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Technical Report for the HIV Optimization and Prevention Economics (HOPE) Model

Version 7

Appendix to the manuscript, “Impact of Improved HIV Care and Treatment and Implementing PrEP in the United States, 2016–2020”

Based on Model Version 4.03

populated with calibration set AS\_1

Most of the material in this technical report has been previously published (O’Leary et al., 2017). Key material specific to this analysis can be found in sections 9, 11, and 12 (see Section 1 for details).

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Disclaimer: Previous versions of this document were published as supplementary material to the following papers:

* O’Leary A, DiNenno E, Honeycutt A, Allaire B, Neuwahl S, Hicks K, Sansom S. Contribution of anal sex to HIV prevalence among heterosexuals: A modeling analysis. *AIDS Behav*. 2017;21:1–9 doi:10.1007/s10461-016-1635-z.
* Jacobson E, Hicks K, Tucker E, Farnham P, Sansom S. Effects of reaching national goals on HIV incidence, by race and ethnicity, in the United States*. J of Public Health Management and Practice*. In press.

# Introduction

This document presents the technical details of the HIV Optimization and Prevention Economics (HOPE) Model, a differential equation model representing the U.S. HIV epidemic developed by the Centers for Disease Control and Prevention’s (CDC’s) Division of HIV/AIDS Prevention and RTI International. Section 2 gives a brief overview of the model and its purpose. Section 3 explains the core structure of the model, including the modeled population, the compartments used in the model, and the notation applied in this document. Section 4 describes the initial model population. Section 5 discusses the transitions that result in the flow of the population between compartments (except the flow due to infection) and the flow into and out of the model. Section 6 describes how the force of infection is calculated. Section 7 explains the differential equations that are applied in the model. Section 8 describes the interventions included in the model that increase progression along the HIV care continuum when “allocation-based” progression is applied. Section 9 provides important details pertaining to the analysis conducted using the HOPE model in the manuscript entitled “Impact of Improved HIV Care and Treatment and Implementing PrEP in the United States, 2016–2020” that were not otherwise presented in the manuscript text. Section 10 describes the calculation of model outcomes. Section 11 discusses the model’s calibration and validation. Section 12 presents the methods and results of sensitivity and uncertainty analyses. Appendix A includes tables defining the symbols and indices applied in this document.

As noted in the disclaimer at the beginning of this document, several versions of this report have previously been published in manuscripts that use the HOPE Model. Each version has been adapted for the specific analysis presented in that manuscript. Besides reflecting the assumptions and structure of the model version used, the following is a list of how this version of this document has been adapted to specifically represent this analysis:

* Sections 5 and 6: All input tables reflect the set of values used for calibrated inputs for this analysis (the set with identifier “AS\_1”).
* Section 9: Key explanations and details of the specific methods applied for using the HOPE model for conducting this particular analysis.
* Section 11: The calibration methods represent those applied in generating the set of values used to populate all calibrated inputs in this analysis (set AS\_1). The ranges considered for all calibrated inputs and the point estimates and acceptable ranges of output values for all targeted outcomes are also specific to the analysis, as are the final values of the inputs and resulting values of the targeted outcomes when those input values were applied in the HOPE Model.
* Section 12: The sensitivity and uncertainty analyses methods reflect those used in this analysis, specifically, the outcome observed and relevant processes applied. Also, the results of the analyses will reflect those specifically generated for this analysis.

In addition, because this document covers the full functionality of the HOPE Model, the following key portions of that functionality were not used in this analysis:

* Allocation-based method for calculating progression along the care continuum (Section 5.4.1 and Section 8): Allocation-based progression was not applied as a method for calculating progression along the care continuum.
* Heterosexual (HET) interval-based testing method (Section 5.4.1) for calculating progression along the care continuum: HET interval-based testing was not applied as a method for calculating progression along the care continuum.
* Calculation of economic outcomes (Section 10.2): Economic outcomes were not calculated in the analyses for this manuscript.

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# Model Overview and Purpose

The objective of the HOPE model was to estimate the impact on health outcomes related to HIV in the U.S. population resulting from changes in the distribution of people living with HIV along the HIV care continuum and to better understand the impact of different risk behaviors on the prevalence of HIV in the United States. The model used differential equations that are implemented and solved in MATLAB software (Mathworks, Natick, Massachusetts); it may also be solved using discretized difference equations, if indicated by the user. The equations represented the dynamics of the HIV-uninfected and HIV-infected populations, including their interaction and progression through various clinical stages of HIV as well as the care continuum. We consider progression through the care continuum to include HIV diagnosis, linkage to care, ART prescription, and achievement of viral load suppression. Transmission risks from sex acts (vaginal and anal) and shared needles were considered. The model can be used to examine HIV prevention interventions aimed at HIV-infected and HIV-uninfected individuals.

Our model was originally based on a model published by Sorensen and colleagues (2012) that included gay, bisexual, and other men who have sex with men (collectively referred to as MSM) in New York City; we expanded that model to include the national epidemic data for multiple transmission groups (MSM, people who inject drugs [PWID], and HETs). These groups were further categorized by sex (male, female), race/ethnicity (black, Hispanic/Latino, other), age group (13–17, 18–24, 25–34, 35–44, and 45–64 years), and risk level (low, high). We also adjusted the model’s care continuum stages to more precisely represent the effects of antiretroviral therapy (ART) and being viral load suppressed (VLS). The model was dynamic in that the risk of uninfected individuals acquiring HIV at any given time was a function of the current size, disease stages, and HIV care continuum stages of the HIV-infected portion of their pool of sexual and needle partners. As a result, changes that affect the HIV-infected population affected the spread of the disease to the uninfected portion of the population in the model.

Three time periods are observed. The first, 2006 to 2009, is a “run-in period” for the model, which provides a necessary period of stabilization for the differential equations. The second is 2010 to 2015, and the third is 2016 and beyond.

# Model Population and Compartments

The population observed in this model was stratified by age group *j* (*j* = 1, …, 5), risk level *k* (*k* = 1, 2), transmission group *l* (*l* = 1, 2, 3), sex *m* (*m* = 1, 2), circumcision status *n* (*n* = 1, 2), and race/ethnicity *o* (*o* = 1, 2, 3). Table 3.1 lists the categories applied in the model for each of these stratification criteria. PWID are all high-risk, MSM are all male, and only males are stratified by circumcision status; therefore, not all combinations of these stratifications (i.e., 360 = 5x2x3x2x2x3) are represented. Males are stratified by 5 age groups, 5 combinations of transmission group and risk level (MSM high-risk, MSM low-risk, HET high-risk, HET low-risk, PWID), 2 groups based on circumcision status, and 3 groups based on race/ethnicity, resulting in 150 (5x5x2x3) male subpopulations. Females are stratified by 5 age groups, 3 combinations of transmission group and risk level (HET high-risk, HET low-risk, and PWID), and three groups based on race/ethnicity, resulting in 45 (5x3x3) female subpopulations. Accounting for both males and females, there are 195 (150+45) subpopulations *p* (*p* =1, …, 195).

Table 3.1. Population Stratification Criteria and Categories Applied in Each

| Stratification Criterion (Represented by) | Categories (Represented by) |
| --- | --- |
| Age group (*j*) (years) | 13–17 (1) |
| 18–24 (2) |
| 25–34 (3) |
| 35–44 (4) |
| 45–64 (5) |
| Risk level (*k*) | Low (1) |
| High (2) |
| Transmission group (*l*) | HET (1) |
| MSM (2)a |
| PWID (3) |
| Sex (*m*) | Male (1) |
| Female (2) |
| Circumcision status (*n*) | Uncircumcised (1) |
| Circumcised (2) |
| Race/ethnicity (*o*) | Black (1) |
| Hispanic/Latino (2) |
| Other (3) |

Note: HET = heterosexual; MSM = men who have sex with men; PWID = people who inject drugs

a The MSM population is meant to capture all men who have sex with men, not just those who self-identify as MSM.

The model’s 28 compartments (defined by *c*) included 25 main compartments for individuals actively moving through the model and 3 compartments for individuals who were no longer actively followed in the model due to death by causes other than AIDS, death due to AIDS, and aging out. The 25 former compartments were defined by disease stage (*h*) and continuum-of-care stage (*r*).

Figure 3.1 displays how the model’s compartments are applied in the model; each compartment is labeled in that figure with its corresponding number *c*. They are defined by HIV stage and HIV continuum-of-care status. Individuals enter the population as susceptible and not on PrEP (*c* = 1). They may die or age out of the population from any of the main compartments.

The six disease stages (*h* = 0, …, 5) were defined by the presence of HIV infection and, if infected, HIV progression:

* *h* = 0: Susceptible
* *h* = 1: Acute HIV infection (“Acute” hereafter)
* *h* = 2: HIV infection with CD4 count greater than 500 cells/mm3 (but not acute) (“CD4>500” hereafter)
* *h* = 3: HIV infection with CD4 count between 350 cells/mm3 and 500 cells/mm3 (“CD4 350-500” hereafter)
* *h* = 4: HIV infection with CD4 count between 200 cells/mm3 and 350 cells/mm3 (“CD4 200-350” hereafter)
* *h* = 5: AIDS with CD4 less than 200 cells/mm3 (“CD4<200” or “AIDS” hereafter)

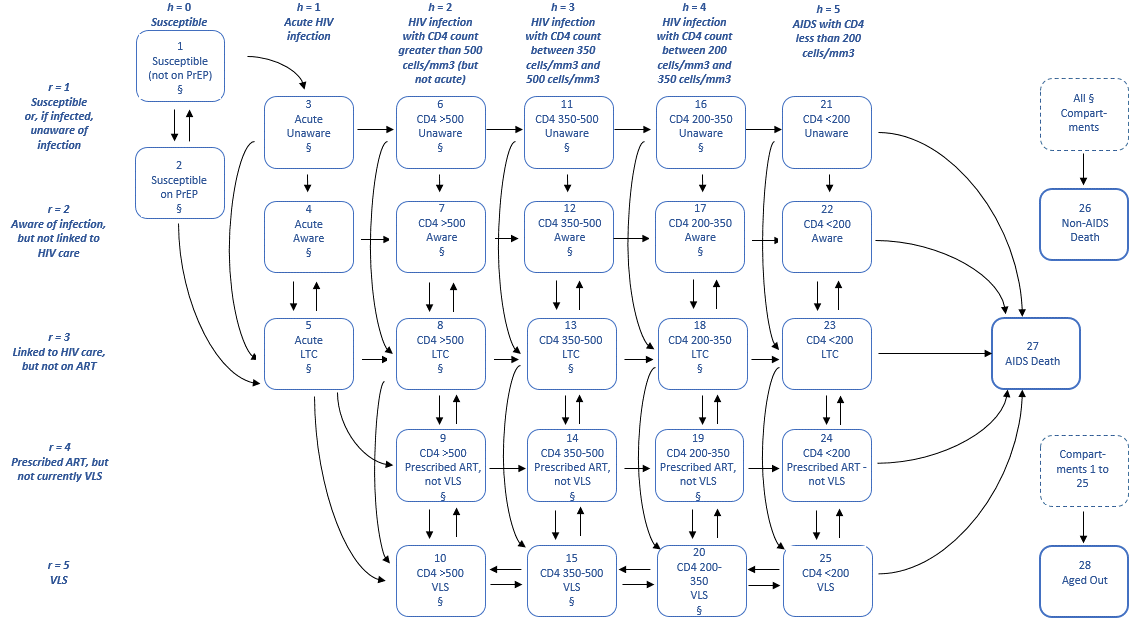
Five continuum-of-care stages (*r* = 1, …, 5) were defined by infection status, awareness of infection, linkage to HIV care, status based on effects of treatment with ART, and VLS status:

* *r* = 1: Susceptible or, if infected, unaware of infection (“Unaware” hereafter)
* *r* = 2: Aware of infection, but not linked to HIV care (“Aware” hereafter)
* *r* = 3: Linked to HIV care, but not prescribed ART (“Linked to HIV care” or “LTC” hereafter)
* *r* = 4: Prescribed ART, but not VLS (“ART-not-VLS” or “ANV” hereafter)
* *r* = 5: VLS (in care and prescribed ART) (“VLS” hereafter)

For the acute disease stage (*h* = 1), compartments were defined by only the first three continuum-of-care stages: susceptible, aware, and LTC (*r* = 1, 2, 3). For each of the four disease stages for individuals with chronic HIV (*h* = 2, 3, 4, 5), compartments were defined by all continuum-of-care stages for infected individuals (*r* = 1, 2, 3, 4, 5). Susceptible individuals (*h* = 0) also were categorized by pre-exposure prophylaxis (PrEP) status (*c* = 1 and c = 2).

The population represented in the model at any given time was distributed among the 25 main compartments. Individuals in the population were defined by the compartment they occupied, as well as by other demographic and behavioral factors. We let  equal the number of individuals in subpopulation *p* in compartment *c* at time *t*. Appendix Table A.1 lists and defines all symbols used in this document.

Figure 3.1. Model Flow Diagram between Compartments due to HIV Infection, Progression along the Care Continuum, Progression of HIV, and Death and Aging



Note: ART = antiretroviral therapy; LTC = linked to HIV care; PrEP = pre-exposure prophylaxis; VLS = viral load suppression.

# Initial Population

The model was initiated so that the observed population was distributed among the model’s 25 main compartments and was characterized to match the total and HIV-infected population in the United States in 2006. The size of the population was set to capture sexually active individuals in the U.S. population; it is flexibly programmed to either include ages 13 to 64 or 18 to 64 based on user settings. The size of and distribution among demographic subpopulations were determined by a set of parameters listed in Tables 4.1 through 4.4.

Table 4.1. Percentage PWID and MSM, Initial Population Size, HIV Prevalence of High- Versus Low-Risk Levels, HIV Prevalence, and Percentage High Risk in Initial Population (2006)

| Parameter | Female | | | | | Male | | | | | | | Total | Source |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Black | Hispanic | Other | | | Black | | Hispanic | | | | Other |
| Percentages of population that are in the PWID and MSM transmission groups | | | | | | | | | | |  | | | |
| PWID | ----------------------0.21%----------------- | | | -----------------------0.36%-------------------- | | | | | | | | | N/A | Lansky et al. (2014), Table 3a |
| MSM (among males only) |  |  |  | ------------------------3.9%-------------------- | | | | | | | | | N/A | Purcell et al. (2012), Table 2b |
| Percentages of PWID and MSM high risk | | | | | | | | |  | | | | | |
| PWID | -----------------------------------------100.0%------------------------------------------------- | | | | | | | | | | | | N/A | Assumedc |
| MSM | ------------------------------------------69.4%------------------------------------------------- | | | | | | | | | | | | N/A | CDC unpublished data based on 2008 NHBS MSM cycle 2.d |
| Percentages of PWID population that is each race/ethnicity, by sex | | | | | | | | | |  | | | | |
|  | 25.68% | 12.72% | 61.60% | | 25.68% | | | 12.72% | | | | 61.60% | N/A | Calculated from Cooper et al. (2005)e |
| Initial population size, total and by transmission group and risk level | | | | | | | | | |  | | | | |
| U.S. population aged 13–64 | 14,111,830 | 17,062,126 | 76,990,484 | | 12,952,528 | | | 17,983,623 | | | | 76,433,745 | 215,534,336 | U.S. Census Bureau (2010) |
| HET |  |  |  | |  | | |  | | | |  |  |  |
| High | 2,698,746 | 1,895,579 | 1,120,531 | | 2,367,723 | | | 1,909,782 | | | | 1,063,334 | 11,055,694 | Calculatedf |
| Low | 11,354,743 | 15,137,665 | 75,730,031 | | 9,980,377 | | | 15,323,332 | | | | 72,151,391 | 199,677,539 | Calculatedg |
| PWID |  |  |  | |  | | |  | | | |  |  |  |
|  | 58,342 | 28,882 | 139,922 | | 99,280 | | | 49,148 | | | | 238,103 | 613,667 | Calculatedh |
| MSM |  |  |  | |  | | |  | | | |  |  |  |
| Overall |  |  |  | | 505,149 | | | 701,361 | | | | 2,980,916 | 4,187,426 | Calculatedi |
| High |  |  |  | | 350,573 | | | 486,745 | | | | 2,068,756 | 2,906,074 | Calculatedd |
| Low |  |  |  | | 154,575 | | | 214,617 | | | | 912,160 | 1,281,352 | Calculatedj |
| Relative HIV prevalence for high- vs. low-risk levels | | | | | | |  | | | | | | | |
| MSM | ---------------------------------------------7.43------------------------------------------------- | | | | | | | | | | | | N/A | Assumptionk |

(continued)

Table 4.1. Percentage PWID and MSM, Initial Population Size, HIV Prevalence of High- Versus Low-Risk Levels, HIV Prevalence, and Percentage High Risk in Initial Population (continued)

| Parameter | Female | | | Male | | | Source |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Black | Hispanic | Other | Black | Hispanic | Other |
| HIV prevalence | | | | | | | |
| HET |  |  |  |  |  |  |  |
| High | 4.582% | 1.644% | 0.707% | 2.862% | 0.731% | 0.378% | CDC (2012b)l |
| Low | 0.222% | 0.080% | 0.034% | 0.139% | 0.035% | 0.018% | CDC (2012b)l |
| PWID |  |  |  |  |  |  |  |
| High | 85.000% | 60.618% | 7.443% | 78.772% | 56.177% | 6.897% | CDC (2012b)l |
| MSM |  |  |  |  |  |  |  |
| Overall |  |  |  | 29.882% | 14.863% | 10.817% | CDC (2012b)l |
| High |  |  |  | 40.645% | 20.217% | 14.714% | Calculatedm |
| Low |  |  |  | 5.470% | 2.721% | 1.980% | Calculatedm |

Note: CDC = Centers for Disease Control and Prevention; HET = heterosexual; HIV = human immunodeficiency virus; MSM = men who have sex with men; N/A = not applicable; NHBS = National HIV Behavioral Surveillance; PWID = people who inject drugs

aEstimate reflects injection drug use in past 12 months.

bEstimate reflects MSM risk behaviors in past 5 years. Note that the percentage with MSM behaviors in the past year was reported as 2.9% in Purcell et al. (2012).

c All PWID assumed to be high risk.

d Identified high-risk MSM based on criteria for PrEP eligibility using 2008 NHBS MSM cycle 2 data. Among MSM aged 18 to 64 who reported at least one occasion of anal sex in the past 12 months (regardless of HIV status), we used the following criteria to identify those at high risk: not in a monogamous partnership with another susceptible man and at least one of the following three risk behaviors: had unprotected anal sex in past 12 months, last partner was HIV-infected or unknown status, or had any sexually transmitted infection diagnosed or reported in past 12 months. In the NHBS analysis, HIV-infected individuals were not eligible to receive PrEP but were included in the high-risk MSM population if they met at least one of the criteria. Number of high-risk MSM calculated as total MSM multiplied by the percentage of MSM population at high-risk.

e Proportions in each race/sex category were based on median proportions of PWID in each category reported by Cooper et al. (2005). However, because those medians did not sum to 100, we proportionally adjusted the sizes of the Black and Hispanic populations so that the total proportions summed to 100%.

Table 4.1. Percentage PWID and MSM, Initial Population Size, HIV Prevalence of High- Versus Low-Risk Levels, HIV Prevalence, and Percentage High Risk in Initial Population (continued)

f Estimated number of high-risk HETs using unpublished 2007-2011 Census tract data from the American Community Survey (A. Hutchinson, personal communication, June 25, 2014). We started by obtaining population data for NHBS-HET 2010 metropolitan statistical areas (MSAs) (Sionean et al., 2010). The following 19 MSAs were included: Boston, Nassau-Suffolk Counties, New York City, Newark, Philadelphia, Atlanta, Baltimore, Dallas, Houston, Miami, New Orleans, Washington DC, Chicago, Detroit, Denver, Los Angeles, San Diego, San Francisco, and Seattle. High-risk HETs were then defined as the estimated population from census tracts that were majority minority (<50% white), high poverty (>20% in poverty), and urban areas, as identified by Rural-Urban Commuting Area codes of primary = 1 and secondary = 1. To limit these census tract population sizes to HETs, we reduced the total population sizes by 4.7% for men (to reflect 4.4% MSM and 0.3% PWID) and 0.3% for women (to reflect 0.3% PWID), the estimated proportions of the population that were MSM or PWID in large central metropolitan urban areas (Oster et al., 2015). We then included in the model only the fraction of the HET population that is sexually active (84.1%), based on reports of sex with opposite sex partner in past year, as estimated in Oster et al. (2014).

g Calculated as the total U.S. population by subgroup net of the population sizes of PWID, MSM, and high-risk HETs (not just sexually active high-risk HETs). The sexually active portion of the low-risk heterosexual population was calculated by applying the fraction of the HET population that is sexually active (84.1%), based on reports of sex with opposite partner in past year, as estimated in Oster et al. (2014).

h Calculated as total U.S. population, by sex and race or ethnicity, multiplied by the percentage of the adult population that is PWID.

i Calculated as total U.S. population of men, by race or ethnicity, multiplied by the percentage of the male population that is MSM.

j Calculated as total MSM population multiplied by (1 − percentage of MSM population at high risk).

k CDC used the model described in Sorensen et al. (2012), which included MSM only and assumed that 50% of MSM were high risk, to calculate HIV incidence by risk level. They found that the relative prevalence for high- vs. low-risk MSM was 7.43.

l Surveillance data (CDC, 2012b) reported number of prevalent cases. Model required prevalence as percentage of the population. Percentages were set so that the prevalent cases by race/ethnicity, transmission group, and sex in the initial modeled population matched those reported in surveillance data.

m Calculated as the risk for high-risk MSM divided by the relative HIV prevalence for high- versus low-risk MSM.

Table 4.2. Distribution of Initial Population (2006) across Age Groups, Percentage Circumcised, and Percentage of Each Transmission Group Sexually Active

| Parameter | Value | Source |
| --- | --- | --- |
| Distribution of initial population by disease stage, by age groups (years) | | |
| Uninfected and acute | | |
| 13–17 | 9.9% | Distribution of general population, per U.S. Census Bureau (2010) |
| 18–24 | 14.2% |
| 25–34 | 19.1% |
| 35–44 | 19.1% |
| 45–64 | 37.8% |
| CD4 > 500 | | Age distribution of individuals with new HIV infections in 2007, as reported in CDC (2012a) |
| 13–17 | 8.5% |
| 18–24 | 11.8% |
| 25–34 | 30.5% |
| 35–44 | 28.9% |
| 45–64 | 20.3% |
| CD4 200–350 and 350–500 | | Calculated as estimated distribution across age groups of PLWH who do not have AIDS, as measured by total HIV prevalence in 2008, by age group (CDC, 2012), minus total number of people living with AIDS, by age group, in 2007 (CDC, 2009) |
| 13–17 | 3.9% |
| 18–24 | 5.1% |
| 25–34 | 20.4% |
| 35–44 | 30.7% |
| 45–64 | 40.0% |
| CD4 < 200 | | Age distribution of people living with AIDS, as reported in CDC (2009) |
| 13–17 | 0.6% |
| 18–24 | 1.5% |
| 25–34 | 9.8% |
| 35–44 | 34.3% |
| 45–64 | 53.8% |
| Percentage of males circumcised, by race/ethnicity |  | Introcaso et al. (2013) |
| Black | 75.7% |
| Hispanic/Latino | 44.0% |
| Other | 90.8% |
| Percentage of population sexually active, by transmission risk group | | |
| HET | 84.1% | CDC unpublished data (Oster et al., 2014)a based on NHANES 1999–2010. |
| MSM | 100% | Assumption |
| PWID | 100% | Assumption |

Note: ART = antiretroviral therapy; HET = heterosexual; HIV = human immunodeficiency virus; NHANES = National health and Nutrition Examination Survey; PLWH = people living with HIV

a Fraction of never-MSM and never-PWID who reported an opposite sex partner in the past year; estimated among adults aged 18 to 59.

Table 4.3. Distribution of Initial HIV-Infected Population across Continuum-of-Care Stages by Race/Ethnicity (2006)

| Continuum-of-Care Stage | Black | Hispanic/ Latino | Other | Source |
| --- | --- | --- | --- | --- |
| Unaware (*r* = 1) | 22.7% | 23.3% | 20.2% | Percentages in first three stages (*r* = 1 to 3) calculated from Gardner et al. (2011) and CDC (2013).a | |
| Aware (*r* = 2) | 32.4% | 30.5% | 28.9% |
| Linked to HIV care (*r* = 3) | 24.4% | 22.8% | 26.6% |
| ART-not-VLS (*r* = 4) | 6.2% | 5.7% | 4.3% | Calculated from Gardner et al. (2011) and Hall et al. (2013).b­ Gardner et al. report the percentage aware who are on treatment. | |
| VLS (*r* = 5) | 14.3% | 17.8% | 20.1% | Calculated from Gardner et al. (2011) and Hall et al. (2013).b | |

Note: ART = antiretroviral therapy; HIV = human immunodeficiency virus; VLS = viral load suppressed

a Race-specific data were unavailable for 2006 and were calculated by applying the relative proportions of each race/ethnicity at each continuum-of-care stage in 2010 (CDC, 2013a) to the non-race specific distribution of the HIV-infected population reported by Gardner et al. (2011).

b Race-specific data were unavailable for 2006 and were calculated by applying the relative proportions of each race/ethnicity at each continuum-of-care stage in 2009 (Hall et al., 2013) to the non-race specific distribution of the HIV-infected population reported by Gardner et al. (2011).

Table 4.4. Distribution of Initial HIV-Infected Population across HIV Stages, by Continuum-of-Care Stage

| Continuum-of-Care Stage | Acute | CD4  > 500 | CD4 350–500 | CD4  200–350 | CD4  < 200 | Source |
| --- | --- | --- | --- | --- | --- | --- |
| Unaware  (*r* = 1) | 1.2% | 40.1% | 34.9% | 15.4% | 8.5% | Average distribution of disease stages at diagnosis produced in this model, given status quo testing rates. Applied that distribution as a proxy. |
| Aware  (*r* = 2) | 1.2% | 40.1% | 34.9% | 15.4% | 8.5% |
| Linked to HIV care (*r* = 3) | 0.0% | 44.5% | 44.5% | 10.0% | 1.0% | Assumption that no individuals with acute infection were linked to HIV care, almost no individuals linked to HIV care but not prescribed ART would have AIDS, and the vast majority would be in earlier stages of HIV. |
| ART-not-VLS (*r* = 4) | 0.0% | 0.0% | 30.0% | 30.0% | 40.0% | Assumption based on the recommendations in 2006 that all PLWH would have initiated ART at CD4<350 but some would have progressed to higher CD4 counts. Those that had would be almost evenly distributed across CD4 categories <500. |
| VLS (*r* = 5) | 0.0% | 25.0% | 25.0% | 25.0% | 25.0% | Assumed that in 2006 individuals who were VLS would be evenly distributed across CD4 stages. All would have initiated ART at CD4<350 but many would have progressed to higher CD4 counts. |

Note: ART = antiretroviral therapy; PLWH = people living with HIV; VLS = viral load suppressed

# Movement into and out of the Model, between Subpopulations, between Compartments (Except Due to Infection), and within Compartments

The number of individuals in the model’s population changes over time by individuals aging into or out of the population, dying from AIDS, or dying from other causes. Individuals move between subpopulations solely due to aging. They move between compartments due to disease progression and progression along the HIV care continuum. The values of the parameters that affect these dynamics are specified in Tables 5.1 through 5.6. Many of these parameter values were calibrated within defined ranges to match specific target outcomes; further details on the calibration process are provided in Section 10.1.

## Transitions into and out of the Model

Individuals can only enter into the model by aging into the population (at either age 13 or 18, depending on user settings about whether age 13–17 is included in the population). The number of people who age in is constant over time for all subpopulations; it is equal to the rate of aging in multiplied by the number of people in that subpopulation in the initial population. All enter the susceptible (and not on PrEP) stage (*c* = 1). If the 13- to 17-year-old age group is included in the modeled population, the rate of aging into the population is equal to 0.2175 per person in the 13 to 17 age group in the initial population. This is calculated as 1 ÷ 5 years in the 13 to 17 age group, and then adjusted slightly to keep the population stable over time. If the 13 to 17 age group is not included, the rate of aging in is equal to 0.1429 per person in the 18 to 24 age group in the initial population (where 0.1429 = 1 ÷ 7 years in the 18 to 24 age group). As a result of this calculation method, the age distribution of individuals across demographic subpopulations is proportional to the age distribution of the initial population.

Individuals leave the model by dying (from AIDS or other causes) or by aging out of the population. Death leads them to either the “AIDS Death” (if they had AIDS at death) or “Non-AIDS Death” states (if they did not have AIDS at death); individuals move to the “AIDS Death” stage only from the AIDS stage (CD4 < 200; *h* = 5). Mortality rates are determined by four methods; the values and sources for the inputs used to calculate those rates are listed in Table 5.1:

* For individuals with CD4<200 (AIDS) and not prescribed ART (*c* = 21 to 23), their mortality rate is equal to 1 / the number of years spent with AIDS under natural history disease progression, as specified by *Number of years in each stage if HIV infected and not prescribed ART* for CD4<200.
* For individuals who are HIV-infected and VLS (*c* = 10, 15, 20, 25), their mortality rates are equal to *Annual probability of death if HIV infected and VLS, by disease stage.*
* For all other individuals who are HIV-infected (*c* = 3 to 9, 11 to 14, 16 to 19, 24), their mortality rates are equal to *Annual probability of death if HIV infected and VLS, by disease stage* times a multiplier that is specific to the continuum-of-care stage (*r*).
* For all individuals who are susceptible (*c* = 1, 2), mortality is assumed to be based on Life Tables in Arias (2008), as specified by *Annual probability of death if HIV uninfected.*

The number of people aging out of the population is equal to the rate of aging out of age group 45–64 (*j* = 5) multiplied by the number of individuals in age group 45–64 (*j* = 5).

The number of people living with HIV (PLWH) who have aged out of the modeled population (aged 65 or older and still alive) is estimated over time based on the initial prevalence of PLWH over the age of 65 in 2006 (28,200, per CDC, 2012b), the cumulative number of PLWH who have aged out since 2006, and the cumulative number of deaths among PLWH aged 65 or older since 2006 (assuming an annual death rate of 0.0954, the average annual probability of death for persons between the ages of 65 and 99 reported in Life Tables in Arias [2008]). This population is only considered for calculating specific outcomes and has no effect on the modeled compartments. PLWH aged 65 or older are stratified by sex, race/ethnicity, and transmission group, resulting in 15 subpopulations.

## 

Table 5.1. Rate of Aging into Population and Inputs that Determine All HIV Progression and Death Rates

| Parameter | 13–17 Years | 18–24 Years | 25–34 Years | 35–44 Years | 45–64 Years | Source |
| --- | --- | --- | --- | --- | --- | --- |
| Annual rate of aging into population per person in youngest age group by race/ethnicity and transmission group | | | | | | |
|  | ------------0.2175 if youngest age group = 13–17-------------  -------------0.1429 if youngest age group = 18–24------------ | | | | | Assumeda |
| Number of years in each stage if HIV infected and not prescribed ART (*r* = 1, 2, 3) | | | | | | |
| Acute | -----------------------------0.17---------------------------------- | | | | | Fiebig et al. (2003) |
| CD4 > 500 | -----------------------------3.50---------------------------------- | | | | | Assumed 7 years in latent asymptomatic state (non-acute, CD4 >350) distributed evenly between CD4 350–500 and CD4 > 500 based on Dorrucci et al. (2007); CGAIHS (2000); Mellors et al. (1997); Antiretroviral Therapy Cohort Collaboration (2007) |
| CD4 350–500 | -----------------------------3.50---------------------------------- | | | | |
| CD4 200–350 | -----------------------------3.00---------------------------------- | | | | | Juusola et al. (2012) applied 3 years in late symptomatic stage, citing Long et al. (2009, 2010); Mellors et al. (1997); and Dunn et al. (2008) |
| CD4 < 200b | -----------------------------3.00---------------------------------- | | | | | Juusola et al. (2012), increased to 3 years to produce # of deaths consistent with CDC surveillance data. |
| Annual rate of progressing one disease stage (to lower CD4 count) if prescribed ART, but not VLS (*r* = 4) | | | | | | |
| CD4 > 500 | -----------------------------0.026--------------------------------- | | | | | Determined by calibrationc |
| CD4 350–500 | -----------------------------0.025--------------------------------- | | | | |
| CD4 200–350 | -----------------------------0.026--------------------------------- | | | | |
| Annual rate of progressing by one disease stage (to lower CD4 count) while VLS (*r* = 5) | | | | | |  |
| CD4 > 500 | ------------------------------0.045-------------------------------- | | | | | Determined by calibrationc |
| CD4 350–500 | ------------------------------0.045-------------------------------- | | | | |  |
| CD4 200–350 | ------------------------------0.045-------------------------------- | | | | |  |

(continued)

Table 5.1. Rate of Aging into Population and Inputs that Determine All HIV Progression and Death Rates (continued)

| Parameter | 13–17 Years | 18–24 Years | 25–34 Years | 35–44 Years | 45–64 Years | | Source |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Annual rate of improving one disease stage (to higher CD4 count) while VLS (*r* = 5) | | | | | | |  |
| CD4 350–500 | -----------------------------0.43------------------------------- | | | | | | Determined by calibrationc |
| CD4 200–350 | -----------------------------0.43------------------------------- | | | | | |
| CD4 < 200 | -----------------------------0.40------------------------------- | | | | | |
| Annual probability of death if HIV infected and VLS in second time period, by disease stage (*r* = 5; range across race/ethnicities) | | | | | | | |
| CD4 > 200 | 0.0065 | 0.0065 | 0.0065 | 0.0122 | 0.0203 | | NA-ACCORD (2014)d |
| CD4 < 200 | 0.0212 | 0.0212 | 0.0212 | 0.0232 | 0.0330 | |
| Annual probability of death if HIV infected and VLS in third time period, by disease stage (*r* = 5; range across race/ethnicities) | | | | | | | |
| CD4 > 200 | 0.0060 | 0.0060 | 0.0060 | 0.0095 | 0.0188 | | NA-ACCORD (2014)d |
| CD4 < 200 | 0.0108 | 0.0108 | 0.0108 | 0.0126 | 0.0326 | |
| Relative risk of death vs. VLS in second and third time periods | | | | | | | |
| Not prescribed ART (*r* = 1,2,3) | ----------------------------1.00------------------------------- | | | | | Assumed due to lack of data demonstrating differences in death rates due to VLS. | |
| Prescribed ART, but not VLS (*r* = 4) | ----------------------------1.00------------------------------- | | | | |
| Relative risk of death if uninfected for PWID vs. non-PWID population | | | | | | | |
| PWID | ----------------------------2.54-------------------------------- | | | | | | Vlahov et al. (2008)e |

(continued)

Table 5.1. Rate of Aging into Population and Inputs that Determine All HIV Progression and Death Rates (continued)

| Parameter | 13–17 Years | 18–24 Years | 25–34 Years | 35–44 Years | 45–64 Years | Source |
| --- | --- | --- | --- | --- | --- | --- |
| Annual probability death if HIV uninfected | | | | | | |
| HET or MSM |  |  |  |  |  |  |
| Female | 0.0002 | 0.0004 | 0.0006 | 0.0013 | 0.0048 | Arias (2012) |
| Male | 0.0005 | 0.0013 | 0.0014 | 0.0021 | 0.0079 |
| PWID |  |  |  |  |  |  |
| Female | 0.0006 | 0.0011 | 0.0016 | 0.0032 | 0.0121 | Calculatede |
| Male | 0.0013 | 0.0032 | 0.0036 | 0.0054 | 0.0201 | Calculatede |

Note: ART = antiretroviral therapy; B = black; H = Hispanic/Latino; O = other race; CDC = Centers for Disease Control and Prevention; HET = heterosexual; HIV = human immunodeficiency virus; MSM = men who have sex with men; NCHS = National Center for Health Statistics; PLWH = people living with HIV; PWID = people who inject drugs

a If the youngest age group is 13 to 17, the rate was set approximately equal to 1 ÷ (number of years in the 13 to 17 age group) and adjusted so that the population size was stable over time (until 2015). If the youngest age group is 18 to 24, the rate of aging into the model is equal to 1 ÷ (number of years in the 18 to 24 age group).

b Departure from CD4 < 200 stage leads to death from AIDS.

c It is assumed that PLWH who are ART-not-VLS experience slowed disease progression and that those who are VLS experience mostly improvement in CD4 rather than disease progression. These assumptions were found to be mathematically essential for the model to simultaneously replicate both the incidence and prevalence trends reported in CDC surveillance data. See Section 9 for further details on the calibration process.

d Source based on ages 18 or older. The probabilities are assumed to be the same for ages 13 to 17, 18 to 24, and 25-34. Values calculated directly from NA-ACCORD data based on mortality rates of NA-ACCORD participants.

e Calculated as the risk from CDC/NCHS life tables multiplied by the relative risk of death for PWID versus non-PWID population.

Table 5.2. Inputs for Calculating Rates of Undiagnosed HIV-Infected and HIV-Uninfected Individuals Getting Tested

| Parameter | Value | Source |
| --- | --- | --- |
| Annual rate of HIV-infected individual getting tested for reference case in second and third time periods (HET, Black, CD4 > 500) | | |
|  | 0.141 | Determined by calibration |
| Multiplier for annual rate of getting tested by HIV stage, race/ethnicity, and transmission group versus the reference case in second and third time periods a | | |
| HIV status (reference: non-acute, CD4 > 500) |  | |
| Uninfected | 0.43 | Derived from CDC (2013b)b |
| Acute | 1.15 | Determined by calibration |
| CD4 350–500 | 2.08 |
| CD4 200–350 | 4.34 |
| CD4 < 200 | 6.87 |
| Race/ethnicity (reference: Black) |  |  |
| Hispanic/Latino | 0.71 | Determined by calibration |
| Other | 0.64 |
| Transmission group (reference: HET) |  | Determined by calibration |
| PWID | 1.79 |
| MSM | 1.99 |

Note: HET = heterosexual; HIV = human immunodeficiency virus; MSM = men who have sex with men; PWID = people who inject drugs

a Literature also suggested that testing rates varied by age (CDC, 2012a); but as a simplifying assumption, we applied constant testing rates by age

b Estimated so that the percentage of uninfected individuals getting tested across all races and transmission groups is consistent with published data on the total number of tests conducted and the percentage of HIV tests that are positive (CDC [2013b]).

Table 5.3. Calculated Annual Rate of an HIV-Infected Undiagnosed or HIV-Uninfected Individual Getting Tested in Second and Third Time Periods

| Parameter | Black | Hispanic | Other | Source |
| --- | --- | --- | --- | --- |
| Calculated annual rate of getting tested in second and third time periods | | | | |
| HET |  |  |  |  |
| Uninfected | 0.066 | 0.072 | 0.088 | Calculateda |
| Acute | 0.157 | 0.172 | 0.210 |
| CD4 > 500 | 0.152 | 0.166 | 0.202 |
| CD4 350–500 | 0.321 | 0.351 | 0.429 |
| CD4 200–350 | 0.554 | 0.605 | 0.739 |
| CD4 < 200 | 0.974 | 1.065 | 1.301 |
| PWID |  |  |  |  |
| Uninfected | 0.159 | 0.174 | 0.212 | Calculateda |
| Acute | 0.380 | 0.416 | 0.508 |
| CD4 > 500 | 0.366 | 0.400 | 0.489 |
| CD4 350–500 | 0.777 | 0.849 | 1.038 |
| CD4 200–350 | 1.338 | 1.463 | 1.787 |
| CD4 < 200 | 2.355 | 2.574 | 3.144 |
| MSM |  |  |  |  |
| Uninfected | 0.183 | 0.200 | 0.245 | Calculateda |
| Acute | 0.438 | 0.479 | 0.585 |
| CD4 > 500 | 0.422 | 0.461 | 0.564 |
| CD4 350–500 | 0.895 | 0.978 | 1.195 |
| CD4 200–350 | 1.542 | 1.685 | 2.059 |
| CD4 < 200 | 2.713 | 2.965 | 3.622 |

Note: HET = heterosexual; HIV = human immunodeficiency virus; MSM = men who have sex with men; PWID = people who inject drugs

a Calculated as the product of the annual rate of getting tested for a reference group (black HIV-infected HET with CD4 >500) and relative risk values specific to that individual’s transmission group, race/ethnicity, and HIV status, as reported in Table 5.2.

Table 5.4. Testing Performance Parameters

| Input | Value | Source |
| --- | --- | --- |
| Test sensitivity,a acute HIV |  |  |
| Rapid screen | 0.0173 | Average of Oraquick and Clearview tests from Pilcher et al. (2013)b |
| Conventional screen | 3G: 0.5090 | 3G: Hutchinson et al. (2013) |
| 4G: 0.8276 | 4G: Hutchinson et al. (2013), which cited Chavez et al. (2011) |
| Confirmatory test | Western blot: 0.0 | Assumption based on length of Western blot window period (Feibig et al., 2003) |
| Test sensitivity, chronic HIVc |  |  |
| Rapid screen | 0.993 | OraQuick ADVANCE:  Rapid HIV-1/2 Antibody Test package insert |
| Conventional screen | 3G: 0.9968  4G: 0.9986 | Hutchinson et al. (2013), which cited package insert data (3G) and Chavez et al. (2011) (4G) |
| Confirmatory testd | Western blot: 1.0 | Assumption in Hutchinson et al. (2013) |
| Percent compliance with testing at a specified interval (without outreach) | | |
| Ages 18–64 |  |  |
| Low risk | 35.0% | Chou et al. (2012) |
| High risk | 60.0% |
| Ages 13–17 |  |  |
| Low risk | 31.5% | Freeman et al. (2009) found uptake of 82% among teens and 91% among adults, which was equivalent to a 10% reduction in uptake in teens versus adults. Applied same relative reduction to ages 13 to 17 versus 18 to 64 for both risk levels. |
| High risk | 54.1% |
| Effect of outreach, as measured by relative increase in compliance with testing | 30.0% | Assumption based on a hypothetical outreach program with 30% effectiveness at increasing compliance. |

a The window period during which acute HIV is not detectable is factored into the calculation of test sensitivity for individuals with acute HIV.

b Calculated as average test sensitivity for Oraquick and Clearview tests for acute HIV.

c Early infection, the time after acute infection but before viral set point when transmission risk per contact is elevated and testing is less sensitive is not accounted for in the model.

d Because all negative confirmatory tests are followed up by a nucleic acid amplification test (NAT) with 100% sensitivity, the sensitivity of the screening process to determine progression does not consider sensitivity of the confirmatory test. The only effect is on cost.

Table 5.5. Annual Probability of Being Prescribed ART in Second and Third Time Periods

| Parameter | Acute | CD4 > 500 | CD4  350–500 | CD4  200–350 | CD4 < 200 | Source |
| --- | --- | --- | --- | --- | --- | --- |
| Annual probability of being prescribed ART, for reference case in second and third time periods | | | | | | |
|  | 0.000 | 0.540 | 0.600 | 0.750 | 0.920 | Fleishman et al. (2012)a |
| Relative risk of being prescribed ART in second and third time periods, by race/ethnicity | | | | | | |
| Black | ---------------------------------------------1.88---------------------------------------- | | | | | Determined by calibration |
| Hispanic | ---------------------------------------------1.26---------------------------------------- | | | | |
| Other | ---------------------------------------------2.577---------------------------------------- | | | | |

Note: ART = antiretroviral therapy; HIV = human immunodeficiency virus

a Examined ART use as a function of sex, race/ethnicity, HIV risk group, age, and CD4 history (no test< 500 cells/mm3, one or more tests between 500 and 350 cells/mm3, one test ≤ 350 cells/mm3, and two or more tests ≤ 350 cells/mm3). Fleishman et al., (2012) reported the proportion of patients in care who initiated ART in 2008 with CD4 levels of interest based on the HIV Research Network (HIVRN) study of HIV-infected adults (> 18 years of) age who first presented for clinical care during the period from January 1997 to December 2007. We assumed that one test with ≤ 350 cells/mm3 is approximation for CD4 250-350 in our model and two tests with ≤ 350 cells/mm3 is for CD4<200.

Table 5.6. Other Continuum-of-Care Probabilities

| Parameter | Black | Hispanic | Other | Source |
| --- | --- | --- | --- | --- |
| Percentage of tests that are rapid vs. conventional | 50% | 50% | 50% | Assumption based on expert opinion of Angela Hutchinson (2014) |
| Probability of being notified of status if tested with the following: | | | | |
| Conventional test | -------------------------0.80------------------------------- | | | Huang et al. (2015) |
| Rapid test | -------------------------1.00------------------------------- | | |
| Annual probability of diagnosed individual linked to HIV care at diagnosis in second and third time periods | | | | |
|  | 0.790 | 0.830 | 0.860 | CDC (2015) |
| Annual probability of diagnosed individual linked to HIV care each year after first year if CD4>350 (*h* = 1, 2, 3) in second and third time periods | | | | |
|  | 0.200 | 0.184 | 0.163 | Determined by calibration |
| Relative risk of linkage to HIV care in second and third time periods, after diagnosis if CD4 ≤ 350, by disease stage (reference: CD4>350) | | | |  |
| CD4 200–350 (*h* = 4) | ------------------------------6.120------------------------- | | | Determined by calibration |
| CD4 < 200 (*h* = 5) | ------------------------------4.529------------------------- | | |
| Annual probability of dropping out of care if linked to HIV care (from *r* = 3 to *r* = 2) in second and third time periods | | | |  |
|  | 0.280 | 0.237 | 0.252 | Determined by calibration |
| Annual probability of dropping out of ART and moving to linked-to-HIV-care (from *r* = 4 to *r* = 3) in second and third time periods | | | |  |
|  | 0.140 | 0.155 | 0.116 | Determined by calibration |
| Annual probability of dropping out of ART (from *r* = 4 to *r* = 2)b | 0.000 | 0.000 | 0.000 | Flow not considered in base model. |
| Annual probability of loss of VLS if VLS (from *r* = 5 to *r* = 4) in second and third time periods | 0.253 | 0.200 | 0.252 | Determined by calibration |

(continued)

Table 5.6. Other Continuum-of-Care Probabilities (continued)

| Parameter | Black | Hispanic | Other | Source |
| --- | --- | --- | --- | --- |
| Annual probability of transitioning from VLS to LTC no ART affects (from r = 5 to r = 3) b | 0.000 | 0.000 | 0.000 | Flow not considered in base model. |
| Annual probability of transitioning from VLS to Aware (from r = 5 to r = 2)b | 0.000 | 0.000 | 0.000 | Flow not considered in base model.  Determined by calibration. |
| Annual probability of becoming VLS if ART-not-VLS (from r = 4 to r = 5) in second and third time periods | 0.236 | 0.404 | 0.147 |
| Percentage of individuals prescribed ART (from linked to HIV care) who become viral load suppressed | ---------------------------80.0%--------------------------- | | | Althoff et al. (2010) |

Note: ART = antiretroviral therapy; CDC = Centers for Disease Control and Prevention; DHHS = Department of Health and Human Services; HIV = human immunodeficiency virus; VLS = viral load suppressed

a A detailed description of the distribution of individuals who are prescribed ART but not VLS is provided in Section 5.5.

b Since all values for these transitions are currently 0, the arrows representing these transitions are not included in the current model flow diagram

## Transitions between Subpopulations (Aging Only)

Individuals can only transition between demographic subpopulations by aging. That is, all of an individual’s demographic characteristics remain the same for the duration of the model except their age. The rate of aging out of age group *j* and into age group *j*+ 1 (where *j* < 5) or out of the population (where *j* = 5),is equal to 1 ÷ (the number of years in age group *j*).

In reality, individuals in the U.S. population move between subpopulations in other ways, such as transitioning between transmission risk groups or risk levels, or going from uncircumcised to circumcised; however, as a simplifying assumption, those transitions are not considered in this model.

## Transitions between Compartments Due to Disease Progression

Transitions between disease stages occur by infection and by HIV progression. The rates at which individuals transition from any disease stage *h* (where *h ≥ 1*) to *h* + 1 or *h* − 1 (or to death in the case of *h =*5) are assumed to be constant. For stages in which patients are not prescribed ART (*r* = 1, 2, 3), the rates from *h* to *h* + 1 are equal to 1 ÷ (duration of stage *h*). Otherwise, the rates are specified directly. For VLS stages (*r* = 5), progression may occur from disease stage *h* to *h* + 1 or to *h* − 1, but for all other continuum-of-care stages, progression may only occur from *h* to *h* + 1. All inputs that determine these progressions are specified in Table 5.1.

## Transitions between Compartments Due to Progression along the Care Continuum

Transitions between continuum-of-care stages occur because HIV-infected individuals become aware of their status through testing and notification of positive results either without immediate linkage to HIV care (*r* = 1 to *r* = 2) or with immediate linkage to HIV care (*r* = 1 to *r* = 3), are linked to HIV care after diagnosis (*r* = 2 to *r* = 3), depart from care (*r* = 3 to *r =*2), are prescribed ART (*r* = 3 to *r* = 4 or *r* = 3 to *r =*5), drop off of ART (*r =*4 to *r =*3), or resume or lose viral load suppression (*r* = 4 to *r =*5 or *r* = 5 to *r =*4).

We assume that individuals with acute HIV are not prescribed ART. Individuals who are ART-not-VLS (*r =*4) experience declines in their CD4 counts but have a slower disease progression than the natural history of HIV (where natural history is the progression that occurs without exposure to treatment). Individuals who are VLS (*r =*5) are very different from individuals in other continuum stages in that they can experience either increases or decreases in their CD4 counts and, in fact, they are more likely to experience an increase than a decrease in their CD4 counts.

Uninfected individuals may participate in PrEP. Details about initiating and stopping that participation are discussed in Section 5.4.3.

Individuals who depart from care are assumed to return to the aware stage, which includes individuals who have never been in care. This assumption of aggregating individuals who have never been in care with those who have dropped out of care was a simplifying assumption. The parameters that determine these transitions are outlined in Tables 5.2 to 5.6. Inputs that determine progression for the first time period are omitted from these tables since they represent the model run-in period. The different methods that can be applied to calculate progression along the care continuum are explained in Section 5.4.1. A detailed explanation of the methods applied for calculating testing rates is presented in Section 5.4.2.

### Methods for Calculating Progression along the Care Continuum

The model uses three methods for calculating progression along the HIV care continuum. Two of those methods can only be applied in the third time period; they exist to allow for exploration of hypothetical scenario analyses. The method is user-selected from the following options:

* Status quo method: User-inputted annual probabilities or rates and, in some cases, relative risk factors by subpopulation or disease stage
* HET interval-based testing method (affecting testing in third time period only): User-inputted testing intervals and symptomatic testing for high-risk HETs and low-risk HETs in the third time period only; otherwise all progression for other stages, subpopulations, and time periods is the same as under the status quo method.
* Allocation-based method (third time period only): Selected rates and probabilities of progression in the third time period are determined by (a) base rates and probabilities of progression without CDC funding for interventions and (b) progression that is determined by the levels of funding allocated to a select set of interventions. It is applied in the third time period; in all other time periods and for all other steps of progression (besides the selected set affected by this method), progression is the same as under the status quo method. This method must be applied to observe the impact of funding to specific interventions on the epidemic.

The default is to apply the status quo method for all time periods. Table 5.7 identifies the steps of progression that are affected by the method selected. Progression along the care continuum in the first and second time periods is always determined by the status quo method.

Table 5.7. Progression along the Care Continuum (and Initiation of PrEP) Affected by Using Interval-Based Testing or Allocation Method (in Third Time Period Only)

| Rates and Probabilities that Determine Progression Along Care Continuum (and Initiation of PrEP) | Different than SQ Rates When Using | |
| --- | --- | --- |
| Interval-Based Testing Method | Allocation-Based Method |
| Testing rates (which affect the *r* = 1 to *r* = 2 and *r* = 1 to *r* = 3 transitions) | X (for HETs only) | X |
| Probability of linkage to HIV care at diagnosis (which affects *r* = 1 to *r* = 2 and *r* = 1 to *r* = 3 transitions) |  | X |
| Rate of loss of VLS (*r* = 5 to *r* = 4) |  | X |
| PrEP initiation rate (*c* = 1 to *c* = 2) |  | X |
| All other rates and probabilities that determine progression along care continuum |  |  |

Note: HET = heterosexuals; SQ = status quo; PrEP = pre-exposure prophylaxis

#### Status Quo Method

Under the status quo method, annual rates of progression are calculated directly from user-inputted annual probabilities or rates and, in some cases, relative risk factors by subpopulation or disease stage. If probabilities of transition are entered, rates are calculated by using Equation (5.1). If relative risk factors apply, they are multiplied by the annual rates by subpopulation or disease stage as appropriate. The inputs used to determine progression under the status quo method are specified in Tables 5.2 to 5.6. Many of those were estimated through a calibration process so that their values resulted in model outcomes (e.g., the percentages of the HIV-infected population that were diagnosed and VLS in both 2009 and 2012 and the number of new infections in 2009 and 2013) that closely matched surveillance data (CDC, 2015, 2014, 2012a), as outlined in Section 10.1.

Annual rate = −ln(1 ‒ Annual probability of transition) (5.1)

We consider the testing rate as an example of how the status quo method is used to calculate one of the steps of progression. The eligible testing pool includes all HIV-uninfected and undiagnosed HIV-infected individuals. The annual rates varied by subpopulation *p* and HIV status *h* (defined by infection status and, if infected, HIV stage) and were calculated as a product of a base rate and multipliers specific to race/ethnicity, transmission group, and HIV status, as defined by Equation (5.2). Both the base rate and the multipliers were estimated through the model’s calibration process. The parameters that determine the status quo testing rates in the second and third time periods are defined in Table 5.2; the calculated rates based on those parameters are listed in Table 5.3.

=   
(*Annual base testing rate of HIV-infected individuals who are HET, Black, CD4 > 500 at t*)   
x (*HIV-status testing multiplier*c at time *t*)   
x (Race/ethnicity testing multiplierp at time *t*)   
x (Transmission group testing multiplierp),

for *c* = {3, 6, 11, 16, 21} (5.2)

where

* = rate of testing of undiagnosed individuals in compartment *c*, at time *t*, by demographic subpopulation *p*.

#### HET Interval-Based Testing Method

The HET interval-based testing method applies user-inputted testing intervals for high-risk HETs and low-risk HETs separately in the third time period only. Otherwise all progression for other stages, subpopulations, and time periods is the same as under the status quo method. Under the HET interval-based testing method, testing rates for HETs are calculated based on testing intervals using Equations (5.3) and (5.4). It is applied only for certain model scenarios during the third time period to the subpopulations *p* that are HETs; all other subpopulations *p* remain at the status quo testing rates. Symptomatic testing is also included under this method for HETs with AIDS (CD4 ≥ 200).

The method implicitly assumes that for the high-risk and low-risk HETs tested at the rates determined by the intervals (versus symptomatic testing, explained in detail below), (a) testing rates are independent of race/ethnicity; (b) with the exception of individuals with AIDS (CD4 ≥ 200), testing rates are independent of HIV status; (c) each year, a portion of the population is compliant with screening at the specified interval (that portion is < 100% for all intervals except under the no-screening scenario, in which no non-symptomatic testing is done); and (d) the remaining noncompliant portion of the population is screened on average once every 20 years. The model allows scenarios to be run that include an outreach testing intervention to increase the portion of the eligible population screened at the specified intervals. Relevant parameter values are included in Table 5.4. Equation (5.3) describes the calculation of screening rates for undiagnosed HIV-infected people without AIDS (CD4 ≥ 200) when using the HET interval-based testing method.

, for *c* = {3, 6, 11, 16},   
 *t* ≥ third time period, *p* = {High-risk HET and low-risk HET subpopulations} (5.3)

where

* = average interval between tests in months by subpopulation *p*, and
* = percentage of subpopulation *p* compliant with testing at the given interval.

For undiagnosed HIV-infected people with AIDS (CD4 < 200), the HET interval-based testing method also considers symptomatic testing by assuming that if the testing rate for HIV-infected people with AIDS (CD4 < 200) under the status quo method is greater than the rate determined by the specified interval, then the testing rate determined by the status quo method is applied. Equation (5.4) reflects this assumption.

= max {,

[(*Annual base testing rate of HIV-infected individuals who are HET, Black, CD4 > 500 at t*)   
x (*AIDS testing multiplier* at time *t*)   
x (Race/ethnicity testing multiplierp at time *t*)},

for *c* = {21}, *t* ≥ third time period, *p* = HET subpopulations only (5.4)

#### Allocation-Based Method

Using the allocation-based method, selected rates and probabilities of progression in the third time period (as specified in Table 5.7) are determined by (a) base rates of progression without the budget under consideration and (b) progression that is determined by the levels of funding allocated to a select set of interventions. It applies rates calculated using Equation (5.5). All other rates and probabilities (besides the selected set) are the same as under the status quo method.

(5.5)

for all j\* = {Testing high-risk HETs, Testing low-risk HETs, Testing high-risk MSM, Testing low-risk MSM, Testing PWID, Linkage to HIV care at diagnosis, Linkage to HIV care later after diagnosis, ART prescription, ART adherence for becoming VLS}

where

* = annual funding allocation for implementing intervention j\*;
* = rate of progression targeted by intervention j\* for subpopulation p in compartment c at time t, given allocated funding for intervention j\* from budget under consideration;
* = rate of progression targeted by intervention j\* for subpopulation p in compartment c at time t, given no allocated funding for intervention j\* from budget under consideration;
* = number of individuals in subpopulation p eligible for intervention j\* at time t, calculated by Equation (5.6):

(5.6)

* = number of times intervention j\* funded for individuals in subpopulation p over time step t, given allocated budget , calculated by Equation (5.7):

(5.7)

* = per-person cost of implementing intervention j\*, as incurred by the agency funding the intervention;
* = binary indicator of eligibility for intervention j\* for individuals in compartment c (1 = eligible, 0 = not eligible);
* = binary indicator that subpopulation p is targeted by intervention j\* (1 = included, 0 = not included);
* = Number of individuals in the population in compartment *c* and demographic subpopulation *p* at time *t* givenallocated budget (relevant only when progression along the HIV continuum of care is determined by allocation-based progression)
* = maximum reach for intervention j\* in any one year among individuals eligible for that intervention;
* = maximum annual rate of the transition targeted by intervention j\* for j\* = {1,…,5,7,…10} among individuals eligible for that intervention, calculated by Equation (5.8):

for j\* = {1,…,5,7,…10} (5.8)

* = maximum annual probability of transition targeted by intervention *j\** for j\* = {6} among individuals eligible for that intervention, calculated by Equation (5.9):

for j\* = {6} (5.9)

### Diagnosis Rates

The annual diagnosis rate of unaware HIV-infected individuals is a function of the testing rate (, as determined by any of the methods used to generate testing rates), the use of rapid (versus conventional) tests, the sensitivity of the tests used, and the likelihood of individuals getting notified of results. The diagnosis rates are calculated using Equation (5.10) and vary by time *t* and HIV status *h* (captured in compartment *c*), and by race/ethnicity, transmission group, and risk level (captured in subpopulation p):

(5.10)

where

* = diagnosis rate based on test and notification of unaware infected individuals in compartment *c*, progressing them from unaware(*r =*1) to aware (*r* = 2 or *r =*3), by subpopulation *p*, for *c* = {3, 6, 11, 16, 21};
* = percentage of screens that are rapid (type of test *g* = 1), by subpopulation *p* and time *t;*
* = probability of notification given a confirmed positive test result for a previously undiagnosed individual in subpopulation *p* and type of test *g* at time *t*; and
* *wc,g =* test sensitivity by compartment *c* and type of test *g*.

Undiagnosed infected individuals who are diagnosed progress either to the aware stages without immediate linkage to HIV care (*r =*1 to *r* = 2) or to the aware stages with immediate linkage to HIV care (*r =*1 to *r* = 3). HIV-uninfected individuals cannot be diagnosed and do not transition between the main compartments; if tested, they remain in the susceptible stage (*h* = 0); the only effect of their testing in the model is to incur costs. The model assumed 100% test specificity.

### PrEP Participation

Uninfected individuals may initiate or stop participation in PrEP each year in the third time period, but they do not otherwise transition between the continuum-of-care stages. The model’s base case assumes no use of PrEP (rates of PrEP initiation and stopping = 0); it is only explored in alternate analyses.

Those uninfected individuals who are in the “on PrEP” compartment (c = 2) incur costs for PrEP. They also have reduced incidence of HIV infection (further discussed in Section 6.4).

# Force of Infection

This section outlines the methods applied for calculating the force of HIV infection, represented by lambda (λ). Infection via both vaginal and anal sex acts occurs for all transmission groups. Infection via shared needles occurs for PWID only. Infection risk is calculated per person in the susceptible population.

The force of infection for susceptible individuals who are not on PrEP (c = 1) is equal to λ. For susceptible individuals who are on PrEP, their force of infection is equal to λ reduced by a multiplicative reduction in infection risk.

## Sexual and Needle-Sharing Partnerships

The partner pool of each transmission group was restricted so that unlikely transmissions, such as those between HET males and HET males, did not occur and that transmissions come from likely partners, such as from HET males to HET females. To implement this assumption, we created two mixing matrices to represent the distributions of sexual and needle-sharing partners, respectively, of the susceptible population on average within any given year by transmission group, sex, risk level, race/ethnicity, and age group. Because infection risk is calculated from the perspective of the susceptible individual, only the mixing patterns of the susceptible population are relevant.

The distribution of sexual partners was defined by sex and transmission group, race/ ethnicity, age group, and risk level. Tables 6.1 through 6.4 outline the values used to determine the distribution of sexual partners by these categories; Tables 6.5 through 6.7 outline the values used to determine the distribution of needle-sharing partners. The values in several of these mixing matrices (as specified in the *Source* columns) were calibrated to ensure that the annual number of infections in 2009 and 2013 estimated by the model closely matched surveillance data from CDC (2012a). We assumed random mixing within each partner pool.

Table 6.1. Distribution of Sexual Partners by Sex and Transmission Group

| Partnering populations | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| Sex and Transmission Group | HET  Males | HET Females | MSM | PWID Males | PWID Females | Source |
| HET males |  | 99.5% |  |  | 0.5% | Determined by calibration |
| HET females | 97.2% |  | 2.6% | 0.2% |  | Determined by calibration |
| MSM |  | 39.3% | 60.5% |  | 0.3% | Determined by calibration |
| PWID male |  | 69.8% |  |  | 30.2% | Determined by calibration |
| PWID female | 36.9% |  | 1.0% | 62.1% |  | Determined by calibration; PWID females—MSM partnerships assumed |

Note: HET = heterosexual; MSM = men who have sex with men; PWID = people who inject drugs

Table 6.2. Distribution of Sexual Partners by Race/Ethnicity

| Race/Ethnicity | Black | Hispanic | Other | Source |
| --- | --- | --- | --- | --- |
| Black | 89.4% | 2.8% | 7.8% | Determined by calibration |
| Hispanic | 4.8% | 67.5% | 27.8% |
| Other | 4.6% | 6.1% | 89.3% |

Table 6.3. Distribution of Sexual Partners by Age

| Age Group | 13–17 | 18–24 | 25–34 | 35–44 | 45–64 | Source |
| --- | --- | --- | --- | --- | --- | --- |
| 13–17 | 91.05% | 2.24% | 2.24% | 2.24% | 2.24% | Calculated from Glick et al. (2012) |
| 18–24 | 2.24% | 91.05% | 2.24% | 2.24% | 2.24% |
| 25–34 | 9.46% | 9.46% | 62.18% | 9.46% | 9.46% |
| 35–44 | 5.25% | 5.25% | 5.25% | 79.00% | 5.25% |
| 45–64 | 5.25% | 5.25% | 5.25% | 5.25% | 79.00% |

Table 6.4. Distribution of Sexual Partners by Risk Level, by Transmission Group

| Transmission Group | Risk Level | Low | High | Source |
| --- | --- | --- | --- | --- |
| HET | Low | 96.44% | 3.56% | Determined by calibration. Mixing for high-risk level HETs and PWIDs are assumed to be equal. |
| High | 22.39% | 77.61% |
| PWIDa | High | 22.39% | 77.61% |
| MSM | Low | 96.15% | 3.85% |
| High | 23.12% | 76.88% |

Note: HET = heterosexual; PWID = people who inject drugs; MSM = men who have sex with men

a All PWID are high-risk.

Table 6.5. Distribution of Needle-Sharing Partners by Sex (PWID Only)

| Sex | Males | Females | Source |
| --- | --- | --- | --- |
| Males | 62.99% | 37.01% | Assumed proportional to PWID population size from Lansky et al. (2014) |
| Females | 62.99% | 37.01% |

Note: PWID = people who inject drugs

Table 6.6. Distribution of Needle-Sharing Partners by Race/Ethnicity (PWID Only)

| Race/Ethnicity | Black | Hispanic | Other | Source |
| --- | --- | --- | --- | --- |
| Black | 80% | 5% | 15% | Assumed based on Lasry et al. (2012) |
| Hispanic | 5% | 80% | 15% |
| Other | 15% | 5% | 80% |

Note: PWID = people who inject drugs

Table 6.7. Distribution of Needle-Sharing Partners by Age Group (PWID Only)

| Age Group | 13–17 | 18–24 | 25–34 | 35–44 | 45–64 | Source |
| --- | --- | --- | --- | --- | --- | --- |
| 13–17 | 91.05% | 2.24% | 2.24% | 2.24% | 2.24% | Assumed same as sexual mixing by age. |
| 18–24 | 2.24% | 91.05% | 2.24% | 2.24% | 2.24% |
| 25–34 | 9.46% | 9.46% | 62.18% | 9.46% | 9.46% |
| 35–44 | 5.25% | 5.25% | 5.25% | 79.00% | 5.25% |
| 45–64 | 5.25% | 5.25% | 5.25% | 5.25% | 79.00% |

Note: PWID = people who inject drugs

## Per-Partnership Transmission Risk

We calculated the risk of infection per serodiscordant partnership for uninfected individuals according to a Bernoulli process that was a function of per-act transmission risk estimates and the number of sex acts and shared needles per partnership. In this model, per-act transmission risk represents the probability of transmission per sex act or shared needle between an HIV-infected and HIV-uninfected person. This method implicitly assumes that sex acts and shared needles within a partnership are independent, each with the same likelihood of infection based on an average weighted by the likelihood of condom use (Pinkerton et al., 1998). Tables 6.8 through 6.12 list the values applied for all parameters that determined these per-partnership risks, as well as the sources from which those values were obtained.

Table 6.8. Per-Act HIV Transmission Risk and Reductions in Risk Due to Circumcision, Viral Load Suppression, and Condom Use

| Parameter | Value | Source |
| --- | --- | --- |
| Base probability of transmission per unprotected sex act (given, if male, uncircumcised HIV-uninfected partners) | | |
| Vaginal insertive | 0.00041 | Determined by calibration |
| Vaginal receptive | 0.00061 | Determined by calibration |
| Anal insertive | 0.00064 | Determined by calibration |
| Anal receptive | 0.0089 | Determined by calibration |
| Relative risk of transmission per sex act by disease stagea | | |
| Acute | 6.8333 | Wawer et al. (2005) as cited by Sorensen et al. (2012) |
| CD4 > 500 | 0.5833 |
| CD4 350–500 | 0.5833 |
| CD4 200–350 | 1.1667 |
| CD4 < 200 (AIDS) | 3.5833 |
| Base probability of transmission per shared needle | | |
|  | 0.0016 | Determined by calibration within 95% confidence interval (0.0010–0.0050), as applied in Long et al. (2010). |
| Reduction in HIV transmission per sex act due to condom use | | |
| MSM insertive | 0.630 | Smith et al. (2015) |
| MSM receptive | 0.720 | Smith et al. (2015) |
| HET | 0.802 | Weller & Davis (2002) |
| Reduction in HIV transmission per sex act if HIV-uninfected partner is circumcised vs. uncircumcised | | |
| Vaginal insertive | 0.54 | Siegfried et al. (2009) |
| Male-male anal insertive | 0.00 | Assumption due to lack of evidence otherwise. |
| Male-female anal insertive | 0.00 | Assumption due to lack of evidence otherwise. |
| Reduction in HIV transmission per act if partner is VLS vs. not VLS | | |
| Shared needle | 0.665 | Determined by calibration. |
| Sex act | 0.96 | Cohen et al. (2011) |

Note: ART = antiretroviral therapy; HET = heterosexual; HIV = human immunodeficiency virus; MSM = men who have sex with men; VLS = viral load suppressed

a Early infection, the time after acute infection but before viral set point, when transmission risk per sex act or shared needle is elevated and testing is less sensitive, is not accounted for in the model.

Table 6.9. Sexual Partners and Sex Acts

| Parameter | Female | | | Male | | | Source |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Black | Hispanic | Other | Black | Hispanic | Other |
| Annual number of sex acts per partner for HIV-uninfected individuals | | | | | | | |
| HET |  |  |  |  |  |  |  |
| High | ----------------47.3----------------- | | | ----------------27.5------------------ | | | Calculateda, b |
| Low | ----------------35.0----------------- | | | ----------------32.3------------------ | | | Calculateda, b |
| PWID |  |  |  |  |  |  |  |
| High | 6.6 | 1.5 | 3.7 | 9.8 | 12.6 | 11.9 | Calculatedc |
| MSM |  |  |  |  |  |  |  |
| High | N/A | N/A | N/A | 8.2 | 9.7 | 8.6 | Calculatedc |
| Low | N/A | N/A | N/A | 30.9 | 29.4 | 33.1 | Calculatedc |
| Annual number of sexual partners per HIV-uninfected person | | | | | | | |
| HET |  |  |  |  |  |  |  |
| High | 5.1 | 3.7 | 3.1 | 9.3 | 6.3 | 4.5 | Calculated from CDC unpublished datab |
| Low | 1.0 | 0.8 | 0.8 | 1.4 | 1.1 | 0.8 | Calculated from CDC unpublished datab |
| PWID |  |  |  |  |  |  |  |
| High | 10.2 | 43.6 | 18.4 | 6.9 | 5.4 | 5.7 | CDC unpublished data based on 2009 NHBS IDU cycle 2 |
| MSM |  |  |  |  |  |  |  |
| High | N/A | N/A | N/A | 8.3 | 7.0 | 8.0 | CDC unpublished data based on 2008 NHBS MSM cycle 2 |
| Low | N/A | N/A | N/A | 2.2 | 2.3 | 2.0 |
| Annual number of sex acts with all partners per HIV-uninfected person | | | | | | | |
| HET |  | | | | | |  |
| High-risk | -------------------------------------200--------------------------------------- | | | | | | Estimated so that HIV prevalence in low-risk and high-risk HETs was stable over time.d |
| Low-risk | --------------------------------------30--------------------------------------- | | | | | |
| PWID and MSM | --------------------------------------68--------------------------------------- | | | | | | Calculated from Reece et al. (2010a); Herbenick et al. (2010). Further detail on the calculation is available from the corresponding author. |

(continued)

Table 6.9. Sexual Partners and Sex Acts (continued)

|  | Female | | | Male | | | Source |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Black | Hispanic | Other | Black | Hispanic | Other |
| Percentage of uninfected individuals’ vaginal sex acts with infected partners that are protected with a condom when partners are undiagnosed | 30.9% | 25.4% | 17.1% | 30.9% | 25.4% | 17.1% | Reece et al. (2010b) |
| Percentage of uninfected individuals’ anal sex acts with infected partners are protected with a condom when partners are undiagnosed | | | | | | | |
| With male partners | --------------13.2%----------------- | | | ---------------50.0%---------------- | | | Value for female-male partnerships from Reece et al. (2010b)  Value for male-male partnerships from Crepaz et al. (2009); Marks et al. (2001, 2005, 2006, 2009); Sorenson et al. (2012) |
| With female partners | N/A | N/A | N/A | ---------------17.8%---------------- | | | Calculated from Reece et al. (2010b)e |

Note: HET = heterosexual; HIV = human immunodeficiency virus; IDU = injection drug user; MSM = men who have sex with men; NHBS = National HIV Behavioral Surveillance; PWID = people who inject drugs

a Annual number of sex acts per partner were calculated as (annual number of sex acts with all partners if HIV-uninfected or HIV-infected and undiagnosed) ÷ (annual number of sexual partners). Because the denominator (annual number of partners) was stratified by race and the numerator (annual number of sexual acts) was not, we used data from the same source as the denominator (Leichliter, et al., 2010) to calculate overall non-race-specific estimates of annual number of partners. Those non-race-specific estimates were then used in the calculations.”

b CDC unpublished data reported 1.14 partners for all HET and 5.73 for high-risk HETs. Those were combined with race- and sex-specific ratios from Leichliter et al. (2010) to back out race- and sex- specific estimates of number of partners for low-risk and high-risk HETs, respectively.

c Calculated as (annual number of sex acts with all partners if HIV-uninfected or HIV-infected and undiagnosed) ÷ (annual number of sexual partners).

d Applying the same number of sex acts for low-risk and high-risk HETs (68 sex acts, based on Reece et al. [2010a] and Herbenick et al. [2010]) resulted in HIV prevalence that dropped to very low levels in high-risk and rose to very high levels in low-risk HETs over time. No sources were identified for risk-level specific sex acts; therefore, we back-calculated the number of sex acts that resulted in stable prevalence over time for both groups.

e Reece et al. (2010b) report the percentage of condom use for all males and MSM. The HET male-specific percentages were derived by taking the all-male condom use as a weighted average of HET and MSM condom use.

Table 6.10. Percentage of Sexual Acts That Are Anal (vs. Vaginal) in Male-Female Partnerships with Anal Intercourse by Sex- and Age-Group-Specific Population in 2010 and Beyond

| Sex | 13–17 | 18–24 | 25–34 | 35–44 | 45–64 | Source |
| --- | --- | --- | --- | --- | --- | --- |
| Female | 14.3% | 19.0% | 20.6% | 16.6% | 17.3% | NSSHB data from Reece et al. (2010a) |
| Male | 31.6% | 24.6% | 21.9% | 20.5% | 20.9% | NSSHB data from Herbenick et al. (2010) |

Note: NSSHB = National Survey of Sexual Health and Behavior

Table 6.11. Percentage of People Who Have Anal Intercourse in their Male-Female Sexual Partnerships by Sex-, Age Group-, and Race/Ethnicity-Specific Population in 2010 and Beyond

| Sex and Age Group | Black | Hispanic/Latino | Other | Source |
| --- | --- | --- | --- | --- |
| Percentage of people who have anal intercourse in their male-female partnershipsa | | | | |
| Female |  |  |  |  |
| 13–17 | 2.7% | 5.6% | 3.7% | Calculated from Herbenick et al. (2010), Reece et al. (2010a), Dodge et al. (2010), and Finlayson et al. (2011) |
| 18–24 | 14.3% | 29.5% | 20.1% |
| 25–34 | 14.4% | 28.8% | 24.1% |
| 35–44 | 12.2% | 21.0% | 18.2% |
| 45–64 | 9.6% | 12.0% | 7.0% |
| Male |  |  |  |
| 13–17 | 3.0% | 5.3% | 2.5% |
| 18–24 | 6.5% | 11.6% | 5.4% |
| 25–34 | 23.3% | 28.6% | 25.3% |
| 35–44 | 15.8% | 27.0% | 22.8% |
| 45–64 | 10.2% | 18.2% | 12.6% |

a It is assumed that all male-female sexual partnerships include vaginal intercourse.

Table 6.12. Other Risk Behaviors

| Risk Behavior | Value | Source |
| --- | --- | --- |
| Annual number of injections across all partners per year | 299.85 | Calculated from Jenness et al. (2011)a |
| Percentage of injections that are shared | `12.63% | Determined by calibration |
| Annual number of needles shared across all partners | 37.87 | Calculatedb |
| Annual number of needle-sharing partners for PWID | 9.5 | Assumption based on number of sexual partners from CDC unpublished data based on 2009 NHBS IDU cycle 2 |
| Number of needles shared per partner | 3.99 | Calculatedc |
| Percentage of uninfected MSM’s sex acts with other MSM that are insertive (vs. receptive) | 50% | Sorensen et al. (2012) |
| Among people who have AI, percentage of their male-female partnerships with AI and VI in second and third time periods | 80.07% | Determined by calibration |
| Increase in percentage of uninfected individuals' sex acts with HIV-infected partners that are protected with a condom when partner is diagnosed vs. undiagnosed | 53% | Marks et al. (2005) (assumed same for both time periods) |
| Percentage of sex acts in which condom provides effective protection | | |
| VI | 80.2% | Weller and Davis (2002) |
| AI | 70% | Smith et al. (2015) |
| Reduction in number of needles shared with HIV-infected partners who are diagnosed versus undiagnosed or HIV-uninfected | 27% | Assumption based on approximately half of condom use effect from diagnosis on needle-sharing behaviors |

Note: AI = anal intercourse; NHBS = National HIV Behavioral Surveillance; PWID = people who inject drugs; VI = vaginal intercourse

a Calculated as (365 days in a year) x (Percentage of PWID who reported injecting at least one time a day) x (1 injection per day) + (Percentage of PWID who reported injecting less than one time per day) x (0.5 injections per day) = 365 x [(0.643 x 1) + (0.357 x 0.5)] = 299.85.

b Calculated as (Annual number of injections across all partners per year) x (Percentage of injections that are shared) = 299.85 x 12.63% = 37.87.

c Calculated as (Number of needles shared across all partners) ÷ (Annual number of needle-sharing partners for PWID) = 37.87 ÷ 9.5 = 3.99.

### Per-Sex-Act Sexual and Needle Transmission Probabilities

The probability of an HIV-uninfected person acquiring HIV from a sex act with an HIV-infected partner varies by the disease stage and continuum-of-care status of the HIV-infected partner; circumcision status of the HIV-uninfected person; condom usage; transmission group; and type of sex act (i.e., vaginal vs. anal and insertive vs. receptive) (Boily et al., 2009; Leynaert et al., 1998; Osmond et al., 1988; Porco et al., 2004). The probabilities were each calculated as the product of a base probability for an HIV-infected person having unprotected sex act with an uncircumcised (if male) HIV-uninfected partner and the relative risk of transmission by disease stage (base probabilities and relative risks listed in Table 6.8). Multiplicative reductions were then applied to those probabilities for sex acts involving circumcised HIV-uninfected partners, protected sex acts, and sex acts with HIV-infected partners who are VLS.

The base probabilities of transmission per unprotected sex act (given, if male, uncircumcised HIV-uninfected partners) were calibrated. We applied the same sources and methods as were applied in Sorensen et al. (2012) to estimate the relative risk of transmission by disease stage. Sorensen and colleagues used clinical trial data, citing Wawer et al. (2005), on transmission risk from heterosexual partnerships by disease stage of the HIV-infected partner and overall per-act sexual risk to calculate transmission risk by disease stage.

The probability of transmission from a shared needle was calibrated within the confidence intervals reported by Long et al. (2010) and was assumed in the base case not to vary by disease stage in the HIV-infected partner. For needles shared with an HIV-infected partner with VLS, a multiplicative reduction to that probability was applied.

### Number of Sex Acts and Needles Shared per Partner

The number of sex acts per partner was calculated as the annual number of sex acts with all partners divided by the annual number of sexual partners. We assumed no reduction in the number of sex acts across all partners for HIV-infected, diagnosed individuals versus HIV-uninfected individuals and HIV-infected, undiagnosed individuals. The number of sexual partners varied by transmission group, sex, risk level, and race/ethnicity (see Table 6.9).

The number of needles shared per partner was calculated as the annual number of injections across all partners per year multiplied by the percentage of injections that are shared divided by the annual number of needle-sharing partners.

### Calculation of Per-Partnership Transmission Risk

Per-partnership transmission risk is represented by  (beta), which is the probability of transmission for an HIV-uninfected individual in subpopulation *p1* per sexual or needle-sharing partnership from transmission risk type *z* (vaginal, anal, or needle) in a partnership type *y* (male-female partnership with vaginal intercourse only, male-male partnership with anal intercourse only, male-female partnership that includes both vaginal and anal intercourse, or needle-sharing) with a partner who is in subpopulation *p2* and compartment *c*. If the partner is uninfected, the risk is zero. The values of the betas for sexual and needle-sharing partnerships are calculated by using Equations (6.1) and (6.2), respectively.

Equation (6.1) is complex but has a simple structure:

1 − [(Probability of not getting infected by unprotected receptive sex acts)\*  
(Probability of not getting infected by protected receptive sex acts)\*  
(Probability of not getting infected by unprotected insertive sex acts)\*  
(Probability of not getting infected by protected insertive sex acts)].

 =

for z = {vaginal intercourse and anal intercourse}, *y* = {male-female partnerships with vaginal intercourse only, male-male partnership with anal intercourse only, male-female partnership with both vaginal and anal intercourse}, and p1 and p2 = {all subpopulations} (6.1)

 =

for *z* = {needle-sharing}, *y* = {needle-sharing}, and *p1* and   
*p2* = {PWID subpopulations} (6.2)

where

* Sp = number of annual sex acts for an HIV-uninfected individual per partner, HIV-uninfected or undiagnosed, by subpopulation *p*;
* Gz,p,c = percentage of sex acts of risk type z protected with a condom, given partner in compartment *c*, by subpopulation *p*;
* = percentage reduction in per-act transmission probability due to VLS, by compartment c and transmission risk type z;
*  and = per-sex-act transmission probability for unprotected receptive and insertive acts, respectively, of type z (vaginal or anal intercourse) with infected partner in compartment *c*; calculated as a product of *base probability of transmission per unprotected sex act* and *relative risk of transmission per sex act by disease stage*, the latter of which varies by *c*;
* dz = percentage reduction in per-sex-act transmission probability from an act of type z due to condom use;
* bp1,p2,z = percentage reduction in per-insertive sex act transmission probability from an act of type z due to circumcision for an HIV-uninfected individual in subpopulation *p1* with an HIV-infected partner in subpopulation *p2* (0 if subpopulation *p1* is uncircumcised male or female);
* Vp1,p2 = proportion of male-male sex acts by individuals in subpopulation *p1* with individuals in subpopulation *p2* that are receptive (0 if subpopulation *p1* or *p2* is not MSM);
* Ωp1,p2,z,y= proportion of sexual acts by individuals in subpopulation *p1* in partnerships of type *y* with individuals in subpopulation *p2* that are risk type *z* (where *z* = vaginal or anal);
* E = number of needles shared annually per needle-sharing partner by PWID who has never been diagnosed with HIV;
* Τp1,p2,c = reduction in number of needles shared between PWID populations *p1* and *p2* for diagnosed versus undiagnosed or uninfected (0 if compartment *c* is for undiagnosed or uninfected compartments); and
* Θc = probability of HIV transmission per needle shared with an HIV-infected partner in compartment *c*; calculated as a product of *base probability of transmission per shared needle* and *relative risk of transmission per sex act by disease stage*, the latter of which varies by *c*.

## Calculation of Force of Infection

The force of infection λ is defined as the rate of infection per uninfected person across all sources. The method that we applied to calculate force of infection is based on the method applied in Long et al. (2010) but adapted to include multiple transmission groups, and mixing is determined explicitly by inputs defining percentage of partners by race/ethnicity, transmission groups, risk levels, and age groups. Long et al. was based on the heterosexual population only and assumed proportional mixing, in which “persons with many sexual partners are more likely to select a partner who similarly has many partners” (p. 779).

The force of HIV infection is a function of the number of vaginal intercourse, anal intercourse, and needle-sharing partners, per-partnership transmission risk (described in Section 6.2), prevalence of HIV among partners, and the distribution of HIV-infected partners among the different disease and care continuum stages.

The force of HIV infection for non-HIV infected individuals of any given subpopulation *p* is calculated as the sum of the contact rates from five different sources of infection, four sexual contact rates and one needle-sharing contact rate (listed and further described in Table 6.13), as stated in Equation (6.3):

(6.3)

Table 6.13. Five Sources of Infection that Contribute to Overall Force of Infection for Each Subpopulation

| Source of Infection | Relevant Subpopulations (*p*) and Sexual Transmission Participation Type (*x*) | Risk Type (*z*) | Betas () Used in Calculation of Lambda |
| --- | --- | --- | --- |
| VI in people who only participate in VI in their male-female partnerships | p = {All}, x = VI only in male-female partnerships (1) | VI (z=1) | Beta for z = VI, y = male-female partnership that only includes VI |
| AI from male-male partnerships | p = {MSM}, x = AI only in male-male partnerships (2) | AI (z=2) | Beta for z = AI, y = male-male partnership that only includes AI |
| VI in people who participate in AI in their male-female partnerships | p = {All}, x = AI and VI in male-female partnerships (3) | VI (z=1) | Beta for z = VI, y = male-female partnership that includes AI;  Beta for z = VI, y = male-female partnership that only includes VI |
| AI in people who participate in AI in their male-female partnerships | p = {All}, x = AI and VI in male-female partnerships (3) | AI (z=2) | Beta for z = AI, y = male-female partnership that includes AI |
| Needle-sharing | p ={PWID}, x = N/A | Needle-sharing (z=3) | Beta for z = needle-sharing, y = needle-sharing |

Note: AI = anal intercourse; HET = heterosexual; MSM = men who have sex with men; PWID = people who inject drugs; VI = vaginal intercourse

Equation (6.4) then describes the calculation of the force of infection from risk type *z* for uninfected individuals in subpopulation *p* who participate in sexual transmission risk behaviors of each type x, at time *t*. Table 6.13 describes the relevant z, x, p, and y values applied in Equation (6.4).

, (6.4)

where

* = Proportion of subpopulation p who participate in transmission risk participation type *x*, which is calculated based on the following:
  + the input *Percentage of people who have anal intercourse (AI) in their male-female partnerships*
  + the assumption that 100% of MSM have AI in their male-male partnerships, and
  + the assumption that 100% of all transmission groups have vaginal intercourse (VI) in their male-female partnerships.
* ξ z,y,p,p2,c (t) = Number of partnerships of type y involving risk type z per uninfected individual in subpopulation p with infected partners in subpopulation p2 in compartment c at time t, which is calculated using the method outlined in Equation (6.5):

(6.5)

where

* = annual number of partners for risk type z per person in p,
* = percentage of individuals in subpopulation p’s partners that are in p2, as determined by the mixing matrix described in Section 6.1,
* = average percentage of partnerships for an individual in subpopulation p that are type y, given that the individual has partnerships of type y. It is calculated based on the following:
  + the input *Among people who have AI in their male-female partnerships, percentage of those partnerships with AI*, which distributes partnerships for people who have AI in male-female partnerships into partnerships with and without AI
  + the assumption that risk from male-female partnerships does not factor into the calculation of force of infection from male-male sexual partnerships with AI only (z = 2, x = 2)
  + the assumption that risk from male-male partnerships does not factor into the calculation of force of infection from VI in male-female partnerships with VI only (z = 1, x = 1) or from either VI or AI in male-female partnerships with both AI and VI (z = 1 or 2, x = 3).
* = binary indicator that model state c is an infected HIV state (1 = infected, 0 = not infected)
* *Number of partnership type y partners in p2 per person in p* =.

This value () equals 0 for uninfected compartments c = {1 or 2}.

This method captures the following effects on HIV transmission:

* the impact of circumcision on the per-partnership transmission risk (beta)
* the impact of viral load suppression on beta
* the impact of vaginal versus anal sexual risk in all transmission groups on beta
* the impact of the prevalence of HIV in the partner populations on the per-person force of infection (lambda)
* the impact of mixing patterns on lambda

This method has the following simplifying assumption:

* Sufficient partner supply always exists to support the distribution of partners specified by the inputs.

## Force of Infection for Individuals on PrEP

Infection risk for susceptible individuals on PrEP (*c* = 2) is calculated as the infection risk for susceptible individuals not on PrEP () reduced by a multiplicative factor. Those multiplicative factors are listed in Table 6.14.

Table 6.14. Percentage Reduction in Infection Risk if on PrEP

|  |  |  |
| --- | --- | --- |
| Risk Group | Value | Source |
| HET | 75% | Baeten et al. (2012) |
| MSM | 73% | Grant et al. (2010) |
| PWID | 49% | Choopanya et al. (2013) |

Note: HET = heterosexual; MSM = men who have sex with men; PWID = people who inject drugs

We assumed that individuals on PrEP are also already engaged in the health care system and tested for HIV regularly and, therefore, when infected with HIV, immediately diagnosed and linked to HIV care.

# Differential Equations that Define the Model

This section outlines the differential equations that define this model. The equations are organized into subsections by compartments *c* based on disease stage *h*. The differential equations in the model are solved using the Dormand-Prince method of Runge-Kutta solvers (i.e., RK5(4)7FM) with a time-step equal to 1 year. If the user opts to apply discretized versions of these equations, a user-selected time step can be indicated; the default is 0.1 year. Table 7.1 lists the model’s 28 compartments.

Table 7.1. Model Compartments

| Number | Description | Row-Column Designation for Each Compartment |
| --- | --- | --- |
| 1 | Susceptible / not on PrEP | A1 |
| 2 | Susceptible/ on PrEP | A6 |
| 3 | HIV-infected / acute stage / unaware of infection | B1 |
| 4 | HIV-infected / acute stage / aware, but not linked to HIV care | B2 |
| 5 | HIV-infected / acute stage / linked to HIV care, but not prescribed ART | B3 |
| 6 | HIV-infected / CD4>500 / unaware of infection | C1 |
| 7 | HIV-infected / CD4>500 / aware, but not linked to HIV care | C2 |
| 8 | HIV-infected / CD4>500 / linked to HIV care, but not prescribed ART | C3 |
| 9 | HIV-infected / CD4>500 / prescribed ART, but not virally suppressed | C4 |
| 10 | HIV-infected / CD4>500 / virally suppressed, which assumes persons are in care and prescribed ART | C5 |
| 11 | HIV-infected / CD4 350–500 / unaware of infection | D1 |
| 12 | HIV-infected / CD4 350–500 / aware, but not linked to HIV care | D2 |
| 13 | HIV-infected / CD4 350–500 / linked to HIV care, but not prescribed ART | D3 |
| 14 | HIV-infected / CD4 350–500 / prescribed ART, but not virally suppressed | D4 |
| 15 | HIV-infected / CD4 350–500 / virally suppressed, which assumes persons are in care and prescribed ART | D5 |
| 16 | HIV-infected / CD4 200–350 / unaware of infection | E1 |
| 17 | HIV-infected / CD4 200–350 / aware, but not linked to HIV care | E2 |
| 18 | HIV-infected / CD4 200–350 / linked to HIV care, but not prescribed ART | E3 |
| 19 | HIV-infected / CD4 200–350 / prescribed ART, but not virally suppressed | E4 |

(continued)

Table 7.1. Model Compartments (continued)

| Number | Description | Row-Column Designation for Each Compartment |
| --- | --- | --- |
| 20 | HIV-infected / CD4 200–350 / virally suppressed, which assumes persons are in care and prescribed ART | E5 |
| 21 | HIV-infected / CD4 < 200 / unaware of infection | F1 |
| 22 | HIV-infected / CD4 < 200 (AIDS) / aware, but not linked to HIV care | F2 |
| 23 | HIV-infected / CD4 < 200 (AIDS) / linked to HIV care, but not prescribed ART | F3 |
| 24 | HIV-infected / CD4 < 200 (AIDS) / prescribed ART, but not virally suppressed | F4 |
| 25 | HIV-infected / CD4 < 200 (AIDS) / virally suppressed, which assumes persons are in care and prescribed ART | F5 |
| 26 | Death due to non-HIV-related cause | N/A |
| 27 | Death from causes related to AIDS | N/A |
| 28 | Aged out of the population | N/A |

Note: ART = antiretroviral therapy; PrEP = pre-exposure prophylaxis; N/A = not applicable

## Number of Susceptible Individuals

The numbers of susceptible individuals not on PrEP (*c =*1) and on PrEP (c = 2) within each subpopulation *p* are determined by Equations (7.1) and (7.2), respectively. For individuals not on PrEP, the number of susceptible individuals increases by aging into the observed population and susceptible individuals on PrEP stopping PrEP and decreases due to PrEP initiation. The number of susceptible individuals on PrEP increases due to initiation of PrEP and decreases due to stopping PrEP. For both compartments, the number of susceptible individuals decreases by HIV infection, death from causes other than AIDS, or aging out of the modeled population. For both compartments, as well as all other *c*, aging also shifts individuals between age groups.

(7.1)

(7.2)

where

*  = number of individuals in the population in compartment *c* and demographic subpopulation *p* at time *t*;
*  = constant rate of aging into the youngest age group in the modeled population per person (based on the size and distribution of that youngest group at *t* = 0) in subpopulation *p*;
* Yp = annual probability of stopping PrEP if susceptible and on PrEP for subpopulation *p*;
* Ψp(t) = annual probability of initiating PrEP, given eligible, for subpopulation *p* at time *t*;
* *i*p = percentage reduction in the annual rate of HIV transmission if HIV-uninfected individual in subpopulation *p* is on PrEP;
*  = mortality rate among uninfected individuals in subpopulation *p*;
*  = aging rates into (+) subpopulation *p* for all *p* in age groups older than the youngest age group included in the population (*j* = 2, 3, 4, 5 if youngest age group is 13 to 17 and *j* = 3, 4, 5 if youngest age group is 18 to 24); and
*  = aging rates out of subpopulation *p*.

## Individuals with Acute HIV Infection

The numbers of individuals with acute HIV infections (*c =*3, 4, 5) within each subpopulation *p* are determined by Equations (7.3) through (7.5), corresponding to continuum-of-care stages (*r*) 1 to 3, respectively. The numbers of individuals calculated in these equations vary in the factors that increase or decrease their values based on their continuum status; hence, the equations vary in the same way. Transitions that increase the values include HIV infection, diagnosis, and linkage to or departure from HIV care. Transitions that decrease the values include HIV progression, testing and notification of results, linkage to HIV care, ART prescription, death from causes other than AIDS, and aging out of the modeled population. Aging also shifts individuals among age groups.

(7.3)

(7.4)

(7.5)

where

*  = rate of natural history HIV progression from compartment *c* to the next disease stage if not prescribed ART;
*  = diagnosis rate from unaware compartment *c* to awarefor subpopulation *p* at time *t*, for *c* = {3, 6, 11, 16, 21};
*  = mortality rate if HIV-infected, by compartment *c* and subpopulation *p* at time *t*;
*  = rate of ART prescription if linked to HIV care, by compartment c and subpopulation *p* at time *t*, for *c* = {8, 13, 18, 23};
* = rate of departure from HIV care if linked to HIV care, by demographic subpopulation *p* at time *t*, for *c* = {5, 8, 13, 18, 23};
*  = percentage of newly diagnosed individuals in subpopulation *p* who immediately link to care at diagnosis at time *t*; and
* = rate of linkage to HIV care among aware (not newly diagnosed) individuals in compartment *c* for subpopulation *p* at time *t*, for *c* = {4, 7, 12, 17, 22}.

## Individuals with Chronic HIV Infection and CD4 ≥ 200

The numbers of individuals with chronic HIV infection and CD4 ≥ 200 (*c =*6 to 20), by demographic subpopulation *p*, are determined by Equations (7.6) through (7.15), corresponding to continuum-of-care stages (*r*) 1 to 5, respectively. Across these compartments, transitions that can increase the number of individuals in a particular compartment include HIV progression, testing and notification of results, linkage to or departure from HIV care, ART prescription (resulting in VLS or not), loss of ART, and loss of viral load suppression. Transitions that can decrease the number of PLWH in any of these compartments include HIV progression, testing and notification of results, linkage to or departure from HIV care, ART prescription (resulting in VLS or not), loss of ART, loss of viral load suppression, death from causes other than AIDS, death if prescribed ART, and aging out of the modeled population. Aging also shifts individuals among age groups.

*Equations for CD4 > 500 (h = 2):*

(7.6)

(7.7)

(7.8)

(7.9)

(7.10)

*Equations for CD4 200–500 (h =3 or 4):*

for c = {11, 16} (7.11)

for c = {12, 17} (7.12)

for c = {13, 18} (7.13)

for c = {14, 19} (7.14)

for c = {15, 20} (7.15)

where

* = annual rate of dropping off of ART if ART-not-VLS, by demographic subpopulation *p* at time *t;*
* = annual rate of becoming VLS if ART-not-VLS, by demographic subpopulation *p* at time *t;*
* Hc = rate of HIV progression to the next disease stage from compartment *c,* if prescribed ART but not VLS;
* u = percentage of individuals who become VLS among those who are prescribed ART;
* = rate of loss of viral load suppression if VLS, by demographic subpopulation *p* at time;
* = rate of HIV progression to the next disease stage from compartment *c,* if VLS; and
* = rate of HIV progression to the previous disease stage from compartment *c*, if VLS.

## Individuals with AIDS (CD4 < 200) (*h* = 5)

The numbers of individuals with AIDS (*c* = 21 to 25), by demographic subpopulation *p*, are determined by Equations (7.16) through (7.20), corresponding to continuum-of-care stages (*r*)1 to 5, respectively. Across these compartments, transitions that can increase the number of individuals in a particular compartment include HIV progression, testing and notification of results, linkage to or departure from HIV care, ART prescription (resulting in VLS or not), loss of ART, and loss of viral load suppression. Transitions that decrease the number of PLWH in any of these compartments include testing and notification of results, linkage to and departure from HIV care, death from AIDS, and aging out of the modeled population. Aging also shifts individuals among age groups. These equations differ from the other sets of equations in that they include AIDS-related mortality.

(7.16)

(7.17)

(7.18)

(7.19)

(7.20)

## Absorbing States

The model’s absorbing states (*c* = 26 to 28) are compartments that hold individuals who have stopped being actively followed because they have died or have aged out of the population aged 13 to 64. The number of individuals by subpopulation *p* in the absorbing states are determined by Equations (7.21) through (7.23), respectively. Transitions that increase the values include aging out of the population, death from AIDS, and death from causes other than AIDS. No transitions decrease the number of individuals in these states.

 (7.21)

 (7.22)

 (7.23)

# Interventions and Optimization of Allocations to Interventions

When the allocation-based method is applied for calculating progression along the care continuum, the model considers the following 13 interventions in five categories, each aimed at increasing or maintaining progression along the HIV care continuum:

* Testing
  + High-risk HETs
  + Low-risk HETs
  + High-risk MSM
  + Low-risk MSM
  + PWID
* Linkage to HIV care
  + At diagnosis
  + After diagnosis
* ART prescription
* ART adherence
  + To become VLS if prescribed ART and not VLS
  + To remain VLS
* PrEP
  + High-risk HETs
  + High-risk MSM
  + PWID

## Intervention Costs and Effects

If the model is using allocation-based progression, the allocation of funding to interventions affects the rates of progression through the model’s compartments for the observed population in the third time period, as described in Section 5.4.1. Table 8.1 lists the effects of allocating funds to each intervention and the eligible populations and costs of each. Section 5.4.1 describes in detail allocation-based progression and specifically how allocation of funds to an intervention affects progression. Table 8.2 lists key model inputs pertaining to the interventions.

Table 8.1. Eligible Populations, Costs, and Effects of Each Category of Interventions

|  | Population Eligible to Receive Intervention | Rate or Probability and Time Period Directly Affected by Intervention | Per-person Cost of Implementing Each Intervention | Effect of Allocating Funds for One Unit of Intervention |
| --- | --- | --- | --- | --- |
| Testing | All uninfected individuals and undiagnosed infected PLWH | Annual testing rate, which affects diagnosis rate of undiagnosed PLWH, in each year over the time horizon | Uninfected individuals: Cost of testing and notification of an HIV-uninfected person  Infected and undiagnosed individuals: Cost of testing and notification of an HIV-infected individual | Test and notify one undiagnosed PLWH |
| Linkage to HIV care at diagnosis | Newly diagnosed PLWH | Probability of linkage to HIV care at diagnosis, which affects rate of linkage to HIV care at diagnosis (model row 1 to 3) and rate of diagnosis without linkage (row 1 to 2), in each year over the time horizon | Cost to effectively link one additional individual to care at diagnosis | Link an additional newly diagnosed individual to care |
| Linkage to HIV care later after diagnosis | Diagnosed PLWH not currently linked to HIV care | Rate of linkage to HIV care (from aware stage), in each year over the time horizon | Cost to effectively link one additional individual to care at a time point beyond initial diagnosis | Link an additional individual to care |
| ART prescription | PLWH linked to HIV care | Rate of ART prescription in each year over the time horizon | Cost to effectively prescribe ART to an additional individual | Prescribe ART for one additional individual |
| ART adherence (to remain VLS) | PLWH who are VLS | Rate of departure from VLS in each year over the time horizon | Cost to effectively maintain one additional person as VLS | Prevent one individual from losing VLS |

(continued)

Table 8.1. Eligible Populations, Costs, and Effects of Each Category of Interventions (continued)

|  | Population Eligible to Receive Intervention | Rate or Probability and Time Period Directly Affected by Intervention | Per-person Cost of Implementing Each Intervention | Effect of Allocating Funds for One Unit of Intervention |
| --- | --- | --- | --- | --- |
| ART adherence (to become VLS if ART- not-VLS) | PLWH who are prescribed ART but not VLS | Rate to VLS if ART –not-VLS in each year over the time horizon | Cost to effectively transition one individual from ART-not-VLS to VLS | Transition one individual who was ART-not-VLS to VLS |
| PrEP | Uninfected high-risk HETs, high-risk MSM, and PWID | First year of third time period: PrEP initiation rate  Remaining years of third time period: No direct effects  (Effect is in first year of the third time period only because costs will be incurred to maintain the individual on PrEP in following years) | Annual cost for drugs, screening, and monitoring per PrEP participant | First year of third time period: Initiate PrEP for one additional eligible individual; PrEP is associated with a reduction in infection rates  Remaining years of third time period: No direct effects. Costs cover continued PrEP provision for individual who initiated in first year of third time period. |

Note: ART = antiretroviral therapy, HET = heterosexual, MSM = men who have sex with men, PLWH = people living with HIV, PWID = people who inject drugs, PrEP = pre-exposure prophylaxis treatment, VLS = viral load suppressed

Table 8.2. Values and Sources for Key Inputs Specific to Interventions

|  |  |  |  |
| --- | --- | --- | --- |
| Input | | Value | Source |
| Per-person cost of implementing each intervention incurred by the agency funding the interventiona | Testing | $23,420 (2015$) per effectively diagnosed HIV-infected person | Dynamically calculated in modelb |
| LTC at diagnosis | $539 (2002$) | Gardner et al. (2005); reduced intervention cost by 10% to remove overhead costs (i.e., assumed that 10% of intervention cost was due to overhead) |
| LTC after diagnosis | $1,078 (2002$) | Source not identified. Assumed that the cost is twice as much as the cost of LTC at diagnosis, due to the fact that linking individuals who are not already in communication with or present at a provider (like they are at diagnosis) will be harder to link to care. |
| ART prescription | $539 (2002$) | Source not identified. Assumed that the costs are the same as LTC at diagnosis since the processes both similarly involve engaging PLWH in the next level of care. |
| All ART adherence interventions | $2,447 (2002$) | Calculated based on Schackman et al., 2005 and assumption of 17% effectiveness (Friedberg et al., 2006; Barnett et al., 2009) ($34.69 \* 12 / 0.17) |
| PrEP | $17,450 (2015$)c | $15,975 annual drug costs (Truven Health Analytics, 2017; Gebo et al., 2010) + $1,475 screening and monitoring costs (Desai et al., 2008) |
| Maximum percentage of eligible individuals for which intervention can be effectiveb | Testing | 85% | Assumed |
| LTC at diagnosis | 90% | Assumed |
| LTC after diagnosis | 70% | Assumed |
| ART prescription | 85% | Assumed |
| ART adherence | 85% | Assumed |
| PrEP | 90% | Assumed |

(continued)

Table 8.2. Values and Sources for Key Inputs Specific to Interventions (continued)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Input | | | Value | Source |
| Current societal funding to interventions (in millions), by targeted subpopulation | Testing | HETs | Low-risk: $250.0  High-risk: $15.8 | Back-calculated based on unit costs of each interventions to create rates of progression that lead to distributions across the care continuum that match published literature (calibration of model to these distributions explained in Section 10.1). |
| MSM | Low-risk: $3.7  High-risk: $7.5 |
| PWID | $1.2 |
| LTC at diagnosis | | $11.6 |
| LTC after diagnosis | | $28.8 |
| ART prescription | | $64.8 |
| ART adherence (to remain VLS) | | $0.4 |
| ART adherence (to become VLS) | | $270.0 |
| PrEP | HETs | $0 |
| MSM |
| PWID |

Note: ART = antiretroviral therapy, HET = heterosexual, LTC = linkage to HIV care, MSM = men who have sex with men, PLWH = people living with HIV, PrEP = pre-exposure prophylaxis treatment, PWID = people who inject drugs, QALY = quality-adjusted life-year, r/e = race/ethnicity

a We assumed that intervention costs were independent of the level of reach and constant per person. All costs were converted to 2015$ in the calculation of economic outcomes.

b Dynamically calculated in HOPE model under the estimated current societal funding to testing interventions based on test sensitivity, which varies by test type and HIV status (Pilcher et al. (2013); Hutchinson et al. (2013), which cites Chavez et al. (2011) (4G) and Pandori et al. (2009) (3G); Feibig et al. (2003); OraQuick ADVANCE: Rapid HIV-1/2 Antibody Test package insert); percentage of tests rapid vs. conventional (assumed); HIV prevalence in tested population (dynamically calculated in the model); test costs and notification costs, as reported in detail in Sections 9.2.1 and 9.2.2 (Hutchinson et al. (2011, 2013); Pinkerton et al. (2010); Farnham et al. (2008); Shrestha et al. (2008)). Includes cost of testing all HIV-negative and HIV-infected individuals per diagnosed HIV-infected PLWH. This cost varied slightly over time since HIV prevalence in the tested population changed over time; the value reported is the average cost in 2017.

c Allocations to PrEP result in increased PrEP initiation in the first year (2017), but no further increases in initiation in later years over the time horizon. Those allocations are instead assumed to pay for continued years of maintenance on PrEP for those who initiated in 2017. This method implicitly assumes that each individual who initiates PrEP stays on PrEP for the entire model time horizon.

These methods apply the following key assumptions:

* Annual allocations to interventions are constant over the observed time horizon.
* Intervention costs and effects are both independent of the level of reach and constant per person.
* Each intervention funded by the allocation is implemented at the same rate with all eligible individuals to whom it is targeted. Therefore, all individuals eligible for an intervention are equally likely to receive that intervention (e.g., all people who are linked to HIV care and not prescribed ART are equally likely to receive the ART prescription intervention, regardless of disease stage, race, or other factors).
* Allocations to PrEP result in increased PrEP initiation in the first year of the third time period, but no further increases in initiation in later years over the time horizon. Those allocations are instead assumed to pay for continued years of maintenance on PrEP for those who initiated in that first year. The model implicitly assumes that each individual who initiates PrEP stays on PrEP for the entire model time horizon.
* The effect of allocating funds to an intervention over a year is estimated based on the number of individuals eligible for that intervention at the beginning of the year, which implicitly assumes that the number eligible is stable over that year. If the number eligible actually decreases over the year, the effect of the intervention will be less than projected; and vice versa for increases in the number eligible. Historical observation of the model has demonstrated that the error due to this assumption is negligible.
* Allocation of funds to PrEP reduces the risk of infection among susceptible individuals which, in turn, reduces the incidence of new infections. Allocation to continuum interventions redistributes HIV-infected individuals across model states so that more are farther along the care continuum; as a result, the risk of PLWH infecting susceptible individuals declines, which ultimately also reduces incidence.

## Optimization of Funding Allocations to Interventions

When selected, the HOPE Model can be run to optimize allocation of funding to the interventions. Based on user selections, the model optimizes allocation funding to the 13 interventions to either minimize total new HIV infections over the selected time horizon or maximize QALYs over the selected time horizon.

Optimization algorithms in the MATLAB Optimization Toolbox are then used to determine the distribution of the specified budget that most efficiently achieves the selected objective.

The HOPE Model’s optimization process ensures that sufficient funding is available from the allocation to cover the provision of treatment and medical care for the entire HIV-infected population. This is accomplished by dynamically calculating the average annual treatment costs over the time horizon and only considering allocations to continuum and PrEP interventions that, together with the resulting treatment costs, sum to no more than the total budget.

# Additional Details Pertaining to the Analysis Conducted in this Manuscript

This section provides the methods and results of supplementary scenario analyses for the manuscript entitled “Impact of Improved HIV Care and Treatment and Implementing PrEP in the United States, 2016–2020” that were not otherwise presented in the manuscript text.

## Effects of Varying PrEP Efficacy, Coverage, and Dropout Rates on HIV Incidence When Current Care Continuum Levels Were Maintained

We considered additional scenarios in which PrEP efficacy, coverage, and dropout rates were varied from their base case values and observed HIV incidence by transmission risk group and overall; the base case care continuum levels were assumed for these scenarios. Those scenarios were then compared to observe how the marginal impact of PrEP on incidence was impacted by variations of these parameters.

We found that the marginal benefit of PrEP increased with increasing efficacy and coverage (Table 9.1). When the current levels of the HIV care continuum were maintained and PrEP efficacy was set at its lower bound, base case, and upper bound, the corresponding marginal benefit of PrEP in preventing additional cases of HIV was 11.6%, 18.1%, and 22.3%, respectively. When the current levels of the HIV care continuum were maintained and the proportion covered among those eligible was set at the lower bound, base case, and upper bound, the marginal benefit of PrEP was 9.2%, 18.1%, and 26.6%, respectively.

We also found that the marginal benefit of PrEP decreased as the annual rate of dropping off of PrEP increased. When the current levels of the HIV care continuum were maintained and PrEP dropout probabilities were 5%, 20%, and 50%, the marginal benefit of PrEP was 16.4%, 12.1% and 6.4%, respectively, in contrast with the 18.1% marginal benefit of PrEP for the scenario when the dropout probability was zero. We performed this analysis for all risk groups. Our calculations showed that the marginal benefit of PrEP would decrease from 25.2% to 9.0% for MSM as the dropout probability increased from 0% to 50%. The corresponding decrease in marginal benefit of PrEP was from 6.2% to 2.2% for HETs and from 5.0% to 1.7% for PWID.

The effects of adherence, coverage, and dropout are interrelated because they all affect the ability of PrEP to prevent HIV infection. However, each issue calls for a different programmatic approach—whether to encourage more complete adherence among those already prescribed PrEP, to expand coverage to more persons eligible for PrEP, or to support continuing with PrEP at a given adherence level, and not dropping out. Because of the different implications for program implementation, we explored all three in scenario analyses.

Table 9.1 Cumulative HIV Incidence in 2016–2020 and the Marginal Benefit of Delivering PrEP as PrEP Parameters Were Varieda, b

|  | MSM | HET | PWID | Total |
| --- | --- | --- | --- | --- |
| **Varying efficacy (coverage and dropout rate set to base case)** | | | | |
| Efficacy |  |  |  |  |
| Lower bound | 85,847 (16.2%) | 41,156 (4.7%) | 16,462 (1.3%) | 143,466 (11.6%) |
| Base case | 76,562 (25.2%) | 40,473 (6.2%) | 15,849 (5.0%) | 132,833 (18.1%) |
| Upper bound | 70,539 (31.1%) | 39,973 (7.4%) | 15,516 (7.0%) | 126,028 (22.3%) |
| **Varying coverage (efficacy and dropout rate set to base case)** | | | | |
| Coverage |  |  |  |  |
| Lower bound | 89,179 (12.9%) | 41,808 (3.1%) | 16,262 (2.5%) | 147,249 (9.2%) |
| Base case | 76,562 (25.2%) | 40,473 (6.2%) | 15,849 (5.0%) | 132,833 (18.1%) |
| Upper bound | 64,461 (37.1%) | 15,439 (9.3%) | 39,161 (7.4%) | 119,061 (26.6%) |
| **Varying dropout rate (efficacy and coverage set to base case)** | | | | |
| Dropout Rate |  |  |  |  |
| 0% | 76,562 (25.2%) | 40,473 (6.2%) | 15,849 (5.0%) | 132,883 (18.1%) |
| 5% | 78,962 (22.9%) | 40,729 (5.7%) | 15,933 (4.5%) | 135,623 (16.4%) |
| 20% | 85,060 (16.9%) | 41,373 (4.2%) | 16,138 (3.2%) | 142,571 (12.1%) |
| 50% | 93,189 (9.0%) | 42,213 (2.2%) | 16,402 (1.7%) | 151,811 (6.4%) |

HET= heterosexual; MSM= men who have sex with men; PWID= people who inject drugs.

*a* Efficacy, coverage, and dropout rate of PrEP were independently varied for the scenario when current care continuum levels were maintained.

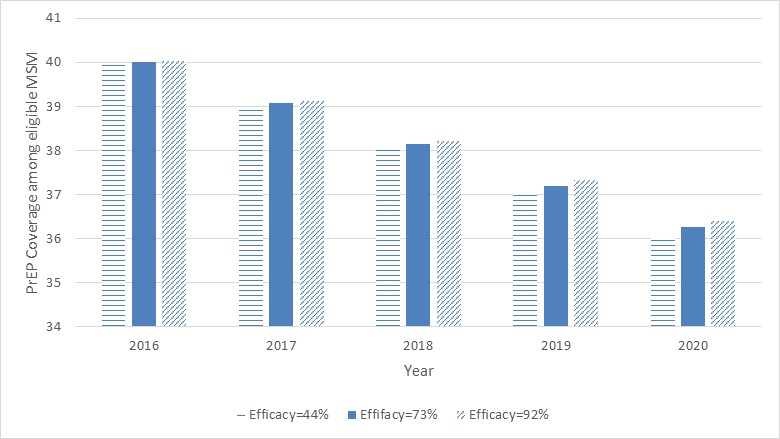
b The numbers in each cell represent the numbers of new infections from 2016 to 2020. The numbers in parentheses represent the corresponding marginal benefit of PrEP (percentage of infections prevented compared to the base case scenario of current continuum-of-care levels without PrEP).

## Effects of Varying PrEP Efficacy and Coverage

PrEP coverage is a function of PrEP initiation, dropout, and other factors such as acquiring HIV and death. We adjusted the annual rate of initiating PrEP per eligible person to yield the desired coverage level of PrEP, both when the base case care continuum levels were assumed and when national goals were met.

A change in PrEP efficacy resulted in a slight change in coverage levels of PrEP for the same values of PrEP initiation rate both for the base case care continuum levels and when national goals were met. Higher efficacy led to a higher coverage of PrEP among the eligible population, given that a more efficacious dose would reduce the size of the susceptible population, thereby increasing overall coverage. As an example, Figure 9.1 shows the coverage among MSM for three levels of efficacy for the scenario when current care continuum levels were maintained. The rate of initiation of PrEP per eligible person was the same for the three values of efficacy in this case. For our analysis, we maintained the initial coverage level of PrEP close to the base case values (40% for MSM, and 10% for both high-risk HETs and PWID) in 2016 for all values of efficacies by adjusting the rate of initiating PrEP per eligible person, when needed.

Figure 9.1. PrEP Coverage of MSM as a Function of Time for Different Levels of Efficacy for the Scenario When Current Care Continuum Levels Were Maintained



MSM = men who have sex with men; PrEP = pre-exposure prophylaxis.

When we held efficacy constant and allowed the coverage level of PrEP to be dynamically determined by the model, the coverage level decreased slightly with time because the number of people on PrEP decreased and the size of the susceptible population increased. The decrease in PrEP coverage with time was observed both when the current care continuum levels were maintained and when national goals were met. As an example, we have shown in Figure 9.1 that, for the scenario when the current care continuum levels were maintained, the coverage of PrEP among eligible MSM populations decreased from 40% in 2016 to about 36% in 2020 for all three values of efficacy. Similar results were also observed for HETs and PWID, where the coverage of PrEP decreased from 10% in 2016 to about 9% in 2020 for all three values of efficacy (not shown).

## Partial Achievement of National Goals

We examined changes in the number of HIV infections from 2016 to 2020 and the marginal benefit of PrEP when national goals were not fully achieved but care and treatment levels were enhanced compared to the current care continuum. We estimated that 90% of PLWH had diagnosed infection, 85% of newly diagnosed persons were linked to care, and 65% of diagnosed PLWH were virally suppressed by 2020 (90/85/65 goals). We first estimated the cumulative incidence for the scenario when these goals were achieved, but PrEP was not implemented. We then repeated the analysis for the scenario when PrEP was also delivered to people at high risk of acquiring HIV. We set the coverage, efficacy, and drop-out values for PrEP at base case values (discussed in detail in the manuscript).

Our results (Table 9.2) showed that achieving (90/85/65) goals led to a 15.8% reduction in new infections (25,600 cases prevented). Implementing PrEP along with reaching these goals resulted in a 14.8% reduction in new infections (24,010 cases prevented), which is the marginal benefit of PrEP compared to reaching the (90/85/65) goals alone.

Table 9.2. Cumulative number of new infections 2016–2020 for varied scenariosa

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Scenario | MSM | HET | PWID | Total |
| Current care-continuum levels - no PrEP (base case) | 102,410 | 43,167 | 16,676 | 162,254 |
| Goals (90/85/65) achieved - no PrEP | 84,691 | 36,781 | 15,122 | 136,594 |
| HIV infections prevented due to achieving goals (percentage) | 17,719 (17.3%) | 6,386  (14.8%) | 1,554  (9.3%) | 25,660  (15.8%) |
| Goals (90/85/65) achieved - with PrEP | 63,704 | 34,506 | 14,374 | 112,584 |
| HIV infections prevented due to achieving goals (percentage) | 38,706 (37.8%) | 8,661  (20.1%) | 2,302 (13.8%) | 49,670 (30.7%) |
| HIV infections prevented due to PrEP | 20,987 (20.5%) | 2,275 (5.3%) | 748 (4.5%) | 24,010 (14.8%) |

MSM= men who have sex with men; HET= heterosexuals; PWID= persons who inject drugs

a Number and percentage of HIV infections prevented for each scenario with respect to the base case.

# Calculation of Model Outcomes

## Health Outcomes

In this section, we define the relevant inputs and methods applied in the calculation of the model’s key (non-economic) health outcomes, including life-years, quality-adjusted life-years (QALYs), HIV incidence, and HIV prevalence. Outcomes were collected for each analysis over a defined outcome collection period, which may or may not cover the entire model time horizon.

### Heath State Utility Inputs

The health state utilities vary by HIV status *h* and are provided in Table 10.1. We assumed that the utilities varied solely by HIV status. The utility values were used to calculate QALYs. The discount rates applied to QALYs, as well as life-years and costs, are provided in Table 10.2.

Table 10.1. Utility Inputs

| HIV Status | Value | Source |
| --- | --- | --- |
| Uninfected | 1 | Assumed |
| Acute | 0.94 | Tengs et al. (2002) |
| CD4 > 500 | 0.94 |
| CD4 350–500 | 0.94 |
| CD4 200–350 | 0.82 |
| CD4 < 200 | 0.7 |

Table 10.2. Discount Rates

|  |  |  |
| --- | --- | --- |
| Application of Discounting | Value | Source |
| Life-years | 0.00 | Assumed |
| QALYs | 0.03 | Gold et al. (1996) |
| Costs | 0.03 | Gold et al. (1996) |

Note: QALYs = quality-adjusted life-years

### Calculation of Health Outcomes

Key health outcomes reported by the model include life-years, QALYs, total number of new infections, and HIV prevalence for all individuals actively moving through the model. They were calculated by using Equations (10.1) to (10.4), respectively.

(10.1)

(10.2)

(10.3)

(10.4)

where

* L = cumulative number of life-years accrued by the modeled population over the outcome collection period;
* W = cumulative number of QALYs accrued by the modeled population over the outcome collection period;
* F = cumulative number of new HIV infections (incidence) over the outcome collection period;
* q(t)­ = length of model’s computational time step, in years, at time *t*;
* Pt = HIV prevalence at time t;
* Q = discount rate for QALYs; and
* Rc = health utility for individuals in compartment *c*.

## Economic Outcomes

In this section, we define the relevant inputs and methods applied in the calculation of the model’s economic outcomes, including the costs of testing, notification, and HIV treatment and care. All economic outcomes were computed using 2015 as a common cost year (Bureau of Labor Statistics, 2015).

### Testing Cost Inputs

Costs are applied for testing and notification. Testing is assumed to be in a clinical setting. During scenarios in which an outreach intervention is applied, an additional outreach cost per test is also applied. Table 10.3 reports the inputs applied in the model used for calculating the costs related to testing.

Table 10.3. Testing Cost Inputs

| Input | Valuea | Source |
| --- | --- | --- |
| Testing cost, including screen and confirmatory test |  |  |
| HIV-uninfected individual, rapid screen | $22.13 (2012$) | Based on cost components from Hutchinson et al. (2011), Pinkerton et al. (2010), and Farnham et al. (2008). |
| HIV-uninfected individual, conventional screen | 4G: $10.36 (2012$) | Based on cost components from Farnham et al. (2008) and Hutchinson et al. (2011, 2013), and adjusted to 2012$. |
| HIV-infected individual, rapid screen | $86.70 (2012$) | Based on cost components from Hutchinson et al. (2011, 2013), Pinkerton et al. (2010), and Farnham et al. (2008) and adjusted to 2012$. Assumes a repeat screen and a Western blot confirmatory test. |
| HIV-infected individual, conventional screen | 4G: $66.81 (2012$) | Based on cost components from Farnham et al. (2008) and Hutchinson et al. (2011, 2013) and adjusted to 2012$. Assumed Western blot confirmatory test. |
| NAT, applied for discrepant Western blot confirmatory test | $160.07 (2012$) | Hutchinson et al. (2013) |
| Notification costs |  |  |
| HIV-uninfected | $0.45 (2009$) | Hutchinson et al. (2011) |
| HIV-infected, conventional screen | $5.88 (2009$) | Hutchinson et al. (2011) |
| HIV-infected, rapid screen | $10.86 (2009$) | Hutchinson et al. (2011) |
| Outreach cost per test (when applied) | $13.67 (2005$) | Shrestha et al. (2008) |

Note: NAT = HIV nucleic acid amplification test

a All cost inputs were converted to 2015$ in the calculation of economic outcomes.

### Calculation of Testing and Notification Costs

We calculated the cost of testing and notification by using Equations (10.5) to (10.9). The cost of testing varies by the type of test (rapid or conventional), the test result (positive or negative), and the test sensitivity, which varies by type of test. The cost for a NAT (HIV nucleic acid amplification test) is applied when the confirmatory test after a positive result is negative. Notification costs also vary by the type of test and test result. We assume the probability of notification does not change if a NAT is conducted. For ease of understanding, the calculations have been provided in words rather than symbols.

#### Number of Tests

Number of positive tests of individuals in *p* with HIV status *h*, taking test type *g*, at time *t* =   
[Number of undiagnosed HIV-infected individuals in *p* with HIV status *h*]   
x [Testing rate over time *t*, by *h* and *p*]   
x [Percentage of tests that are type *g*, by *p*]   
x [Sensitivity of test type *g*, by *h*]  
for *h* = {1 to 5} and all *p*, *g*, and *t*. (10.5)

Number of negative tests of HIV-infected individuals (missed diagnoses) in *p* with HIV status *h*, taking test type *g*, at time *t* =   
[Number of undiagnosed HIV-infected individuals in *p* with HIV status *h*]   
x [Testing rate over time *t*, by *h* and *p*]   
x [Percentage of tests that are type *g*, by *p*]   
x [1 − (Sensitivity of test type *g*, by *h*)]  
for *h* = {1 to 5} and all *p*, *g*, and *t*. (10.6)

Number of negative tests of HIV-uninfected (HIV status *h=0*) individuals in *p*, taking test type *g*, at time *t* =   
[Number of HIV-uninfected individuals in *p*]   
x [Testing rate over time *t*, by *h* and *p*]   
x [Percentage of tests that are type *g*, by *p*]   
for *h* = {0} and all *p*, *g*, and *t*. (10.7)

The total number of tests conducted is the sum of all positive and negative tests of HIV-infected individuals (calculated using Equations [10.5] and [10.6], respectively) and all negative tests of HIV-uninfected individuals (calculated using Equation [10.7]) across all *p*, *h*, *g*, and *t*.

#### Costs of Testing

Cost of testing individuals with HIV status *h* in *p* taking test type *g*, at time *t* = ([Number of positive tests of HIV-infected individuals in *p* with HIV status *h* = {1 to 5}, taking test type *g*, at time *t*] x [(Cost of positive test type *g* at *t*) + (1 − [Test sensitivity of confirmatory screen, by HIV status *h*]) x (Cost of NAT)]   
+ [Number of negative tests of individuals in *p* with HIV status *h*, taking test type *g*, at time *t*] x [(Cost of negative test type *g* at *t*)]   
+ [Outreach cost per test, if applicable]) x (Discount factor at *t*)   
for all *h*, *p*, *g*, and *t.* (10.8)

The total cost of testing is the sum of the cost of testing (calculated using Equation [10.8]) across all *h*, *p*, *g*, and *t*.

#### Notification Costs

Cost of notification of HIV test results for individuals in *p* with HIV status *h* taking test type *g* at time *t* = (Probability of notification, by p and test type *g*, at time t)  
x ([Number of positive tests of individuals in *p* with HIV status *h*, taking test type *g*, at time *t*] x [Cost of notification of positive results from test type *g*] + [Number of negative tests of individuals in *p* with HIV status *h*, taking test type *g*, at time *t*] x [Cost of notification of negative results from test type *g*]) x (Discount factor at *t*)  
for all *h*, *p*, *g*, and *t.* (10.9)

The total notification cost is the sum of the cost of notification (calculated using Equation [10.9]) across all *h*, *p*, *g*, and *t*.

### HIV Treatment and Care Costs

HIV treatment and care costs, listed in Table 10.4, vary by both HIV status and care continuum status. The total HIV treatment and care costs accrued by the modeled population over the outcome collection period are calculated by using Equation (10.10).

Total treatment and care costs are calculated using Equation (10.10):

(10.10)

where

* D = cumulative treatment and care costs over the outcome collection period,
* U= discount rate for costs, and
* Jc = annual treatment and care costs for an individual in compartment c

Table 10.4. Annual HIV Treatment and Care Costs

| HIV Status | Care Continuum Stage | Valuea (2006$) | Source |
| --- | --- | --- | --- |
| Uninfected | N/A | $0 | Assumed |
| Acute | Unaware of infection | $2,055 | Gebo et al. (2010), Farnham et al. (2008), Schackman et al. (2006) |
|  | Aware but not linked to HIV care | $2,055 |
|  | Linked to HIV care but not prescribed ART | $4,468 |
| CD4 >500 | Unaware of infection | $2,055 |
|  | Aware but not linked to HIV care | $2,055 |
|  | Linked to HIV care but not prescribed ART | $4,468 |
|  | Prescribed ART | $13,550 |
| CD4 350–500 | Unaware of infection | $1,843 |
|  | Aware but not linked to HIV care | $1,843 |
|  | Linked to HIV care but not prescribed ART | $4,822 |
|  | Prescribed ART | $13,841 |
| CD4 200–350 | Unaware of infection | $1,811 |
|  | Aware but not linked to HIV care | $1,811 |
|  | Linked to HIV care but not prescribed ART | $6,213 |
|  | Prescribed ART | $16,581 |
| CD4 < 200 | Unaware of infection | $1,976 |
|  | Aware but not linked to HIV care | $1,976 |
|  | Linked to HIV care but not prescribed ART | $14,116 |
|  | Prescribed ART | $25,305 |

a All cost inputs were converted to 2015$ in the calculation of economic outcomes.

### Calculation of PrEP Costs

The monthly costs for PrEP listed in Table 10.5 are incurred for all individuals on PrEP. The total PrEP costs accrued by the modeled population over the outcome collection period are discounted. These costs assume HIV testing while receiving PrEP every 3 months.

Table 10.5. Annual PrEP Costs

|  |  |  |
| --- | --- | --- |
| Cost Category | Value | Source |
| Drug costs | $16,453 (2015$) | Truven Health Analytics (2017); Gebo et al. (2010) |
| Screening and monitoring costs | $1,475 (2015$) | Desai et al. (2008) |
| Total | $17,450 |  |

### Calculation of Incremental Cost-Effectiveness Ratios

The incremental cost-effectiveness ratio (ICER), defined as the incremental cost per QALY gained, was calculated for one scenario (*I*) versus a comparator scenario (*C*) by using Equation (10.11). Scenarios were defined as model runs with alternative input values. The ICER could be calculated for subsets of subpopulations or specific sets of costs.

(10.11)

where A = relevant total costs accrued by the modeled population over the outcome collection period.

# Model Calibration and Validation

## Model Calibration to Published Data

We calibrated a subset of the model’s inputs so that key model outcomes in the first and second time periods approximated surveillance data defining the HIV epidemic. The process that was applied to calibrate the model is outlined in Sections 11.1.1 to 11.1.4.

### Establish Calibration Outcome Targets

The model outcomes targeted to match surveillance data are listed in Table 11.3. We aimed for the model’s outcomes to approximate the published point estimates within an acceptable range. We used 95% confidence intervals for those ranges when available; otherwise we established ranges based on ±20% of the point estimates.

### Establish Inputs to Vary in Calibration

We identified inputs to vary and specified both a priority weight and a range of acceptable values for each (Tables 11.1 and 11.2). Most parameters selected to be varied were selected because limited to no source data were available. We also calibrated all rates of flow along the continuum-of-care so that the distribution of the HIV-infected population matched that observed in surveillance data, despite the fact that estimates of some of those rates (testing, linkage to HIV care, and other rates) are reported in the published literature. In addition, we also varied some inputs to which the model was highly sensitive but for which the published literature did not offer high confidence in specific values; per-act transmission risk was a key example of such an input.

A range of values to consider was established for each input; those ranges were informed by available data or expert opinion. Ranges of values were set so that the following qualitative restrictions were also applied:

1. Testing rates of MSM and PWID are higher than testing rates of HETs;

2. Testing rates increase with progressively more advanced disease stages;

3. Rates of linkage to HIV care after diagnosis increased with more severe symptomatic disease stages; and

4. Per-sex-act risk from insertive AI (VI) was less than that of receptive AI (VI).

Given these restrictions, all input values and combinations of input values within the bounds were considered acceptable.

Table 11.1. Bounds and Final Values of Continuum-of-Care Parameters Varied in Calibration: Second Time Perioda

| Parameter | Calibrated Value | | Lower Bound | Upper Bound |
| --- | --- | --- | --- | --- |
| Annual rate of getting tested per reference case | | |  |  |
| Black, HET, CD4 < 500 | 0.141 | | 0.030 | 0.300 |
| Relative risk of getting tested by race/ethnicity | | |  |  |
| Hispanic/Latino | 0.710 | | 0.300 | 1.500 |
| Other | 0.639 | | 0.100 | 1.500 |
| by transmission group |  | |  |  |
| MSM | 1.986 | | 1.000 | 8.000 |
| PWID | 1.790 | | 1.000 | 8.000 |
| by disease stage |  | |  |  |
| Acute | 1.151 | | 0.500 | 1.500 |
| CD4 350–500 | 2.076 | | 1.000 | 3.000 |
| CD4 200–350 | 4.339 | | 1.250 | 5.000 |
| CD4 <200 | 6.871 | | 1.500 | 8.000 |
| Relative risk of linkage to HIV care after (versus immediately at) diagnosis, by disease stage | | |  |  |
| CD4 200–350 | | 6.120 | 1.000 | 8.000 |
| CD4 < 200 | | 4.529 | 1.000 | 8.000 |
| Annual probability of dropping out of care if linked to HIV care, not prescribed ART | | |  |  |
| Black | | 0.200 | 0.010 | 0.500 |
| Hispanic | | 0.184 | 0.010 | 0.500 |
| Other | | 0.163 | 0.010 | 0.500 |
| Annual probability of dropping off of ART if ART-not-VLS and movement to linked-to- care | | |  |  |
| Black | | 0.280 | 0.004 | 0.300 |
| Hispanic | | 0.237 | 0.010 | 0.300 |
| Other | | 0.252 | 0.010 | 0.300 |
| Annual probability of departing from VLS and movement to ART-not-VLS | | |  |  |
| Black | | 0.253 | 0.025 | 0.350 |
| Hispanic | | 0.200 | 0.025 | 0.350 |
| Other | | 0.252 | 0.025 | 0.350 |

(continued)

Table 11.1. Bounds and Final Values of Continuum-of-Care Parameters Varied in Calibration: Second Time Perioda (continued)

| Parameter | Calibrated Value | Lower Bound | Upper Bound |
| --- | --- | --- | --- |
| Relative risk of ART prescription by race/ethnicity | |  |  |
| Black | 1.884 | 0.500 | 3.000 |
| Hispanic | 1.258 | 0.500 | 3.000 |
| Other | 2.566 | 0.500 | 3.000 |
| Annual probability of becoming VLS if ART-not-VLS | |  |  |
| Black | 0.236 | 0.010 | 0.700 |
| Hispanic | 0.404 | 0.010 | 0.700 |
| Other | 0.147 | 0.010 | 0.700 |

Note: ART = antiretroviral therapy; HET = heterosexual; PWID = people who inject drugs; VLS = viral load suppressed

aCalibrated values reported in this version of the technical report are from calibration set AS\_1.

Table 11.2. Bounds and Final Values of Inputs Defining Behaviors and Infectivity Varied in Calibrationa

| Parameter | Calibrated Value | Lower Bound | Upper Bound |
| --- | --- | --- | --- |
| Percentage of sexual partners by transmission group and sex (mixing matrix) | |  |  |
| HET M: HET F | 0.995 | 0.950 | 0.999 |
| HET F: HET M | 0.972 | 0.960 | 0.980 |
| HET F: PWID M | 0.002 | 0.000 | 0.005 |
| MSM: HET F | 0.393 | 0.000 | 0.450 |
| MSM: PWID F | 0.003 | 0.000 | 0.005 |
| PWID M: PWID F | 0.302 | 0.100 | 0.800 |
| PWID F: PWID M | 0.621 | 0.100 | 0.800 |
| Percentage of sexual partners by risk level (mixing matrix) | |  |  |
| HET/PWID—Low: Low | 0.964 | 0.850 | 0.999 |
| HET/PWID—High: High | 0.776 | 0.600 | 0.990 |
| MSM—Low: Low | 0.962 | 0.850 | 0.990 |
| MSM—High: High | 0.769 | 0.600 | 0.990 |

(continued)

Table 11.2. Bounds and Final Values of Inputs Defining Behaviors and Infectivity Varied in Calibration (continued)

| Parameter | Calibrated Value | Lower Bound | Upper Bound |
| --- | --- | --- | --- |
| Percentage of sexual partners by race (mixing matrix) | |  |  |
| Black: Hispanic | 0.028 | 0.005 | 0.050 |
| Black: Other | 0.078 | 0.035 | 0.120 |
| Hispanic: Black | 0.048 | 0.010 | 0.100 |
| Hispanic: Other | 0.278 | 0.150 | 0.400 |
| Other: Black | 0.046 | 0.010 | 0.100 |
| Other: Hispanic | 0.061 | 0.010 | 0.100 |
| Percentage of needle partners by transmission group and sex (mixing matrix) | | |  |
| PWID M: PWID F | 0.37 | 0.37005 | 0.37015 |
| PWID F: PWID M | 0.63 | 0.6295 | 0.6305 |
| Base probability of transmission per unprotected sex act | |  |  |
| Vaginal insertive | 0.00041 | 0.0001 | 0.0008 |
| Vaginal receptive | 0.00061 | 0.0004 | 0.0009 |
| Anal insertive | 0.0006 | 0.0003 | 0.001 |
| Anal receptive | 0.0089 | 0.0080 | 0.014 |
| Probability of transmission per shared needle | 0.0016 | 0.0010 | 0.005 |
| Percentage of injections that are shared | 0.126 | 0.050 | 0.300 |
| Reduction in transmission per shared needle if VLS vs. not VLS | 0.665 | 0.500 | 0.990 |
| Percentage of M–F partnerships with AI and VI if both AI and VI | 0.801 | 0.650 | 0.950 |
| Length of time (in years) in each HIV stage if ART-not-VLS | |  |  |
| CD4 > 500 | 37.793 | 5.000 | 50.000 |
| CD4 350–500 | 39.583 | 5.000 | 50.000 |
| CD4 200–350 | 38.414 | 5.000 | 60.000 |
| Annual rate of declining one disease stage while VLS | |  |  |
| CD4 > 500 | 0.045 | 0.010 | 0.080 |
| CD4 350–500 | 0.045 | 0.010 | 0.080 |
| CD4 200–350 | 0.045 | 0.010 | 0.080 |
| Annual rate of improving one disease stage while VLS | |  |  |
| CD4 350–500 | 0.432 | 0.250 | 0.650 |
| CD4 200–350 | 0.428 | 0.250 | 0.650 |
| CD4 < 200 | 0.397 | 0.250 | 0.650 |

(continued)

Table 11.2. Bounds and Final Values of Inputs Defining Behaviors and Infectivity Varied in Calibration (continued)

Note: ART = antiretroviral therapy; HET = heterosexual; PWID = people who inject drugs; VLS = viral load suppressed

aCalibrated values reported in this version of the technical report are from calibration set AS\_1.

### Screening for Preliminary Input Sets Using Latin Hypercube Sampling

We used Latin Hypercube Sampling (LHS) to identify potential input sets. LHS is a Bayesian computation scheme that was initially proposed by McKay, Conover, and Beckman (1979) and has been previously applied to HIV disease transmission models by Blower and Dowlatabadi (1994), Sood et al. (2013), and Boily et al. (2013). This method is preferable to random sampling because it covers more of the feasible parameter space with a given number of sets of values.

The user first decides how many parameters to vary (*NumParsVaried*), how many input sets to run (*NumRuns*), and how many outcomes to target (*NumTargets*). A range of feasible values was defined for each of the *NumParsVaried* parameters and divided into *NumRuns* equal-width, contiguous segments. From each segment for every parameter, a value was randomly sampled (i.e., each parameter had a set of *NumRuns* possible values). Then *NumRuns* distinct input sets were defined: for each parameter of a single input set, a value was sampled without replacement from the *NumRuns* potential values for that parameter. This process was repeated *NumRuns* times to define *NumRuns* distinct input sets. The model’s parameters that were not selected for variation were left at base case values. We then iteratively ran the model using each of the input sets and collected the results.

Two measures of the goodness of each input set were calculated, the “Out-of-bounds penalty measure” (inspired by a similar measure applied in Tian et al. [2016]) and the “target error measure,” as defined in Equations 11.1 and 11.2.

(11.1)

where the penalty was set to 1000 if model outcome *i* was outside of the target range and 1 otherwise.

(11.2)

We also observed the number of outcomes that were out of bounds for each set.

We generated exactly 10,000 LHS sets (i.e., *NumRuns* = 10,000). We selected the eleven sets with the lowest out-of-bounds penalty measures to apply to the base and uncertainty analyses and then included an additional set to offer one alternative for consideration, totaling twelve sets.

### Identification of Base and Alternative Input Sets Using Optimization Techniques

We then used MATLAB’s Optimization Toolbox (Mathworks; Natick, Massachusetts) to identify the local optimal input set starting with each of the twelve sets identified using LHS, with optimal defined as a minimized out-of-bounds penalty measure. Priority weights of 1 were assigned to all outcomes. Among those optimized sets, we then selected one set to apply in the base analysis and 10 sets for the uncertainty analysis; they were selected based on the out-of-bounds penalty measures, target error measures, and the number of targets that were out of bounds. The values in the identified base analysis set that affected either all time periods or the second time period are shown in Tables 11.1 and 11.2; values for inputs that affect only the first time period are not included because they affect the run-in period of the model only. The model’s outcomes given the identified base analysis set are shown in Table 11.3; all those outcomes were between their targeted bounds.

Table 11.3. Values Generated by the Model using the Base Analysis Set vs. Target Values and Bounds Considered for Outcomes Targeted in Calibration

| Outcome Namea | Model Values | Target Value | Lower Bound | Upper Bound | Source for Target Values and Bounds |
| --- | --- | --- | --- | --- | --- |
| Estimated number of new infections in the United States in 2009b | | | | | CDC (2012a) |
| HET male | 3,833 | 3,800 | 3,040 | 4,560 |
| HET female | 8,863 | 8,800 | 7,040 | 10,560 |
| MSM | 31,978 | 28,080 | 22,464 | 33,696 |
| PWID male | 2,476 | 2,310 | 1,848 | 2,772 |
| PWID female | 1,827 | 2,010 | 1,608 | 2,412 |
| Total | 48,977 | 45,000 | 36,000 | 54,000 |
| Number of aware PLWH deaths | | | | | CDC (2014) |
| 2009 | 18,611 | 19,058 | 15,246 | 22,870 |
| 2013 | 16,368 | 16,281 | 13,025 | 19,537 |
| HIV prevalence |  |  |  |  | Expert opinionc |
| 2009 | 1,068,133 | 1,006,500 | 905,850 | 1,107,150 |
| 2012 | 1,062,858 | 1,082,100 | 973,890 | 1,190,310 |

(continued)

Table 11.3. Model vs. Target Values and Bounds Considered for Outcomes Targeted in Calibration (continued)

| Outcome Name | Model Values | Target Value | Lower Bound | Upper Bound | Source for Target Values and Bounds |
| --- | --- | --- | --- | --- | --- |
| Distribution of HIV-infected population across continuum-of-care in 2009 | | | | | Expert opinionc |
| Diagnosed | 80% | 81% | 79% | 83% |
| Viral load suppressed (among diagnosed) | 39% | 36% | 29% | 43% |
| Distribution of HIV-infected population across continuum-of-care in 2012 | | | | | CDC (2015) |
| Diagnosed | 85% | 83% | 81% | 85% |
| Viral load suppressed (among diagnosed) | 51% | 50% | 40% | 60% |
| Estimated number of diagnoses of HIV infection in the United States in 2013 | | | | | CDC (2014) |
| HET male | 3,190 | 3,545 | 2,836 | 4,254 |
| HET female | 7,267 | 7,213 | 5,770 | 8,656 |
| MSM | 26,625 | 28,493 | 22,795 | 34,192 |
| PWID male | 1,764 | 1,757 | 1,406 | 2,109 |
| PWID female | 1,305 | 1,255 | 1,004 | 1,506 |
| Total | 40,150 | 42,566 | 34,053 | 51,079 |
| Estimated number of new infections in the United States in 2013 | | | | | CDC (2014)d |
| Total | 37,919 | 39,800 | 35,820 | 43,780 |
| Ratio of overall prevalence in 2012 vs 2006 | 1.00 | 1.15 | 1.00 | 1.30 | CDC (2012b) |
| Ratio of HET prevalence in 2015 vs 2006, by risk level | | | | | Assumptione |
| Low-risk | 1.10 | 1.00 | 0.90 | 1.10 |
| High-risk | 0.97 | 1.00 | 0.90 | 1.10 |

Note: ART = antiretroviral therapy; HET = heterosexual; PWID = people who inject drugs; VLS = viral load suppressed

a Priority weights of 1 were assigned to all outcomes.

b Infections reported for the MSM/PWID transmission category in CDC (2012a) were allocated between MSM and PWID males.

c Ranges provided by CDC from unpublished analyses using CDC surveillance data. Target values were set to the midpoints of the ranges.

d Bounds were calculated as 75% and 100%, respectively, of the number of new diagnoses in 2013 by race/ethnicity, per CDC (2014) Table 1a, which reports the diagnoses of HIV infection, by year of diagnosis and selected characteristics. Target values were set to the midpoints of those ranges. This method was recommended by CDC expert opinion.

e Assumed that calibration must show relatively stable prevalence within HET risk groups over time.

## Internal and External Validation of the Model

We conducted a thorough quality check of the model’s inputs, calculations, and differential equations. An earlier version of this model was also reviewed by experts in differential equation modeling of HIV, Drs. Michael Pickles and Marie-Claude Boily, both of the Imperial College of London.

We compared our model’s outcomes to CDC surveillance data as listed in Table 11.3. Estimated new infections by transmission group and distributions of the HIV-infected population across the continuum-of-care stages were used for calibration as described in Section 11.1. The model’s values for all outcomes targeted were within their target ranges; most were within 5% of the target data point.

# Model Sensitivity and Uncertainty Analyses

To explore the HOPE model’s sensitivity to its input values for this particular analysis, we applied the elementary effects method and conducted one-way sensitivity analysis. We also studied the HOPE model’s uncertainty. Details on the methods and results of these analyses are outlined in the sections below.

## Elementary Effects Method

The elementary effects method (based on Morris [1991]) is recognized as an efficient and effective mechanism for conducting screening (Saltelli et al., 2004; Wu et al., 2013) to identify inputs to which a model’s output is sensitive. This method is often used to select inputs to vary in a calibration or uncertainty analysis.

Unlike the commonly used one-way sensitivity analysis method, elementary effects measure the effects of changes in each input at multiple locations across the possible parameter space. The elementary effects method calculates the effects of changes in each input over multiple model iterations. With an increasing number of iterations, there is increased coverage of the parameter space and consideration of interaction effects between parameters. If only a single iteration is performed, then the elementary effect is highly dependent on the initial point in the parameter space and does not account for interactions between parameters (Herman et al., 2013). Using the elementary effects method, two measures are computed for each input: (a) the mean of the absolute values of elementary effects of the input, which is a measure of the overall effect of the input on the outcome; and (b) the standard deviation of the elementary effects of the input, which is a measure of the nonlinearity of that input’s effect on the outcome. These two statistics can then be used to identify the degree of effect of each input the observed outcome. The mean of absolute elementary effects and the standard deviation of elementary effects are denoted by the Greek letters μ and σ, respectively. We note that these two Greek letters are used elsewhere in this document to represent selected model parameters (see Table A.1 in the appendix for definitions); however, we are using them in this section to represent the key outcomes of the elementary effects method to be consistent with standard elementary effects terminology (Morris [1991], Saltelli et al., 2004).

When we implemented the elementary effects method in this analysis, we varied 52 inputs; they were selected based on uncertainty about their values and whether their values may depend on program implementation. All selected inputs were varied within ±50% of their base case values in each of 10 iterations. We observed the elementary effect of each input change on the key outcome: total U.S. HIV incidence in 2020.

We conducted the elementary effects method by using the following process:

1. Identified the *Z* = 52 inputs to vary and the key outcome against which the sensitivity of each input is measured, total U.S. HIV incidence in 2020.
2. Specified ranges over which to vary the *Z* inputs. A uniform distribution was assumed for each range. All inputs not selected to vary remained at their base values for every model run.
3. Ran *Л*=10 iterations (*Л*). The number of iterations determined both the number of trials for measuring the elementary effects and the number of equal segments across the input’s range that were considered for sampling input values (without replacement). The number of model runs required to complete the analysis is given by Equation 12.1.

Number of model runs required = (*Z* + 1) × (*Л*) (12.1)

Based on Equation 12.1, this analysis would require 530 model runs ([52 + 1] x [10]).

1. Using LHS, chose for each of the selected inputs one of the 10 segments and applied the randomly selected value from that segment. This process generated *Л* =10 values for each of the *Z* inputs to be considered in the sensitivity analysis by using LHS sampling from each of the *Л* =10 segments of the inputs’ distributions. We will refer to the *шth* sampled value of input *Њ* as *й*Њ*,ш*.
2. Randomly selected one of the *Л* =10 sampled values (*й*Њ*,ш*) for each of the *Z* inputs to be varied. Note that this was the first step of an iteration.
3. Replaced all of the varied inputs’ values with the sampled values in the model. Ran the model and recorded the value of the key outcome, total U.S. HIV incidence in 2020.
4. Selected one (input *Њ*) of the *Z* = 52 inputs and replaced that input’s sampled value (*й*Њ*,ш*) with a value that was systematically adjusted by a constant percentage, *Ж* =0.5, of the width of the range considered for input *Њ* (in a randomly selected direction that results in a sampled value inside the range). The adjusted input values will be referred to as *й*Њ*,ш\**. As an example, if the range for input *Њ* was 0 to 1 and *й*Њ*,ш* = 0.8, then *й*Њ*,ш\**= (0.8) − (1 − 0)\*(0.5) = 0.3. We ran the model using the adjusted input value *й*Њ*,ш\** and recorded the value of the key outcome, total U.S. HIV incidence in 2020.
5. Calculated an elementary effect of this input as the difference in the value of the key outcome from step 7 (when the value of the varied input *Њ* was set to *й*Њ*,ш\**) and the value of the key outcome from the previous run (when the value of the varied input *Њ* was set to *й*Њ*,ш*), divided by *Ж*; this calculation is given by Equation 12.2.

Elementary effect of input Њ from iteration *ш* = (*EEш,Њ*)   
 = ([HIV incidence in 2020 from step 7] − [HIV incidence in 2020  
 from step 6]) / (Ж) (12.2)

1. Repeated steps 7 and 8 until all *Z* inputs had been varied to their alternate values. Each time we adjusted one input’s value, we assessed its elementary effect. For each new input varied, we kept all inputs already varied at their adjusted values, and those not yet varied at the value chosen by LHS. The iteration was complete when all Z inputs were varied and their elementary effects had been calculated.
2. We then repeated steps 5 to 9 for the remaining Л-1 iterations, using values for each iteration drawn by LHS without replacement from the segments of the range of values for each input.
3. When all iterations were complete, calculated the mean, mean of the absolute values, and standard deviation of the elementary effects for each input *Њ*. The mean of elementary effects (denoted by *μ*Њ) for input *Њ* was calculated as the average of the collection of elementary effects collected for input *Њ*. The mean of absolute elementary effects for input *Њ* (denoted by *μ*Њ*\**) was calculated as the average of the collection of absolute values of the elementary effects collected for input *Њ*, as outlined in Equation 12.4; the absolute value is used to offset the canceling out effect of positive and negative elementary effects.

Mean of the absolute values of elementary effects of input Њ =  
 (12.4)

The standard deviation of elementary effects for input *Њ* (denoted by *σ*Њ) was calculated as the standard deviation of the elementary effects collected for the input; its calculation uses Equation 12.5.

Standard deviation of the elementary effects of input Њ =  
 (12.5)

These measures are reported for all inputs in Table 12.1 for total U.S. HIV incidence in 2020. We then plotted the inputs as shown in Figure 12.1.

For total U.S. HIV incidence in 2020, the elementary effects method found that the following inputs had the greatest effect on HIV incidence in 2020: annual number of sexual partners and sex acts per person, the percentage of HET females’ sexual partners with HET males (versus MSM and male PWID), percentage of MSM's sexual partners with MSM (versus HET females and female PWID), and the probability of HIV transmission per condomless anal receptive sex act.

Table 12.1 Elementary Effects Analysis Results for Total U.S. HIV Incidence in 2020: Mean of Absolute, and Standard Deviation of Elementary Effects for 52a Inputs (in Descending Order by Mean of Absolute Elementary Effects)

|  |  |  |  |
| --- | --- | --- | --- |
| Input #a | Inputa | Mean of Absolute Elementary Effects (µ\*)b | Standard Deviation of Elementary Effects (σ)c |
| **26** | **Annual number of sexual partners per person** | 212,688 | 199,915 |
| **1** | **Annual number of sex acts per person** | 206,104 | 138,647 |
| **28** | **Percentage of HET females' sexual partners with HET males (versus MSM and male PWID)** | 127,812 | 190,460 |
| **29** | **Percentage of MSM's sexual partners with MSM (versus HET females and female PWID)** | 121,619 | 143,651 |
| **49** | **Probability of HIV transmission per condomless anal receptive sex act** | 114,055 | 106,314 |
| **27** | **Percentage of HET males' sexual partners with HET females (versus female PWID)** | 103,927 | 139,894 |
| **52** | **Reduction in HIV transmission per sex act if VLS versus not VLS** | 72,588 | 76,251 |
| **19** | **Condom efficacy per sex act for MSM** | 63,259 | 64,564 |
| **47** | **Probability of HIV transmission per condomless vaginal receptive sex act** | 59,801 | 34,138 |
| **23** | **Percentage of anal sex acts protected with condoms** | 58,829 | 62,342 |
| **46** | **Probability of HIV transmission per condomless vaginal insertive sex act** | 51,427 | 40,048 |
| **2** | **Percentage of MSM sex acts that are insertive** | 40,465 | 31,785 |
| **16** | **Annual probability of becoming VLS if prescribed ART but not VLS** | 32,370 | 20,778 |
| **18** | **Condom efficacy per sex act for HETs** | 31,666 | 18,622 |
| **51** | **Reduction in probability of HIV transmission per sex act if circumcised versus uncircumcised** | 30,147 | 30,828 |
| **22** | **Percentage of vaginal sex acts protected with condoms** | 27,949 | 30,446 |
| **4** | **Annual testing rate, 2010+** | 26,110 | 20,649 |
| **15** | **Annual probability of being prescribed ART, given eligible for ART** | 22,769 | 20,351 |
| **14** | **Annual probability of losing VLS and moving to ART-not-VLS** | 22,434 | 17,788 |
| **39** | **Percentage of people who have any AI in their male-female partnerships, 2010+** | 21,839 | 33,952 |

(continued)

Table 12.1 Elementary Effects Analysis Results for Total U.S. HIV Incidence in 2020: Mean of Absolute, and Standard Deviation of Elementary Effects for 52a Inputs (in Descending Order by Mean of Absolute Elementary Effects) (continued)

|  |  |  |  |
| --- | --- | --- | --- |
| Input #a | Inputa | Mean of Absolute Elementary Effects (µ\*)b | Standard Deviation of Elementary Effects (σ)c |
| 20 | Percentage of injections that are shared | 21,447 | 16,421 |
| 17 | Percentage of individuals who become VLS when prescribed ART | 21,277 | 15,501 |
| 5 | Probability of being notified of HIV status if tested | 21,039 | 22,762 |
| 7 | Test sensitivity | 20,545 | 15,358 |
| 21 | Annual number of needle-sharing partners for PWID | 19,556 | 18,104 |
| 36 | Percentage of sexual partners within same age group | 19,438 | 15,603 |
| 44 | Annual rate of improving one CD4 stage if VLS | 18,905 | 8,970 |
| 24 | Increase in percentage of sex acts protected with condoms for diagnosed versus undiagnosed | 18,370 | 18,914 |
| 40 | Among people who have male-female AI, percentage of partnerships with AI | 17,257 | 15,535 |
| 41 | In male-female partnerships with AI, percentage of contacts AI, 2010+ | 16,844 | 13,261 |
| 35 | Percentage of sexual partners within same race | 13,945 | 16,380 |
| 50 | Probability of HIV transmission per shared needle | 12,957 | 14,513 |
| 48 | Probability of HIV transmission per condomless anal insertive sex act | 11,519 | 8,705 |
| 45 | Annual probability of death if HIV+ and VLS, before 2016 | 10,811 | 10,856 |
| 34 | Percentage of MSM sexual partners within same risk level | 10,795 | 7,710 |
| 42 | Number of years in each CD4 stage if not prescribed ART | 9,842 | 6,464 |
| 37 | Percentage of needle-sharing partners within same race | 9,587 | 11,192 |
| 25 | Decrease in needle sharing for diagnosed versus undiagnosed | 6,648 | 7,430 |
| 33 | Percentage of HET/PWID sexual partners within same risk level | 5,744 | 8,107 |
| 11 | Annual probability of diagnosed individual linked to care after (versus immediately at) diagnosis | 5,205 | 3,403 |
| 12 | Annual probability of dropping out of care if in care | 4,630 | 4,830 |

(continued)

Table 12.1 Elementary Effects Analysis Results for Total U.S. HIV Incidence in 2020: Mean of Absolute, and Standard Deviation of Elementary Effects for 52a Inputs (in Descending Order by Mean of Absolute Elementary Effects) (continued)

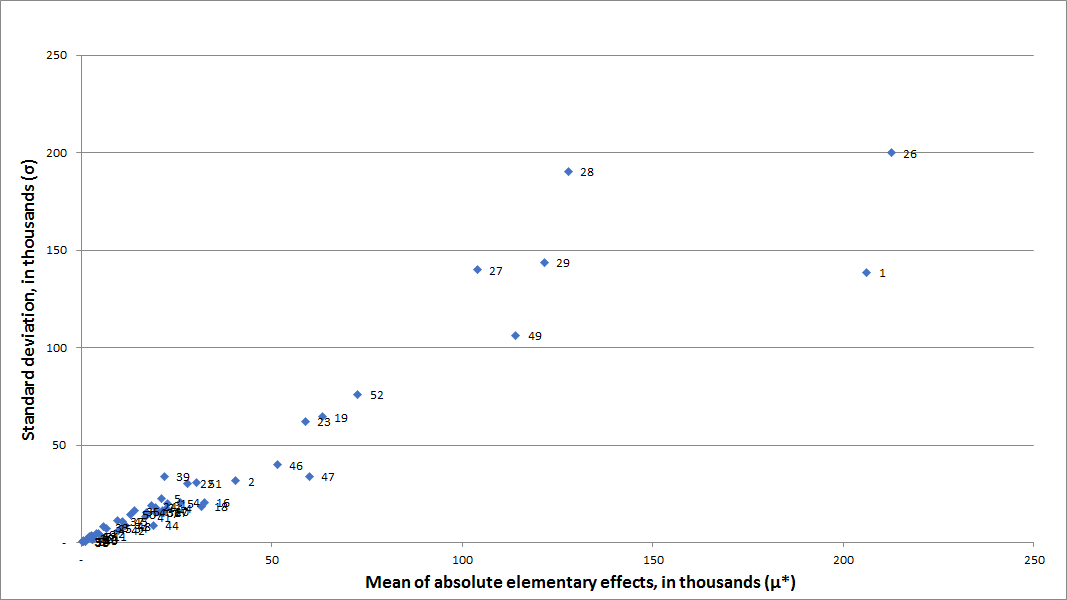
|  |  |  |  |
| --- | --- | --- | --- |
| Input #a | Inputa | Mean of Absolute Elementary Effects (µ\*)b | Standard Deviation of Elementary Effects (σ)c |
| 9 | Probability that a newly diagnosed individual will be immediately linked to care | 4,032 | 4,665 |
| 8 | Probability that a newly diagnosed individual will be immediately linked to care | 3,073 | 3,371 |
| 10 | Annual probability of diagnosed individual linked to care after (versus immediately at) diagnosis | 2,990 | 1,737 |
| 43 | Number of years in each CD4 stage if on ART-not-VLS | 2,889 | 1,484 |
| 13 | Annual probability of dropping off of ART if on ART but not VLS | 2,729 | 3,466 |
| 6 | Percentage of tests that are rapid vs. conventional | 2,188 | 3,310 |
| 30 | Percentage of PWID males' sexual partners with HET females (versus female PWID) | 1,726 | 2,310 |
| 3 | Annual risk of death due to non-HIV-related causes, HETs | 1,147 | 669 |
| 38 | Percentage of needle-sharing partners within same age group | 568 | 512 |
| 32 | Mixing: Percentage of needle sharing partners within each subgroup, PWID, male | 560 | 919 |
| 31 | Percentage of PWID females' sexual partners with HET males (versus MSM and male PWID) | 389 | 599 |

ART = antiretroviral therapy; HET = heterosexual; MSM = men who have sex with men; PWID = people who inject drugs; VLS = viral load suppressed.

a 52 inputs were selected based on uncertainty about their values and whether their values may depend on program implementation. The number and name of the 20 inputs with the largest mean absolute elementary effects are bolded. Those inputs were varied in the one-way sensitivity analysis.

b Calculated using Equation 12.4.  
c Calculated using Equation 12.5.

Figure 12.1 Elementary Effects Analysis Results for Total U.S. HIV Incidence in 2020: Standard Deviation of the Elementary Effects Versus Mean of Absolute Elementary Effects for 52 Inputs (Using Input Numbers Defined in Table 12.1)



## Values and Sources for Key Model Parameters

The values and sources for the 20 inputs with the largest mean absolute elementary effects, and their sources and assumptions, are listed in Table 12.2 in order of the magnitude of the absolute elementary effect.

Table 12.2. Values and Sources of Key Model Parameters

| Input | Value | Source |
| --- | --- | --- |
| Annual number of sexual partners per persona | High Risk HET Males: 9.4/6.3/4.5  High Risk HET Females: 5.1/3.8/3.1  Low Risk HET Males: 1.4/1.1/0.8  Low Risk HET Females: 1.0/0.8/0.8 | Calculated from CDC unpublished data based on NHBSb |
| Annual number of sex acts per person | High-risk HETs: 200  Low-risk HETs: 30 | Estimatedc |
| Percentage of HET females' sexual partners with HET males (versus MSM and male PWID) | 97.2% | Calibration |

(continued)

Table 12.2. Values and Sources of Key Model Parameters (continued)

| Input | Value | Source |
| --- | --- | --- |
| Percentage of MSM's sexual partners with MSM (versus HET females and female PWID) | 60.5% | Calibration |
| Probability of HIV transmission per condomless anal receptive sex act | 0.0089 | Calibration |
| Percentage of HET males' sexual partners with HET females (versus female PWID) | 99.5% | Calibration |
| Reduction in HIV transmission per sexual contact for HETs if virally suppressed | 0.96 | Cohen et al. (2011) |
| Condom efficacy per sex act for MSM | MSM insertive: 63%  MSM: receptive: 72% | Smith et al. (2015)  Smith et al. (2015) |
| Probability of HIV transmission per condomless vaginal receptive sex act | 0.00067 | Calibration |
| Percentage of anal sex acts protected with condoms | Females with male partners: 13.2% | Reece et al. (2010) |
| Males with female partners: 17.8% | Reece et al. (2010b)d |
| Males with Male partners: 50.0% | Sorensen et al. (2012); Crepaz et al. (2009); Marks et al. (2001); Marks et al. (2006); Marks et al. (2005); Marks et al.; Marks et al. (2009) |
| Probability of HIV transmission per condomless vaginal insertive sex act | 0.0004111 | Calibration |
| Percentage of MSM sex acts that are insertive | 50% | Sánchez et al. (2011) |
| Annual probability of becoming VLS if on ART but not VLS | Years 2006–2009:  Black: 0.122  Hispanic/Latino: 0.302  Other: 0.154  Years 2010+:  Black: 0.236  Hispanic/Latino: 0.404  Other: 0.147 | Calibration |
| Condom efficacy per sex act for HETs | 80.2% | Weller et al. (2002) |
| Reduction in probability of HIV transmission per sex act if circumcised versus uncircumcised | Vaginal insertive: 0.54  Male-male anal insertive: 0.00  Male-female anal insertive: 0.00 | Siegfried et al. (2009)  Assumption  Assumption |

(continued)

Table 12.2. Values and Sources of Key Model Parameters (continued)

| Input | Value | Source |
| --- | --- | --- |
| Percentage of vaginal sex acts protected with condoms | Black: 30.9%  Hispanic/Latino: 25.4%  Other: 17.1% | Reece et al. (2010b) |
| Annual testing rate, 2010+ | For reference case (Black, HET, C.CD4 > 500): 0.141 | Calibration |
| Annual probability of being prescribed ART, if eligible for ART | Acute: 0.000  CD4>500: 0.540  CDC 350-500: 0.600  CD4 200-350: 0.750  CD4<200: 0.920 | Based on Fleishman et al. (2012) |
| Annual probability of losing viral suppression | Years :2006–2009  Black: 0.278  Hispanic/Latino: 0.228  Other: 0.462  Years: 2010+  Black:0.253  Hispanic/Latino: 0.200  Other: 0.252 | Calibration |
| Percentage of people who have any AI in their male-female partnerships, 2010+a | Male  Age Group:  13-17: 3.0/5.3/2.5  18-24: 6.5/11.6/5.4  25-34: 23.3/28.6/25.3  35-44: 15.8/27.0/22.8  45-64: 10.2/18.2/12.6  Female  Age Group:  13-17: 2.7/5.6/3.7  18-24: 14.3/29.5/20.1  25-34: 14.4/28.8/24.1  35-44: 12.2/21.0/18.2  45-64: 9.6/12.0/7.0 | Calculated; Herbenick et al. (2010); Reece et al. (2010a); Dodge et al. (2010); Finlayson et al. (2008) |
| Annual rate of initiating PrEP per eligible person | Current continuum of care:  HET:0.1085  MSM: 0.5264  PWID:0.1085  National goals achieved:  HET: 0.1085  MSM: 0.5267  PWID: 01085 | Calculated to give a coverage of  HET: 10%  MSM: 40%  PWID: 10%  Coverage levels assumed based on expert opinion.e |

(continued)

Table 12.2. Values and Sources of Key Model Parameters (continued)

| Input | Value | Source |
| --- | --- | --- |
| PrEP Efficacy | HET: 75%  MSM: 73%  PWID: 49% | Baeten et al. (2012)  Grant et al. (2010)  Choopanya et al. (2013) |
| Annual probability of dropping off of PrEP, if susceptible and on-PrEP | 0% | Assumption |

AI = anal intercourse; ART = antiretroviral therapy; HET = heterosexual; MSM = men who have sex with men; PrEP = pre-exposure prophylaxis; PWID = people who inject drugs; VLS = viral load suppressed.

a The reported values correspond to Blacks, Hispanic/Latinos, and Whites/Other, respectively

b CDC unpublished data generated from National HIV Behavioral Surveillance reported the total number of annual partners among infected and uninfected heterosexuals. We defined high-risk and low-risk heterosexuals depending on the number of partnerships and other factors. Leichliter and colleagues (2010) reported the annual numbers of partners by race and sex for high-risk heterosexuals. We applied their distributions of partnerships by race and sex to our number of total partnerships among low- and high-risk heterosexuals.

c Estimated so that HIV prevalence in low-risk and high-risk HETs was stable over time. See Table 6.9 for further details.

d Reece and colleagues (2010b) reported the percentage of anal sex acts protected with condoms for all males and for MSM, and the sample size for all males and MSM. Based on that, we calculated the proportions of the sample that were MSM or heterosexual males, and the proportion of sex acts protected with condoms for heterosexual males. We used the following equation: Percentage of anal sexual contacts protected with condoms for males with female partners = [(Percentage of anal sex acts protected with a condom for all adult males)-((Percentage of sample that was MSM)\* (Percentage of anal sex acts protected with a condom for MSM))]/[Percentage of sample that was heterosexual male].

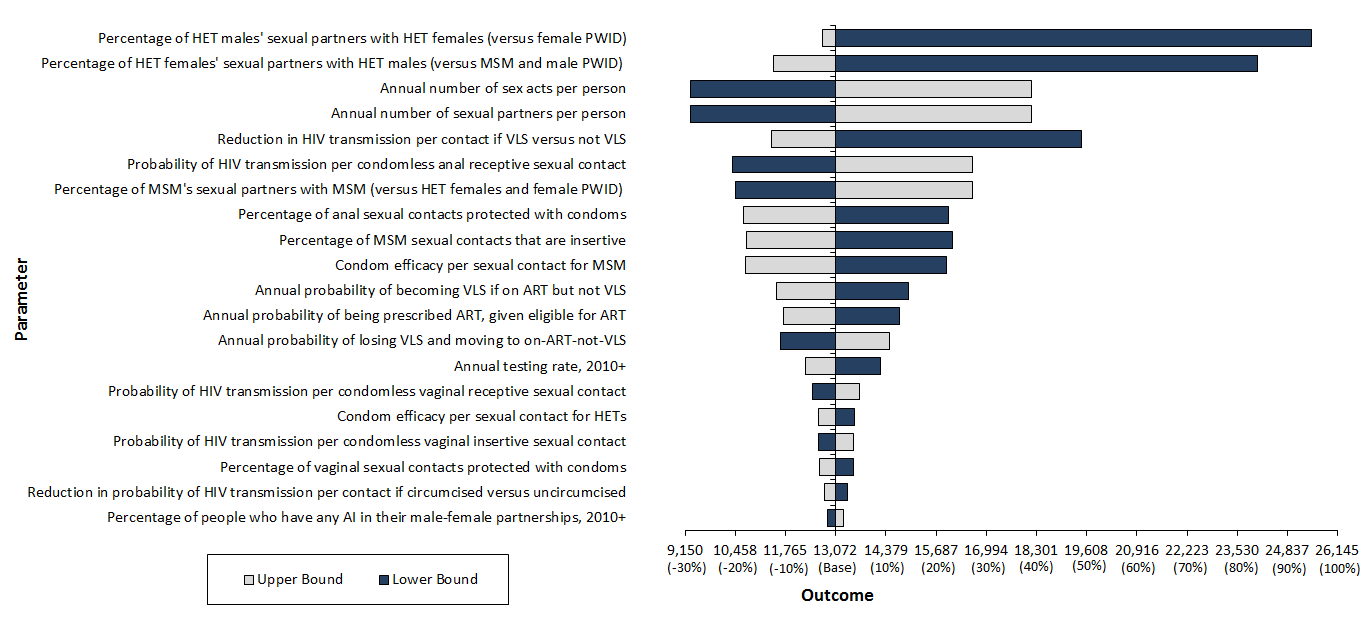
e The rates are for the case when efficacy of PrEP was assumed to be at base case. Annual rates of initiating PrEP per eligible person were adjusted to maintain these coverage levels when efficacy was varied.

## One-Way Sensitivity Analysis

We selected the 20 inputs with the largest mean absolute elementary effects to vary in the one-way sensitivity analysis; those inputs are marked in Table 12.1. Each input’s value was varied in the model by ±20%, and the total U.S. HIV incidence in 2020 for the scenario when national goals were achieved and PrEP was delivered were recorded.

We present the sensitivity analysis outcomes in the form of a tornado diagram (Figure 12.2), showing the parameters that had the greatest impact on the number of HIV infections in 2020 at the top and those that had the least impact at the bottom.

Figure 12.2. One-Way Sensitivity Analysis Results: Impact of ±20% Relative Change in Input Parameter Values on the Total U.S. HIV Incidence in 2020



ART = antiretroviral therapy; HET = heterosexual; MSM = men who have sex with men; PWID = people who inject drugs; VLS = viral load suppressed.

## Uncertainty Analysis

Uncertainty analysis is used to evaluate a model outcome’s variability that is due to the uncertainty of model input values that are estimated. Unlike a one-way sensitivity analysis, which estimates the effect of the changes in the value of an individual input on the model outcome, uncertainty analysis considers the variability of the model outcome based on the collective uncertainty of the estimated input values.

To consider the uncertainty of the cumulative incidence estimates between 2016 and 2020 due to the selected values of the calibrated parameters, we ran the model using 10 additional sets of values for those inputs that resulted in model outcomes that approximated the targeted surveillance measures. The same process and selection criteria were applied as for the set used in the base case analysis, as outlined in Sections 11.1.3 and 11.1.4. We then observed the range of the cumulative incidence estimates between 2016 and 2020 for the scenario when national goals have been achieved and PrEP has been delivered for all transmission groups across all calibrated runs to assess the robustness of our findings (Table 12.3).

We found that total cumulative U.S. HIV incidence from 2016 to 2020 stayed within 25% of the base case outcome, while the cumulative incidence for MSM, HET, and PWID stayed within 20%, 26%, and 50% of the base case outcome, respectively. These outcomes demonstrate the robustness of the findings.

Table 12.3 Uncertainty Analysis Results for Cumulative U.S. HIV Incidence from 2016 to 2020

| Population | Base Case | Minimum | Maximum |
| --- | --- | --- | --- |
| MSM | 49,444 | 40,039 | 57,426 |
| HET | 26,599 | 19,743 | 30,636 |
| PWID | 12,434 | 6,315 | 15,096 |
| Total U.S. population | 88,476 | 67,941 | 98,437 |

HET = heterosexual; MSM = men who have sex with men; PWID = persons who inject drugs.

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Appendix A:  
Definitions

Table A.1. Definitions of Symbols Applied in This Document

| Symbol | Definition |
| --- | --- |
| **Latin Alphabet** | |
| *A* | Cumulative total costs over the time horizon |
|  | Percentage of individuals in subpopulation p1’s partners that are in p2, as determined by the mixing matrix |
| *Bc* | Rate of HIV progression to the next disease stage from compartment *c,* if VLS; applies to individuals with HIV, CD4 ≥ 200, and VLS, (*c* = 10, 15, 20) only |
| *bp1,p2,z* | Percentage reduction in per-insertive sex act transmission probability from an act of type z due to circumcision for an HIV-uninfected individual in subpopulation *p1* with an HIV-infected partner in subpopulation *p2* |
| *C* | Comparator scenario, using alternative user-defined inputs |
| *D* | Cumulative treatment and care costs over the time horizon |
| *dz* | Percentage reduction in per-sex-act transmission probability from an act of type z due to condom use |
| *E* | Number of needles shared annually per needle-sharing partner by a person who injects drugs (PWID) who has never been diagnosed with HIV |
|  | Rate of departure from HIV care if in care but not prescribed ART, by demographic subpopulation *p* at time *t*; applies to (*c =*5, 8, 13, 18, 23) only |
| *F* | Cumulative number of HIV infections over the time horizon |
| *Gz,p,c* | Percentage of sex acts of risk type z protected with a condom, given partner in compartment *c*, by subpopulation *p* |
| *Hc* | Rate of HIV progression to the next disease stage from compartment *c,* if prescribed ART, not VLS; applies to individuals with HIV, CD4 ≥ 200, and prescribed ART, not VLS (*c* = 9, 14, 19) only |
| *I* | Initial scenario, using user-defined inputs |

(continued)

Table A.1. Definitions of Symbols Applied in This Document (continued)

| Symbol | Definition |
| --- | --- |
| **Latin Alphabet (continued)** | |
| *i*p | Percentage reduction in the annual rate of HIV transmission if HIV- individual in subpopulation *p* is on PrEP |
|  | Number of individuals in subpopulation p eligible for intervention j\* at time t |
|  | Percentage of subpopulation *p* compliant with testing at the given interval (relevant for interval-based testing only) |
| *L* | Cumulative life-years in the modelled population over the time horizon |
|  | Binary indicator of eligibility for intervention j\* for individuals in compartment c (1 = eligible, 0 = not eligible) |
|  | Rate of linkage to HIV care among aware (not newly diagnosed) individuals, by demographic subpopulation *p* at time *t*; applies to individuals aware of their infection but not in care or prescribed ART (*c* =4, 7, 12, 17, 22) only |
|  | Annual number of partners of risk type z per person in demographic subpopulation *p* |
|  | Average interval between tests in months by demographic subpopulation *p* (applicable to HET interval-based testing method only) |
| ṅj\* | Annual funding allocation for implementing intervention j\* |
|  | Percentage of subpopulation p’s partnerships that are type y, given partnerships of type y |
| *P(t)* | HIV prevalence at time *t*, defined as the number of individuals with HIV |
| *Q* | Discount rate for QALYs |
| *q(t)* | Length of model’s computational time step, in years, at time t |
| *Rc* | Health utility for individuals in compartment c |
| *Rj\*,1* | Maximum reach for intervention j\* in any 1 year among individuals eligible for that intervention |

(continued)

Table A.1. Definitions of Symbols Applied in This Document (continued)

| Symbol | Definition |
| --- | --- |
| **Latin Alphabet (continued)** | |
| *Rj\*,2* | Maximum annual rate or probability of the transition targeted by intervention j\* among individuals eligible for that intervention |
| *S p* | Number of annual sex acts for an HIV-uninfected individual per partner, HIV-uninfected or undiagnosed, by subpopulation *p* |
| *sc* | Binary indicator that model state *c* is an infected HIV state (1 = infected, 0 = not infected) |
|  | Per-person cost of implementing intervention j\*, as incurred by the agency funding the intervention |
| *Τ*p1,p2,c | Reduction in number of needles shared for diagnosed versus undiagnosed or uninfected (0 if compartment *c* is for undiagnosed or uninfected compartments or if either subpopulations *p1* or *p2* are not PWID) |
|  | Percentage of the individuals who become VLS among those who are prescribed ART |
|  | Binary indicator that subpopulation p is targeted by intervention j\* (1 = included, 0 = not included) |
| *U* | Discount rate for costs |
|  | Proportion of male-male sex acts by individuals in subpopulation p1 with individuals in subpopulation p2 that are receptive (0 if subpopulation p1 or p2 is not MSM), so that (1 − ) is the fraction of insertive sex acts |
| W | Cumulative quality-adjusted life-years in the modelled population over the time horizon |
|  | Test sensitivity by compartment *c* and type of test *g* |
|  | Number of individuals in the population in compartment *c* and demographic subpopulation *p* at time *t*; when progression along the HIV continuum of care determined by allocation-based progression, this variable is also a function of allocated budget and therefore represented by |
| Yp | Annual probability of stopping PrEP, if susceptible and on-PrEP for subpopulation *p* |
|  | Number of individuals in subpopulation p funded to receive intervention j\* over time step t, given allocated budget |
| Z | Number of inputs varied using the elementary effects method |

(continued)

Table A.1. Definitions of Symbols Applied in This Document (continued)

| Symbol | Definition |
| --- | --- |
| **Greek Alphabet** | |
|  | Probability of transmission for an HIV-uninfected individual in subpopulation *p1* per sexual or needle-sharing partnership from risk type *z* (vaginal, anal, or needle) in a partnership type *y* (male-female partnership with vaginal intercourse only, male-male partnership with anal intercourse only, male-female partnership that includes anal intercourse, or needle-sharing) with a partner who is in subpopulation *p2* and compartment *c* |
|  | Per-sex-act transmission probability for insertive unprotected intercourse of type z (vaginal or anal intercourse) with infected partner in compartment *c* |
|  | Rate of ART prescription if linked to HIV care, by compartment c and subpopulation *p* at time *t*; applies to individuals linked to HIV care and not prescribed ART (*c =*5, 8, 13, 18, 23) |
|  | Percentage reduction in per-act transmission probability due to viral load suppression, by compartment c and transmission risk type *z* |
| and | Aging rates into (+) and out of (–) demographic subpopulation *p* |
|  | Annual rate of dropping off of ART if ART-not-VLS, by demographic subpopulation *p* at time *t*; applies to individuals who are ART-not-VLS (*c =*9, 14, 19, 24) only |
|  | Annual rate of loss of viral load suppression if VLS, by demographic subpopulation *p* at time *t*; applies to individuals with HIV and who are VLS (*c* = 10, 15, 20, 25) only |
| Θ *c* | Probability of HIV transmission per needle shared with an HIV-infected partner in compartment c |
|  | Rate of HIV progression to the previous disease stage from compartment *c*, if VLS; applies to individuals with HIV, CD4 ≤500, and VLS, (*c* = 15, 20, 25) only |
|  | Percentage of newly diagnosed individuals in subpopulation *p* immediately linked to HIV care at time *t* |
|  | Constant rate of aging into the modeled population per person in subpopulation *p* at the start of the model |
|  | Force of HIV infection for non-HIV-infected individuals (across all sexual and needle-sharing risks) in subpopulation *p* at time *t* |

(continued)

Table A.1. Definitions of Symbols Applied in This Document (continued)

| Symbol | Definition |
| --- | --- |
| **Greek Alphabet (continued)** | |
|  | Force of HIV infection from risk type *z* for non-HIV infected individuals in subpopulation *p* who participate in sexual transmission risk behaviors of each type x, at time *t* |
|  | Mortality rate from causes other than AIDS, if not prescribed ART, by demographic subpopulation *p* |
| ξ z,y,p1,p2,c | Number of partnerships of type y involving risk type z per uninfected individual in subpopulation p1 with infected partners in subpopulation p2 in compartment c |
| (t) | Rate of testing of undiagnosed individuals in compartment *c*, at time *t* by demographic subpopulation *p* |
| (t) | Probability of notification given a confirmed positive test result for a previously undiagnosed individual in demographic subpopulation *p* and type of test *g* at time *t* |
|  | Proportion of subpopulation p with transmission risk participation type x, which is defined by the percentage of people who have anal intercourse (AI) in their male-female partnerships as well as the assumptions that 100% of MSM have AI in their male-male partnerships and 100% of all transmission groups have vaginal intercourse (VI) in their male-female partnerships |
|  | Mortality rate if HIV-infected, by demographic subpopulation *p* and compartment *c,* at time *t* |
|  | Diagnosis rate based on test and notification of unaware infected individuals in compartment *c*, progressing them from unaware(*r =*1) to aware (*r* = 2 or *r =*3), by subpopulation *p* |
|  | Per-sex-act transmission probability for receptive unprotected intercourse of type z (vaginal or anal intercourse) with infected partner in compartment *c* |
|  | Annual probability of initiating PrEP, given eligible, for subpopulation *p* at time *t* |
| *(t)* | Percentage of screens that are rapid (type of test *g* = 1), by subpopulation *p* and time *t* |
| Ωp1,p2,z,y | Proportion of sexual acts by individuals in subpopulation p1 in partnerships of type y with individuals in subpopulation p2 that are risk type z (where z = vaginal or anal) |
|  | Rate of natural history of HIV progression to the next disease stage from compartment *c*; applies to individuals with HIV, CD4 ≥ 200, and not prescribed ART (*c* = 3 to 5, 6 to 8, 11 to 13, 16 to 18) only |
|  | Annual rate of becoming VLS if ART-not-VLS, by demographic subpopulation *p* at time *t* |

(continued)

Table A.1. Definitions of Symbols Applied in This Document (continued)

| Symbol | Definition |
| --- | --- |
| **Other Symbols** | |
|  | Rate (j\* = {1,…5,7,…10}) or probability (j\* = 6) of progression for the transition targeted by intervention j\* in subpopulation p in compartment c at time t, given no allocated funding from CDC |
|  | Rate (j\* = {1,…5,7,…10}) or probability (j\* = 6) of progression targeted by intervention j\* for subpopulation p in compartment c at time t, given allocated funding ṅj\* for intervention j\* from budget under consideration |
| *Л* | Number of iterations performed using the elementary effects method |
| Њ | Input number being sampled or varied in elementary effects method |
| ш | Iteration number in the elementary effects method |
| *й*Њ*,ш* | The *шth* sampled value of input Њ in the elementary effects method |
| Ж | Constant percentage of base parameter value used for parameter variation in the elementary effects method |

Note: ART = antiretroviral therapy; PrEP = pre-exposure prophylaxis; PWID = people who inject drugs.

Table A.2. Definitions of Indices Applied in This Document

| Index | Definition | Number of Categories | Categories (Represented by) |
| --- | --- | --- | --- |
| c | Compartment | 28 | 25 main compartments for individuals actively moving through the model (further defined by disease stage [*h*] and continuum-of-care stage [*r*]) and 3 compartments for individuals who were no longer actively followed in the model due to death due to causes other than AIDS, death due to AIDS, and aging out.  1: Susceptible / not on PrEP (A1)  2: Susceptible / on PrEP (A6)  3: HIV-infected / acute stage / unaware of infection (B1)  4: HIV-infected / acute stage / aware, but not linked to HIV care (B2)  5: HIV-infected / acute stage / linked to HIV care, but not prescribed ART (B3)  6: HIV-infected / CD4>500 / unaware of infection (C1)  7: HIV-infected / CD4>500 / aware, but not linked to HIV care (C2)  8: HIV-infected / CD4>500 / linked to HIV care, but not prescribed ART (C3)  9: HIV-infected / CD4>500 / prescribed ART, not VLS (C4)  10: HIV-infected / CD4>500 / VLS (C5)  11: HIV-infected / CD4 350–500 / unaware of infection (D1)  12: HIV-infected / CD4 350–500 / aware, but not linked to HIV care (D2)  13: HIV-infected / CD4 350–500 / linked to HIV care, but not prescribed ART (D3)  14: HIV-infected / CD4 350–500 / prescribed ART, not VLS (D4)  15: HIV-infected / CD4 350–500 / VLS (D5)  16: HIV-infected / CD4 200–350 / unaware of infection (E1)  17: HIV-infected / CD4 200–350 / aware, but not linked to HIV care (E2)  18: HIV-infected / CD4 200–350 / linked to HIV care, but not prescribed ART (E3)  19: HIV-infected / CD4 200–350 / prescribed ART, not VLS (E4)  20: HIV-infected / CD4 200–350 / VLS (E5)  21: HIV-infected / CD4 < 200 / unaware of infection (F1)  22: HIV-infected / CD4 < 200 (AIDS) / aware, but not linked to HIV care (F2) |

(continued)

Table A.2. Definitions of Indices Applied in This Document (continued)

| Index | Definition | Number of Categories | Categories (Represented by) |
| --- | --- | --- | --- |
|  |  |  | 23: HIV-infected / CD4 < 200 (AIDS) / linked to HIV care, but not prescribed ART (F3)  24: HIV-infected / CD4 < 200 (AIDS) / prescribed ART, not VLS (F4)  25: HIV-infected / CD4 < 200 (AIDS) / VLS (F5)  26: Non-AIDS death-related cause  27: AIDS death  28: Aged out of the population |
| g | Test type | 2 | Rapid screen (1)  Conventional screen (2) |
| h | Disease status | 6 | No HIV infection (0)  Acute HIV infection (1)  HIV infection with CD4 count greater than 500 cells/mm3 (2)  HIV infection with CD4 count between 350 cells/mm3 and 500 cells/mm3 (3)  HIV infection with CD4 count between 200 cells/mm3 and 350 cells/mm3 (4)  AIDS with CD4 less than 200 cells/mm3 (5) |
| j | Age group | 5 | 13–17 years (1)  18–24 years (2)  25–34 years (3)  35–44 years (4)  45–64 years (5) |

(continued)

Table A.2. Definitions of Indices Applied in This Document (continued)

| Index | Definition | Number of Categories | Categories (Represented by) |
| --- | --- | --- | --- |
| j\* | Interventions aimed at increasing progression along the continuum of HIV care | 13 | Testing intervention targeted to low-risk HETs (1), high-risk HETs (2), low-risk MSM (3), high-risk MSM (4), PWIDs (5)  Linkage to HIV care at diagnosis intervention (6)  Linkage to HIV care later after diagnosis intervention (7)  ART prescription intervention (8)  ART adherence (to move from ART-not-VLS to VLS) intervention (9)  ART adherence (to remain VLS) intervention (10)  PrEP initiation intervention targeted to high-risk HETs (11), high-risk MSM (12), PWIDs (13) |
| k | Risk level | 2 | Low (1)  High (2) |
| l | Transmission group | 3 | HETs (1)  MSM (2)  PWID (3) |
| m | Sex | 2 | Male (1)  Female (2) |
| n | Circumcision status | 2 | Uncircumcised (1)  Circumcised (2) |
| o | Race/ethnicity | 3 | Black (1)  Hispanic/Latino (2)  Other (3) |
| p | Subpopulation | 195 | Combinations defined by age group (j), risk level (k), transmission group (l), sex (m), circumcision status (n), and race/ethnicity (o). PWID are all high-risk, MSM are all male, and only males are stratified by circumcision status, therefore not all combinations of these stratifications are represented. |

(continued)

Table A.2. Definitions of Indices Applied in This Document (continued)

| Index | Definition | Number of Categories | Categories (Represented by) |
| --- | --- | --- | --- |
| r | Care Continuum stage | 5 | Uninfected or unaware of infection (1)  Aware of infection, not prescribed ART or in HIV care (2)  Linked to HIV care, not prescribed ART (3)  Prescribed ART, not VLS (4)  VLS (5) |
| t | Time/timestep | 1 | -- |
| x | Sexual transmission risk participation type | 3 | Vaginal intercourse only in male-female partnerships (1)  Anal intercourse only in male-male partnerships (2)  Anal intercourse in male-female partnerships (3) |
| y | Partnership type | 4 | Male-female partnership that only includes vaginal intercourse (1)  Male-male partnership that only includes anal intercourse (2)  Male-female partnership that includes anal intercourse (3)  Needle-sharing (4) |
| z | Transmission risk type | 3 | Vaginal intercourse (1)  Anal intercourse (2)  Needle-sharing (3) |

Note: ART = antiretroviral therapy; PrEP = pre-exposure prophylaxis; PWID = people who inject drugs.