^{i,j} + \sigma_V(\mathrm{A}_1^{\mathrm{i,j}} + \mathrm{A}_2^{\mathrm{i,j}} + \mathrm{A}_3^{\mathrm{i,j}})$$

Model Parameterization

The model was parameterized using data from the CDC's National HIV Surveillance reports, population-based surveys, meta-analyses, and local epidemiological studies from Seattle, Washington. Since the model begins in 2014, initial conditions for the proportion of HIV-positive individuals who had acute HIV, chronic HIV, or AIDS were based on 2014 data from the CDC's National HIV Surveillance reports. Initial conditions for the proportion of individuals at each stage of the HIV care continuum were based on meta-analysis[3] and data from the National HIV Surveillance System.

Data on the proportion of people in each demographic group who have an increased likelihood of HIV acquisition were estimated using pooled 2016-2020 data from the BRFSS, which asks participants if they had experienced any of the following in the past year: injection drug use, treated for an STI, or given or received money or drugs in exchange for sex. This proportion ranged from 8.4% among trans men to 29.8% among sexual minority cis men. We similarly obtained BRFSS estimates of the proportion of individuals who tested for HIV in the past year for each demographic group stratified by higher/lower likelihood of HIV acquisition. Annual HIV testing ranged from 9.0%-22.0% among individuals with a lower likelihood of HIV acquisition and ranged from 27.4%-59.2% among individuals with a higher likelihood of HIV acquisition.

Lastly, the probabilities for sexual partnerships between all demographic groups is based on 2019-2021 data collected from participants living in Seattle and Washington State (see Chapter 3). A complete list of fixed and calibration parameters are provided in the Supplement.

Table 1. Fixed Parameters

Description	Demographic Group	Value	Source
Population Size	Trans Women	124,246	Back-calculated based on HIV prevalence reported in TransPop study and CDC HIV surveillance Data.[4] Note these are much lower than recent estimates of the size of the transgender population in the US.[5]
Population Size	Trans Men	35250	
Population Size	Non-binary AMAB	4,453	
Population Size	Non-binary AFAB		
Population Size	Sexual Minority Cis Men	4,000,000	3.5% of US male adults age 18-64[6]
Population Size	Sexual Minority Cis Women	4,000,000	3.5% of US female adults age 18-64[6]
Population Size	Heterosexual Cis Men	200,000	0.2% of heterosexual cis men age 18-64[6] and Chapter 3
Fraction of Population with higher likelihood of HIV acquisition	Trans Women	13.7%	BRFSS 2016-20 data
Fraction of Population with higher likelihood of HIV acquisition	Trans Men	8.4%	BRFSS 2016-20 data
Fraction of Population with higher likelihood of HIV acquisition	Non-binary AMAB	23.1%	BRFSS 2016-20 data
Fraction of Population with higher likelihood of HIV acquisition	Non-binary AFAB	14.1%	BRFSS 2016-20 data
Fraction of Population with higher likelihood of HIV acquisition	Sexual Minority Cis Men	29.8%	BRFSS 2016-20 data
Fraction of Population with higher likelihood of HIV acquisition	Sexual Minority Cis Women	16.0%	BRFSS 2016-20 data
Fraction of Population with higher likelihood of HIV acquisition	Heterosexual Cis Men	29.8%	BRFSS 2016-20 data
"Birth" rate	All Groups	0.012	Average US birth rate in 2014-2019
Death rate among HIV-negative	All Groups	0.0025	Average US Death rate, age 15-64
Death rate among acute HIV	All Groups	0.012	[7,8]

Death rate among chronic HIV	All Groups	0.012	[7,8]
Death rate among AIDS	All Groups	0.022	[7]
Death rate among virally suppressed	All Groups	0.0025	Assume same as HIV-negative individuals
Initial Conditions, HIV prevalence (%)	Transgender Women	6.5%	[4]
Initial Conditions, HIV prevalence (%)	Transgender Men	0.8%	[4]
Initial Conditions, HIV prevalence (%)	Non-binary AMAB	5.1%	[4]
Initial Conditions, HIV prevalence (%)	Non-binary AFAB	0.2%	[9]
Initial Conditions, HIV prevalence (N)	Transgender Women	8076	[10]
Initial Conditions, HIV prevalence (N)	Transgender Men	282	[10]
Initial Conditions, HIV prevalence (N)	Non-binary	118	[10]
Initial Conditions, HIV prevalence (N)	Sexual Minority Cis Men	470000	[10]
Initial Conditions, Undiagnosed Fraction	All Groups	15%	[11,12]
Initial Conditions, Proportion of Diagnoses at Acute stage	All Groups	5%	[10]
Initial Conditions, Proportion of Diagnoses at Chronic stage	All Groups	75%	[10]
Initial Conditions, Proportion of Diagnoses at AIDS	All Groups	20%	[10]
Initial Conditions, Proportion of Diagnosed People on ART	All TNB	70%	[3,9,13,14]
Initial Conditions, Proportion of Diagnosed People on ART	Sexual Minority Cis Men	74%	[15]
Initial Conditions, Proportion of Diagnosed People on ART	Sexual Minority Cis Women	73%	[15]
Initial Conditions, Proportion of Diagnosed People on ART	Heterosexual Cis Men	68%	[15]
Initial Conditions, Proportion of Diagnosed People who are Virally Suppressed	All TNB	60%	[3,13–16]
Initial Conditions, Proportion of Diagnosed People who are Virally Suppressed	Sexual Minority Cis Men	60%	[15]
Initial Conditions, Proportion of Diagnosed People who are Virally Suppressed	Sexual Minority Cis Women	55%	[15]
Initial Conditions, Proportion of Diagnosed People who are Virally Suppressed	Heterosexual Cis Men	55%	[15]
Multiplier for increased per act transmission risk for acute stage	All groups	10	[17–19]
Multiplier for increased per act transmission risk for AIDS	All groups	5	[17–19]

Key Model Assumptions

We assumed that the initial number of TNB people diagnosed and living with HIV reported in CDC's HIV Surveillance reports in 2014 (i.e., 8076 transgender women, 282 transgender men, and 118 non-binary people) was accurate and corresponded with the self-reported HIV positivity reported in the TransPop Study (6.5%, 0.8%, and 5.1% respectively).[4] From this assumption, we back-calculated the total TNB population size to be approximately 164,000. Notably, this is 8-fold smaller than recent estimates that at least 1.3 million TNB adults currently live in the US.[5] This is likely an artifact of the significant underreporting of prevalent HIV diagnoses among TNB people in HIV surveillance data.

We also assumed that 75% of HIV diagnoses occurred among individuals with a higher likelihood of acquiring HIV. This assumption allowed for the HIV prevalence among individuals with a higher likelihood of acquiring HIV to approximate the HIV prevalence reported in recent meta-analyses based on convenience and clinical samples: approximately 19% among transgender women and 3% among transgender men.[20] Lastly, we did not differentiate between sexual role (i.e., insertive/receptive anal or vaginal/front hole sex). We instead parameterize the model based on an average transmission probability per sex act.

2. Model Calibration

We calibrated the model starting in 2014 and ending in 2020 by fitting the model outputs to data on HIV prevalence and the HIV care cascade for each demographic group (Table 4.1). We used count data on the number of prevalent HIV diagnoses reported in the CDC's National HIV surveillance report from 2015-2020, which are based on laboratory testing; however, as discussed in the primary text, these data are likely an undercount due to the misclassification of TNB people in the National HIV Surveillance Database. For the HIV care cascade, we used 2018-2020 data on viral suppression as well as data on engagement in care from the CDC's National HIV surveillance report as a proxy for current ART use.

Table 2. Calibration targets

Target	Description	Source	Demographic Group	Value/Range
HIV Prevalence (Counts)	Number of prevalence HIV diagnoses; time series of 5 years	National HIV Surveillance Data, 2018-2020	Trans Women	10,507 – 11,949
			Trans Men	419 - 509
			Non-binary People	182 - 243
			Sexual minority cis men	574,555 – 599,433
On ART (%)	Percent who received any HIV care[1] as a proxy for receipt of ART	National HIV Surveillance Data, 2018-2020	Trans Women	83.7 – 84.4%
			Trans Men	87.1 – 85.4%
			Non-binary People	85.7 – 88.8%
			Sexual minority cis men	77.3 – 77.7%
			Sexual minority cis women[2]	75.5 – 78.8%
			Heterosexual cis men	71.1 – 71.3%
Viral Suppression (%)	Percent of diagnosed people living with HIV who are virally suppressed; 2 years of data	National HIV Surveillance Data, 2018-2020	Trans Women	64.5 – 67.0%
			Trans Men	68.3 - 71.5%
			Non-binary People	68.7 – 70.6%
			Sexual minority cis men	67.3 – 68.1%
			Sexual minority cis women[2]	63.0 – 63.1%
			Heterosexual cis men	59.8 – 64.4%
PrEP Use (%)	Percent of HIV-negative people currently using PrEP, 2019	Chapter 3	Trans Women	20%
			Trans Men	10%
			Non-binary People AMAB	30%
			Non-binary People AFAB	8%
			Sexual minority cis men	35%
			Sexual minority cis women[2]	2%
			Heterosexual cis men	15%

[1]Defined as having at least 1 CD4 or viral load test

[2]CDC does not disaggregate data specifically for sexual minority cis women. Therefore, we are using the overall rates of ART use and Viral Suppression among cisgender women overall.

We use a Bayesian Markov chain Monte Carlo (MCMC) framework to calibrate our model to the calibration targets described above. Bayesian frameworks enable us to update a *prior* probability distribution for a parameter, $p(\theta)$, using new data (referred to as the *likelihood*, or $p(Y|\theta)$)[21] to obtain a *posterior* distribution, $p(\theta|Y)$. This relationship can be mathematically expressed as $p(\theta|Y) \propto p(\theta) \times p(Y|\theta)$. Bayesian calibration methods thus allow us to combine three different sources of information and uncertainty: uncertainty in model parameters (e.g. by specifying *priors* for each calibration parameter), model outcomes (e.g. the *likelihood* of HIV prevalence and other calibration targets), and structural assumptions incorporated into our ODE-based mathematical model.[22] For calibration parameters, we defined priors using a uniform distribution of plausible ranges informed by the literature. We defined the likelihood using a weighted normal probability density function. We fit the model to calibration targets using 100,000 iterations to ensure MCMC convergence.

We conducted model calibration in two steps. First, we calibrated the prevalence of current PrEP use within the HIV-negative simulated population to obtain estimates of PrEP initiation and discontinuation for each demographic strata. We assumed that people with a higher likelihood of HIV acquisition were also more likely to be on PrEP than people with

a lower likelihood of HIV acquisition. The resulting posterior distributions were then used as the priors in the full calibration model where we calibrate our model to HIV prevalence and the treatment cascade. After the second calibration step, we chose the best fit parameters as the maximum a posteriori (MAP), or the mode of the posterior distribution for each parameter. We then consider 100 random draws from the posterior parameter space to quantify model uncertainty. Calibration results are presented in Figure 4.2.

Table 3. Calibration Parameters

Description	**Demographic Group**	**Range**	**Source**
HIV transmission probability per sex act (for vaginal sex or insertive anal sex)	All groups	0.001 – 0.01	[23,24]
Disease Progression from acute to chronic among individuals not on ART	Same for all groups	1/0.25 – 1/0.125 (equivalent to a duration of 1.8-3 months)	
Disease Progression from chronic to AIDS among individuals not on ART	Same for all groups	1/10 – 1/6 (equivalent to a duration of 6-10 years)	
Disease Progression from acute to chronic among individuals on ART	Same for all groups	1/0.25 – 1/0.125 (equivalent to a duration of 1.5-3 months)	
Disease Progression from chronic to AIDS among individuals on ART	Same for all groups	1/40 – 1/10 (equivalent to a duration of 10-40 years)	
PrEP initiation	Varies by demographic group	0.001 – 0.25	
ART initiation	Varies by demographic group	1-3	
Rate of Viral Suppression	Same for all groups	1-10	
PrEP discontinuation	Varies by demographic group	0.001 – 0.1	
ART discontinuation	Varies by demographic group	0.1 – 0.3	
Drop rate for viral suppression	Same for all groups	0.01 – 0.1	
Annual HIV Testing/ Diagnosis	Trans Women, higher likelihood of HIV acquisition	36.8% - 50.6%	BRFSS 2016-20 data
Annual HIV Testing/ Diagnosis	Trans Men, higher likelihood of HIV acquisition	30.1% - 49.1%	BRFSS 2016-20 data
Annual HIV Testing/ Diagnosis	Non-binary AMAB, higher likelihood of HIV acquisition	31.7% - 46.4%	BRFSS 2016-20 data
Annual HIV Testing/ Diagnosis	Non-binary AFAB, higher likelihood of HIV acquisition	31.7% - 46.4%	BRFSS 2016-20 data
Annual HIV Testing/ Diagnosis	Sexual Minority Cis Men, higher likelihood of HIV acquisition	56.5% - 61.8%	BRFSS 2016-20 data

Annual HIV Testing/ Diagnosis	Sexual Minority Cis Women, higher likelihood of HIV acquisition	37.8% - 44.8%	BRFSS 2016-20 data
Annual HIV Testing/ Diagnosis	Heterosexual Cis Men, higher likelihood of HIV acquisition	26.0% - 28.8%	BRFSS 2016-20 data
Annual HIV Testing/ Diagnosis	Trans Women, lower likelihood of HIV acquisition	9.7% - 13.2%	BRFSS 2016-20 data
Annual HIV Testing/ Diagnosis	Trans Men, lower likelihood of HIV acquisition	9.5% - 13.2%	BRFSS 2016-20 data
Annual HIV Testing/ Diagnosis	Non-binary AMAB, lower likelihood of HIV acquisition	10.1% - 14.9%	BRFSS 2016-20 data
Annual HIV Testing/ Diagnosis	Non-binary AFAB, lower likelihood of HIV acquisition	10.1% - 14.9%	BRFSS 2016-20 data
Annual HIV Testing/ Diagnosis	Sexual Minority Cis Men, lower likelihood of HIV acquisition	20.5% - 23.5%	BRFSS 2016-20 data
Annual HIV Testing/ Diagnosis	Sexual Minority Cis Women, lower likelihood of HIV acquisition	17.0% - 19.4%	BRFSS 2016-20 data
Annual HIV Testing/ Diagnosis	Heterosexual Cis Men, lower likelihood of HIV acquisition	8.7% - 9.2%	BRFSS 2016-20 data
Reduction in transmissibility associated with being on ART but not virally suppressed	Same for all groups	50% - 70%	
Efficacy of condoms in preventing HIV transmission	Same for all groups	70% – 80%	
Efficacy of PrEP preventing HIV transmission	Same for all groups	90% – 95%	
Multiplier for reduced sexual activity during AIDS		0.2 – 0.5	
Annual number of partners	Lower likelihood of HIV acquisition (Varies by demographic group)	1 –2	
Annual number of partners	Higher likelihood of HIV acquisition (Varies by demographic group)	30 – 50	[20]
Number of sex acts per partnership per year	Lower likelihood of HIV acquisition (Varies by demographic group)	20 – 40	
Number of sex acts per partnership per year	Higher likelihood of HIV acquisition (Varies by demographic group)	1 – 5	
Proportion of sex acts using a condom	Lower likelihood of HIV acquisition (Varies by demographic group)	0.4 – 0.7	[20,25]
Proportion of sex acts using a condom	Higher likelihood of HIV acquisition (Varies by demographic group)	0.4 – 0.7	[20,25]

Assortative mixing by higher/lower likelihood of HIV acquisition	Same for all groups	0.7 – 0.95	

3. Interventions and Simulation Approach

Simulations

The calibrated model was used to simulate the HIV epidemic from 2020-2030 under the current standard of care to provide a reference scenario for evaluating the impact of each intervention scenario. We consider a range of different intervention scenarios for TNB people. First we consider the impact of increasing the rate of HIV testing (i.e., $\sigma_{\mathrm{D}}^{i,j}$, see Figure 4.1) alone by 10%, 25%, 50%, 75% and 100%; the impact of increasing the rate of PrEP uptake (i.e., $\sigma_{\mathrm{PrEP}}^{i,j}$) alone by 10%, 25%, 50%, 75% and 100% while keeping the rate of PrEP discontinuation (i.e. $\tau_{\mathrm{PrEP}}^{i,j}$) constant; and the impact of increasing both HIV testing and PrEP initiation by 10%, 25%, 50%, 75% and 100% among all TNB people. Second, we examine the impact of targeted combined interventions (e.g. HIV testing and PrEP) only among TNB people with a higher likelihood of HIV acquisition.

Intervention Impact

We evaluated the effectiveness of each intervention scenario over the 10-year period of 2020-2030 by comparing the simulated intervention scenarios to the reference scenario. The impact was measured as the cumulative fraction of HIV transmissions prevented as well as the absolute number HIV transmissions prevented. Lastly, we estimated the percent reduction in annual HIV incidence in 2030 relative to the incidence in 2020. Notably, we will compare the estimated reduction in HIV incidence in 2030 to the EHE target of a 90% reduction in new HIV diagnoses.

4. Model Results

In the reference scenario, we estimated that HIV incidence in 2020 was 3.6 per 10,000 person-years among transgender women, 2.2 per 10,000 person-years among transgender men, and 4.2 per 10,000 person-years among non-binary people (Figure 4.3). Maintaining constant rates of HIV testing and PrEP uptake, we predict that 2,461 transgender women, 532 transgender men, and 103 non-binary people will acquire HIV over the 10-year period of 2020-30, such that 16,455 transgender women, 1,523 transgender men, and 453 non-binary people would be living with HIV in the US in 2030. In the reference scenario, our model projects that HIV incidence would significantly decrease over the 10-year period, equivalent to a 70%, 63% and 71% reduction in the HIV incidence compared to 2020 among transgender women, men, and non-binary people, respectively.

We then modeled the impact of increasing the rate of HIV testing and/or PrEP uptake, assuming a constant rate of PrEP discontinuation. Table 4.2 reports the proportion of TNB people who would test for HIV annually and be on PrEP by 2030 assuming 10%, 25%, 50%, 75% and 100% increases in the rate of testing and PrEP uptake, respectively.

Across all demographic groups, increasing PrEP uptake alone had a much larger population impact compared to HIV testing alone (Figure 4.4-4.5). Combination interventions (e.g. increase both HIV testing and PrEP) provided only marginal increases in the number and percentage of HIV acquisitions that were prevented over the 10-year intervention period. Across all intervention scenarios, universal intervention approaches had a greater population-level impact for HIV prevention compared to targeted interventions (e.g. only increasing HIV testing and PrEP among individuals with a higher likelihood of HIV acquisition). The effectiveness of targeted inventions was positively correlated with the fraction of the population with a higher likelihood of HIV acquisition, which was highest among non-binary people (19%) and transgender women (14%) and lowest among transgender men (8%). Similarly, across all intervention scenarios, a larger increase in the rate of PrEP uptake is needed to prevent a similar proportion of HIV acquisition among transgender men because our model estimates a lower HIV incidence rate among transgender men compared to transgender women and non-binary people.

A moderate 50% increase in the rate of both HIV testing and PrEP uptake among all TNB people (i.e., a universal combination intervention scenario) was estimated to prevent 400 HIV acquisitions during the 10-year intervention period relative to the reference scenario, equivalent to preventing 15%, 6%, and 10% of the new HIV acquisitions projected in the reference scenario between 2020-2030 among transgender women, transgender men, and non-binary people, respectively (Figure 4.5). This scenario is equivalent to reducing HIV incidence by 67-78% by 2030, relative to 2020 (Figure 4.6).

An optimistic scenario with a doubling (100% increase) in the rate of both HIV testing and PrEP uptake among all TNB people was estimated to prevent 679 HIV acquisitions during the 10-year intervention period relative to the reference scenario, equivalent to preventing 25%, 10%, and 17% of the new HIV acquisitions between 2020-2030 among transgender women, transgender men, and non-binary people, respectively. This scenario is equivalent to reducing HIV incidence by 70-86% by 2030, relative to 2020 (Figure 4.6). Thus, even a doubling of the rate of HIV testing and PrEP uptake was not sufficient to reach the EHE target of reducing HIV incidence by 90% by 2030.

DISCUSSION

We developed a novel mathematical model of HIV transmission among all TNB people in the US that more accurately represents the sexual network of TNB people. To our knowledge, this is also the first model to include transgender men and non-binary people, despite these populations being disproportionately impacted by HIV. In our reference scenario, we predict that at least 3,096 TNB people will acquire HIV by 2030 assuming current rates of HIV testing and PrEP among TNB people in the US. Notably, this figure is almost certainly a significant underestimate given limitations of the HIV surveillance data used to calibrate our model.

Similar to other modeling studies, our findings suggest that the EHE targets will be difficult to achieve among TNB populations. We project that moderate increases in the rate of HIV testing and PrEP uptake would achieve a 67-78% reduction in HIV incidence among TNB people, which is comparable to estimates of 67% by Bradley et al.[26] and 68% by Fojo et al.[27] Overall, our findings suggest that increasing access to PrEP was significantly more effective than HIV testing at preventing HIV transmission at a population level. This points to the need to focus prevention efforts on improved access to and retention for PrEP for TNB populations.

Multilevel interventions are needed for TNB people to address the structural barriers to accessing HIV prevention and treatment.[28–30] Despite high reported willingness to take PrEP among transgender women and men, PrEP uptake has been low among TNB populations.[31–34] Qualitative studies have identified trans-specific barriers to PrEP, including concerns that PrEP may interact with hormone therapy, the absence of trans-inclusive marketing and public health campaigns for PrEP, stigma, and medical distrust.[35–40] Transgender participants also cited barriers that were not trans-specific, such as low awareness of PrEP, difficulty taking daily pills, side effects, and cost.[41]

An unmet need for gender-affirming health care may also hinder access HIV prevention tools for TNB people. Therefore, delivery of HIV prevention and PrEP along with gender-affirming health care, including access to gender-affirming hormones, may be effective an increasing PrEP uptake and adherence.[42,43,44] Qualitative studies based in the US have also demonstrated that fear of mistreatment in medical settings and competing priorities for accessing hormones are both barriers to PrEP uptake among transgender women. The TRIUMPH (Trans Research–Informed communities United in Mobilization for the Prevention of HIV) PrEP demonstration project found that co-administration of hormone therapy alongside PrEP significantly improved knowledge, acceptability, uptake and retention for PrEP among TNB participants.[45] Thus, receiving PrEP from trans-competent providers with training in healthcare for TNB people may be critical for PrEP uptake and adherence.[32,35]

Limitations

The development and calibration of our model was limited by the quality of data. Most notably, due to limited availability of longitudinal data on HIV prevalence for TNB people, our model assumed that the HIV prevalence reported by the CDC's National HIV Surveillance report was accurate. In actuality, these numbers are likely a gross underestimate of the true number of TNB people living with HIV, especially for transgender men and non-binary people, who are likely misclassified as cisgender. Therefore, the absolute reductions and HIV incidence rates estimated in our study are also likely significant underestimates of the impact of the intervention scenarios considered. This modeling exercise underscores the importance of trans-inclusive data collection and reporting in HIV/STI surveillance,[46] since the relevance of these analyses for informing public health decision-making is strongly dependent on the validity of the calibration targets. Therefore, it is necessary for local, state, and federal public health jurisdiction implement best practices in collecting gender identity data.

Our model should also be considered in light of the following limitations. Although there are significant racial inequities in HIV among TNB people, we were unable to include race/ethnicity our model due to very limited data available on sexual behavior, HIV prevalence, the HIV care cascade, testing or PrEP use among TNB people stratified by both gender identity and race/ethnicity. In addition, our calibrated model overestimated engagement in the HIV care cascade, and assumes an overall high level of ART use and viral suppression.

Conclusions

Modeling can be an important tool for planning public health interventions for TNB populations who are disproportionately impacted by HIV. Although we found that improving access to PrEP was effective at preventing a modest proportion of HIV transmissions by 2030, our model suggests that achieving the EHE targets among TNB populations will be difficult. This modeling exercise highlights the need to for trans-inclusive HIV data collection, the importance of reporting data disaggregated by gender identity and race/ethnicity, and the need for multilevel interventions to address structural barriers TNB people face in accessing HIV prevention services.

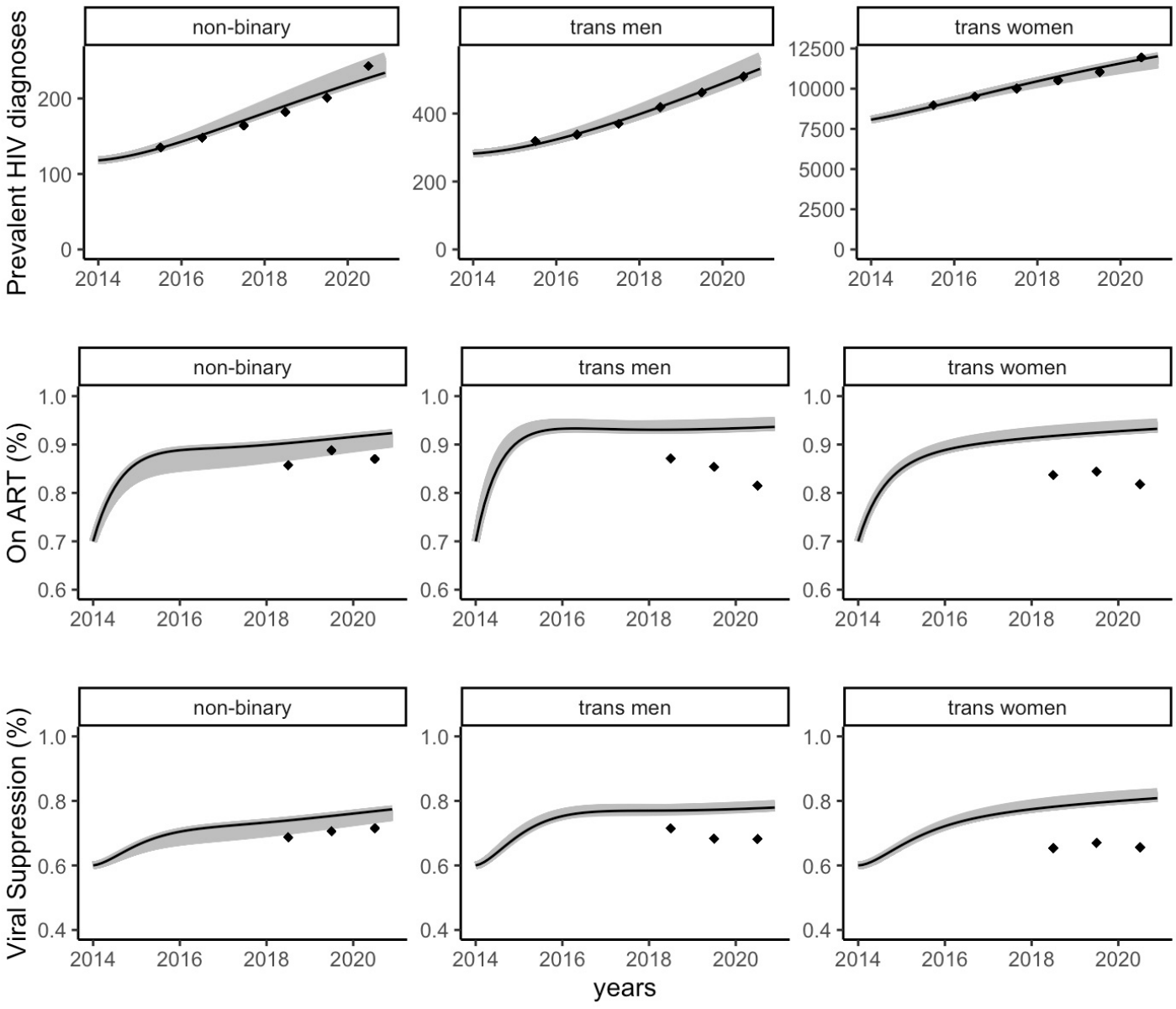

Figure 2. Model Calibration Results for Transgender and Non-binary Populations.
Black line indicates the best fit based on the maximum apriori (MAP) of the posterior distribution for all calibration parameters. Gray shading indicate model uncertainty based on random draws from the posterior distribution.

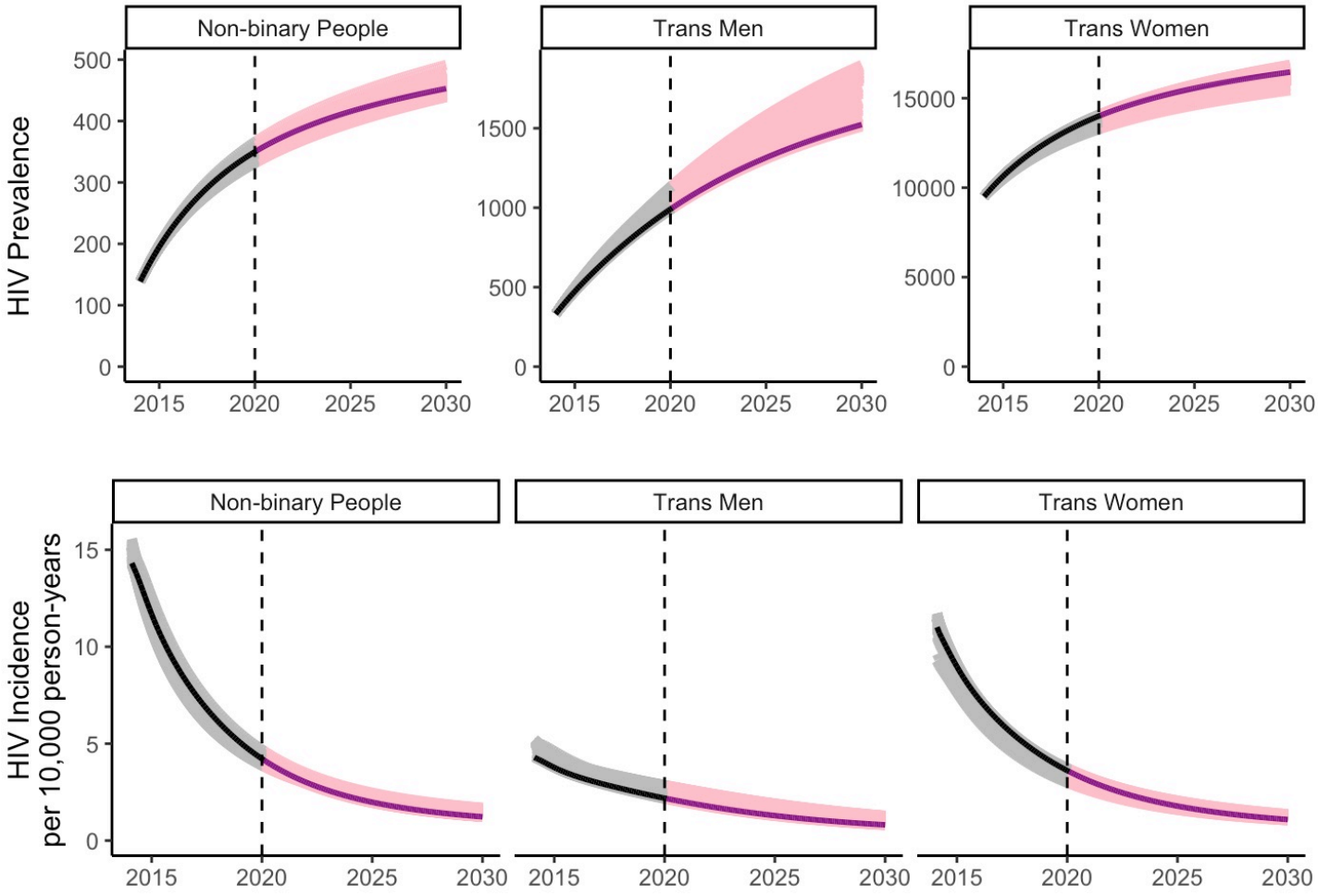

Figure 3. Projected HIV Prevalence and Incidence for Reference Scenario.

Line indicates the best fit based on the maximum apriori (MAP) of the posterior distribution for all calibration parameters. Shading indicate model uncertainty based on random draws from the posterior distribution. Grey/black indicate model calibration up to the year 2020, while pink/magenta indicate model projections into the future.

Table 3. Predicted Population Coverage for Annual HIV Testing and PrEP Use by 2030 for each Intervention Scenario, Stratified by Demographic Group and Higher/Lower Likelihood of HIV Acquisition

	Reference Scenario	Intervention Scenario: Percent Increase in the Rate of HIV Testing and PrEP Uptake				
		10%	25%	50%	75%	100%
Proportion Testing for HIV Annually by 2030						
Non-binary People						
Lower Likelihood of Acquiring HIV	8.2%	9.0%	10.2%	12.3%	14.3%	16.4%
Higher Likelihood of Acquiring HIV	30.5%	33.5%	38.1%	45.7%	53.4%	61.0%
Transgender Men						
Lower Likelihood of Acquiring HIV	8.2%	9.0%	10.2%	12.2%	14.3%	16.3%
Higher Likelihood of Acquiring HIV	25.1%	27.6%	31.4%	37.7%	43.9%	50.2%
Transgender Women						
Lower Likelihood of Acquiring HIV	17.5%	19.2%	21.8%	26.2%	30.6%	34.9%
Higher Likelihood of Acquiring HIV	43.7%	48.1%	54.7%	65.6%	76.5%	87.4%
Proportion on PrEP by 2030						
Non-binary People						
Lower Likelihood of Acquiring HIV	19.7%	20.9%	22.6%	25.4%	28.0%	30.4%
Higher Likelihood of Acquiring HIV	57.4%	59.4%	62.1%	66.0%	69.2%	71.8%
Transgender Men						
Lower Likelihood of Acquiring HIV	15.2%	16.2%	17.6%	19.9%	22.1%	24.3%
Higher Likelihood of Acquiring HIV	56.3%	58.6%	61.7%	66.1%	69.7%	72.8%
Transgender Women						
Lower Likelihood of Acquiring HIV	29.5%	31.1%	33.6%	37.4%	41.0%	44.3%
Higher Likelihood of Acquiring HIV	65.4%	67.5%	70.3%	74.2%	77.3%	79.8%

The proportion of participants with a higher likelihood of acquiring HIV is based on 2016-2020 data from the Behavioral Risk Factor Surveillance System (BRFSS), which asks participants if they "have injected any drug other than those prescribed for you in the past year; have been treated for an STD in the past year; or have given or received money or drugs in exchange for sex in the past year". We estimated that 14.1% of non-binary people assigned female at birth, 23.1% of non-binary people assigned male at birth, 8.4% of transgender men, and 13.7% of transgender women responded yes to this question.

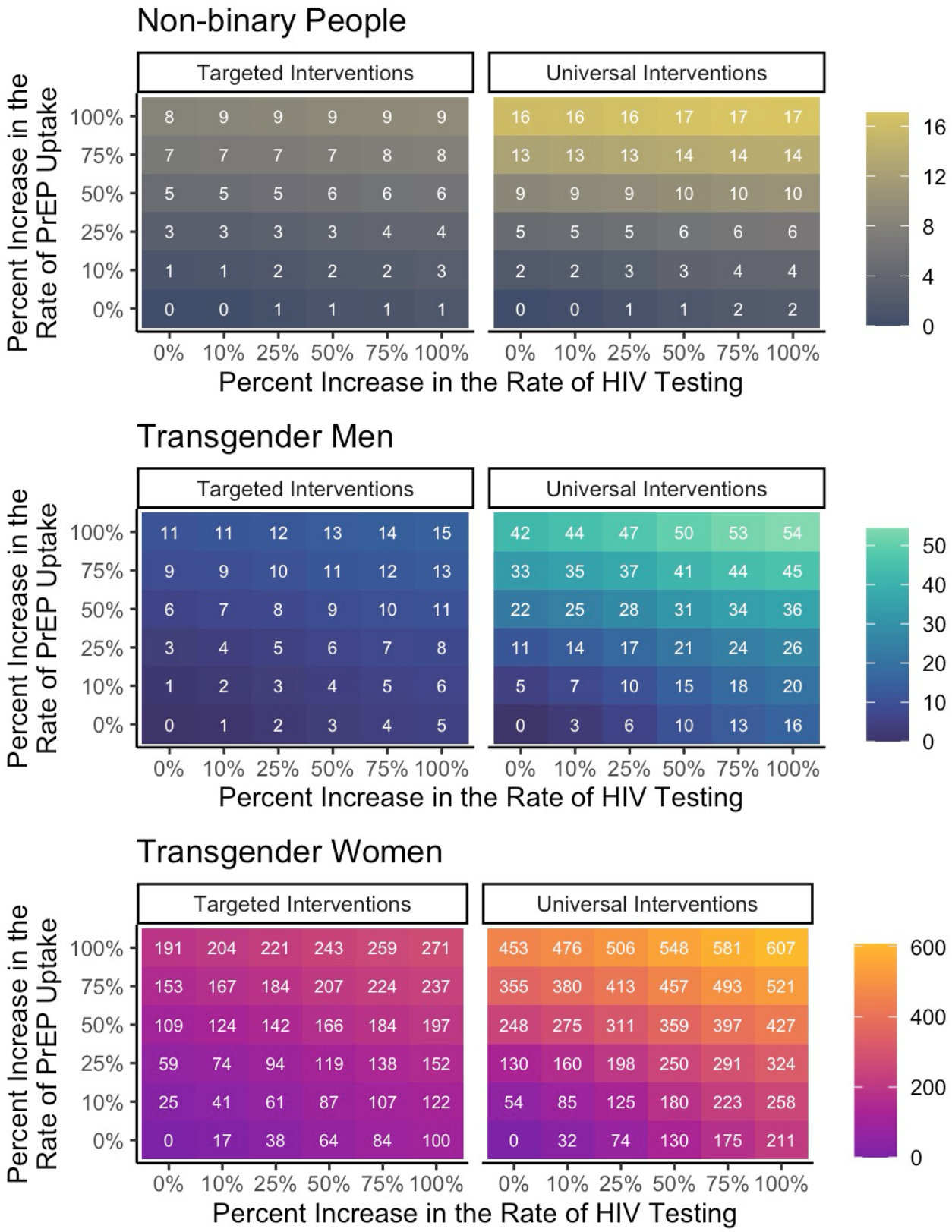

Figure 4. Absolute Number of New HIV Acquisitions Prevented between 2020-2030 Relative to the Reference Scenario.

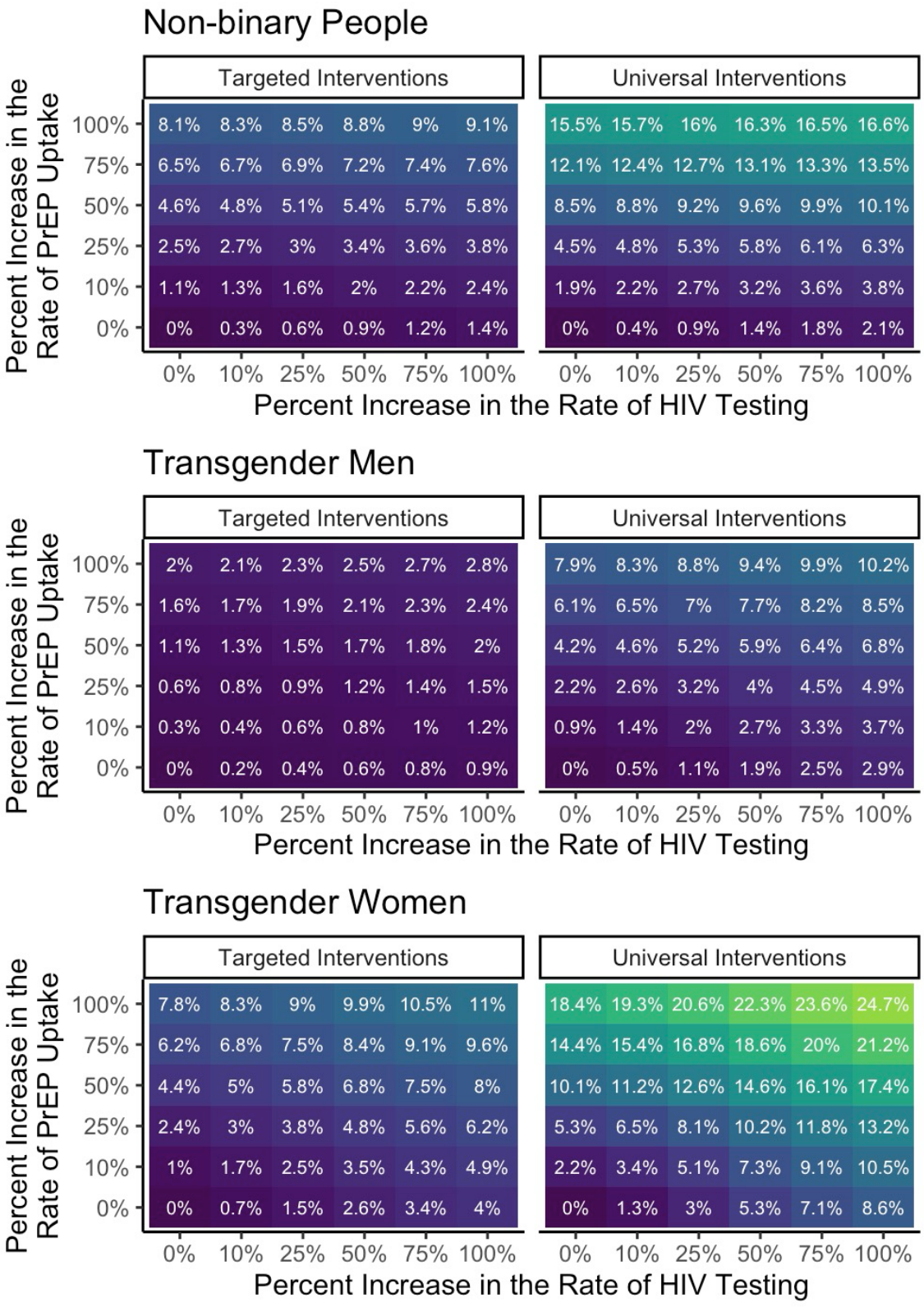

Figure 5. Cumulative Fraction of New HIV Acquisitions Prevented between 2020-2030 Relative to the Reference Scenario.

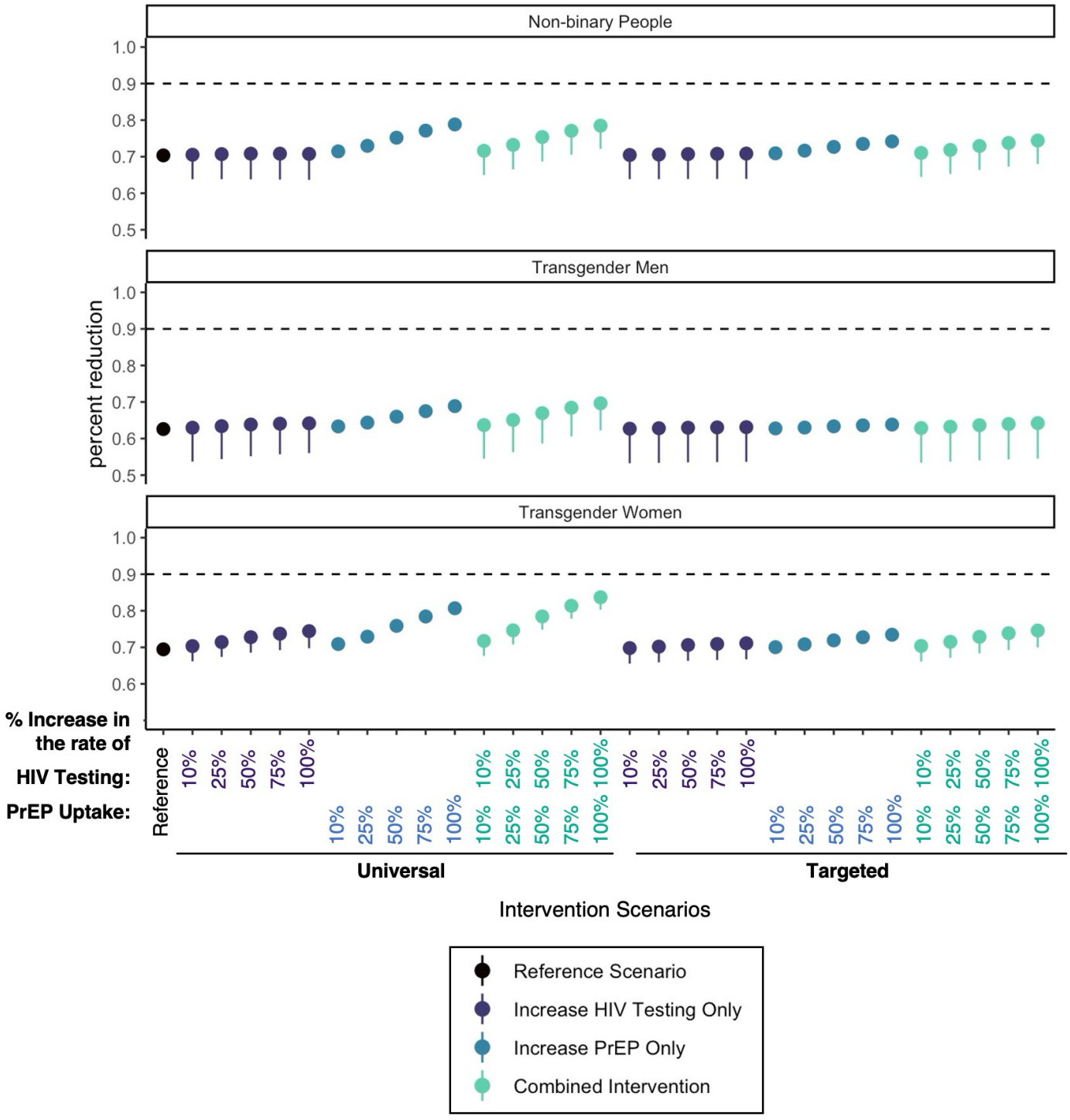

Figure 6. Percent Reduction in HIV Incidence Rate by 2030 Relative to 2020, by Intervention Scenario. *Point estimate indicates the best fit based on the maximum apriori (MAP) of the posterior distribution for all calibration parameters. The lines indicate model uncertainty based on random draws from the posterior distribution. Dashed line indicates the Ending HIV Epidemic goal of reducing HIV incidence by 90% by 2030.*

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