Impact of Improved HIV Care and Treatment on PrEP Effectiveness in the United States, 2016–2020

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Background: The effect of improving diagnosis, care, and treatment of persons living with HIV (PLWH) on pre-exposure prophylaxis (PrEP) effectiveness in the United States has not been well established.

Methods: We used a dynamic, compartmental model that simulates the sexually active US population. We investigated the change in cumulative HIV incidence from 2016 to 2020 for 3 HIV care-continuum levels and the marginal benefit of PrEP compared with each. We also explored the marginal benefit of PrEP for individual risk groups, and as PrEP adherence, coverage and dropout rates varied.

Results: Delivering PrEP in 2016 to persons at high risk of acquiring HIV resulted in an 18.1% reduction in new HIV infections from 2016 to 2020 under current care-continuum levels. Achieving HIV national goals of 90% of PLWH with diagnosed infection, 85% of newly diagnosed PLWH linked to care at diagnosis, and 80% of diagnosed PLWH virally suppressed reduced cumulative incidence by 34.4%. Delivery of PrEP in addition to this scenario resulted in a marginal benefit of 11.1% additional infections prevented. When national goals were reached, PrEP prevented an additional 15.2% cases among men who have sex with men, 3.9% among heterosexuals, and 3.8% among persons who inject drugs.

Conclusions: The marginal benefit of PrEP was larger when current HIV-care-continuum percentages were maintained but continued to be substantial even when national care goals were met. The high-risk men who have sex with men population was the chief beneficiary of PrEP.

Key Words: HIV, PrEP, national HIV goals, HIV care-continuum

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INTRODUCTION

In the United States, more than 1.1 million persons were living with HIV at the end of 2014,[1] and approximately 40,000 persons are diagnosed with HIV each year.[2] However, 15% of persons living with HIV (PLWH) were unaware of their infection at the end of 2014.[1] Based on surveillance data, of PLWH diagnosed by the end of 2013 and alive at the end of 2014, only 58% had suppression of viral replication, hereafter referred to as viral suppression.[1] Two key strategies to reduce HIV incidence in the United States are (1) improving diagnosis, care, and treatment of PLWH, and (2) delivering pre-exposure prophylaxis (PrEP) to persons at risk for acquiring HIV. PrEP, which consists of daily oral antiretroviral medication for persons at high risk of acquiring HIV, is a highly effective intervention that may reduce the risk of disease transmission from sexual contact by more than 90%.[3]

In 2010, the White House first released a set of national goals that identified a set of priorities and strategic action steps for HIV prevention and treatment.[4] This document, which was updated in 2015, provided strategy goals and indicators of progress up to 2020.[5] The health service goals for increasing the proportion of PLWH who achieve each step of the HIV care continuum included increasing to 90% the proportion of PLWH who have diagnosed HIV, increasing to 85% the proportion of newly diagnosed PLWH linked to care within 1 month of diagnosis, and increasing to 80% the proportion of diagnosed PLWH who achieve and maintain viral suppression.

Clinical trials have established both a large reduction in HIV transmission risk among PLWH who achieve viral suppression[6] and the efficacy of PrEP in preventing HIV among men who have sex with men (MSM), persons who inject drugs (PWID), and high-risk heterosexuals (HRH).[7–9] However, the effectiveness of PrEP when layered onto improvements in the diagnosis, care, and treatment of PLWH has not been well established. Our objective is to estimate the number of infections prevented from 2016 to 2020 when populations at high risk of acquiring HIV are on PrEP either under the current continuum-of-care levels or under improved continuum-of-care levels that result in achievement of the three 2020 national goals listed above. Our goal is to investigate the

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marginal benefits of PrEP compared with different levels of treatment, delivered to different risk groups, and under different program implementation strategies.

METHODS

We used the HIV Optimization and Prevention Economics (HOPE) model (Version 4.03), which simulates the sexually active US population aged 13 to 64 years beginning in 2010,[10] to analyze the effects of reaching the national goals and implementing PrEP. The population in the model is stratified into 195 subpopulations by transmission group, sex, race/ethnicity, age group, male circumcision status, and HIV risk level as defined for this model based on previously published methods.[11,12] We provide details on the subpopulations in Section 3, Supplemental Digital Content http://links.lww.com/QAI/B158.

The model distributes each of the subpopulations across 25 compartments. All HIV-uninfected individuals are in 2 susceptible model compartments stratified by use of PrEP. PLWH are distributed among 23 compartments defined by disease progression (according to decreasing CD4 count) and continuum-of-care stage (moving from unaware of infection to viral suppression).

The differential equations were solved using the Dormand–Prince method of Runge–Kutta solvers (ie, RK5(4) 7FM) over each year, using MATLAB software (MathWorks; Natick, MA). The time steps were dynamically determined by the solver and varied between and within each year, such that the number of time steps in a given year varied from 10 to more than 20. However, in most years, the solver applied ten 0.1-year time steps. The Appendix describes the model's differential equations, force of infection calculations, model inputs and sources, calibration, and other model specifications.

Key Model Inputs

The model required data to describe the initial US population aged 13 through 64 years, HIV-risk behaviors and their associated transmission risks, efficacy of HIV prevention and treatment, and the movement of PLWH along the care-continuum and disease stages. To obtain estimated values for each model input, we reviewed and summarized the published, peer-reviewed literature, and surveillance data.

For inputs for which data were limited or uncertain, we obtained input values through a calibration process by varying those values within expected bounds.

The top 20 parameters for our model that have the greatest effect on our outcomes have been listed in Table 12.2, Supplemental Digital Content, http://links.lww.com/QAI/B158.

Estimation of PrEP-Eligible Population

According to the US Public Health Service (USPHS) 2014 guidelines, PrEP is recommended for people who are at substantial risk of HIV acquisition.[3] We defined high-risk subsets for each HIV-transmission category and assumed only those populations were eligible for PrEP. All PWID were assumed to be at high risk of HIV infection, whereas MSM and heterosexuals (HET) were both split into low- and high-risk categories.

To estimate the percentage of MSM that are high risk, we used sexual behavior survey data that closely matched the PrEP eligibility indicators in the 2014 PrEP guidelines.[3] We used the following indicators to define high-risk MSM (aged 18–64 years) (1) had at least one anal sex act in the past 12 months (regardless of HIV status); and (2) were both not in a monogamous partnership with an uninfected man and had at least one of the following: unprotected anal sex in the past 12 months, their last partner was HIV-infected or unknown, or had a sexually transmitted infection diagnosed or reported in the past 12 months. The percentage of MSM with these behavioral indicators was calculated from unpublished data using the CDC National HIV Behavioral Surveillance system (NHBS)[13] MSM cycle 2. As a result, we estimated 69.4% of MSM were high risk and eligible for PrEP if HIV negative. We then estimated the total number of MSM as 3.9% of men aged 13–64 years,[14] where the total number of men aged 13–64 years was derived from the US Census Bureau (2010). The number of PrEP-eligible MSM was calculated by excluding the number of HIV-positive, high-risk MSM, which was estimated in the model for each year. The number of PrEP-eligible, high-risk MSM at the beginning of 2016 was estimated to be 2,206,379.

We estimated the number of HRH using 2010 Census tract data. We started by obtaining population data for NHBS-HET 2010 metropolitan statistical areas.[15] HRH were then defined as the estimated population from census tracts that were from minority white (<50% white), high-poverty (>20% in poverty), and urban areas. To limit these census tract population sizes to HET, we reduced the total population sizes by 4.7% for men (to reflect MSM and PWID) and 0.3% for women (to reflect PWID), the estimated proportions of the population that were MSM or PWID in large central metropolitan urban areas.[16] 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 an opposite sex partner in the past year, as estimated by Oster.[17] Based on these calculations, we estimated the total number of sexually active HRH in the initial population. After adjusting for HIV prevalence, we estimated that the number of HRH eligible for PrEP at the beginning of 2016 was 9,045,474.

We estimated the number of PWID using the results from Lansky et al,[18] who conducted a meta-analysis using data from 4 national probability surveys. PWID were defined as the US population aged 13 years or older who reported use of injection drugs in the past 12 months. Lansky et al[18] estimated that 0.36% (0.26%–0.47%) of men and 0.21% (0.10%–0.32%) of women injected drugs in the past year. We applied these gender-specific estimates to the population sizes from the US Census Bureau (2010) to obtain the initial number of PWID, and we assumed that all of them either were infected with HIV or at high risk of infection. After adjusting for HIV prevalence, the total number of PWID eligible for PrEP at the beginning of 2016 was estimated to be 386,209.

Scenarios and Model Outcomes

We examined changes in the number of HIV infections from 2016 to 2020 under different scenarios that varied by both progression of PLWH along the care continuum and

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whether PrEP was implemented with eligible populations during the same period. We estimated that 87% of PLWH had diagnosed infection, 82% of newly diagnosed PLWH were linked to care, and 52% of diagnosed PLWH were virally suppressed at the beginning of 2016. Under current care-continuum levels, these percentages were maintained from 2016 to 2020. We first estimated the cumulative number of new HIV infections from 2016 to 2020 for the base-case scenario in which the current care-continuum levels were maintained, and PrEP was not implemented. We then repeated the analysis with the scenario for which the national health services goals have been achieved by 2020: 90% of PLWH had diagnosed infection, 85% of newly diagnosed PLWH were linked to care, and 80% of diagnosed PLWH were virally suppressed. Finally, we conducted an analysis for the scenario for which national health goals were achieved only partially (90% of PLWH had diagnosed infection, 85% of newly diagnosed PLWH were linked to care, and 65% of diagnosed PLWH were virally suppressed).

We then assumed that PrEP was delivered to the high-risk populations based on predetermined coverage levels (see below). We assumed that PrEP was delivered to MSM and heterosexuals who were considered to be at high risk of acquiring HIV. However, we collected the cumulative incidence of HIV among all MSM and heterosexuals as our outcome. The model allowed for a portion (defined as the coverage level) of the eligible population to initiate PrEP in 2016, and some portion of people on PrEP to dropout each year from 2016 to 2020. Therefore, the number of people on PrEP at any given time between 2016 and 2020 was determined based on the initial coverage and subsequent (in scenario analyses) dropout rates, as well as on rates of people leaving the model because of aging, death, or HIV infection. We assessed the marginal benefit of PrEP (ie, the additional number of infections prevented by PrEP) in each scenario.

Scenario Analyses: Varying PrEP Parameters

Efficacy

The efficacy of PrEP varies significantly based on adherence. In the base case, we assumed PrEP efficacy, defined as the reduction in HIV incidence among people on PrEP, was 73%,[7] 75%,[8] and 49%[9] for MSM, HRH, and PWID, respectively (Table 1). The assumed efficacy for MSM was that estimated among persons with high-level adherence in the iPrEX trial.[7] For HRH, the efficacy was set to the relative reduction in incidence with oral tenofovir disoproxil fumarate coformulated with emtricitabine among participants in the Partners PrEP trial.[8] The assumed efficacy of PrEP for PWID was based on the Bangkok Tenofovir Study.[9]

In the scenario analysis, we examined the effect of variations in PrEP efficacy/adherence on HIV incidence. We assumed the lower bound of efficacy for MSM was the same as that among all iPrEX trial participants, and the upper bound was that among iPrEX participants whose adherence was confirmed with a laboratory test.[7] Similarly, for PWID and HRH, we selected as the lower bound in scenario analyses the lower bounds of the 95% confidence intervals for the efficacy results in the PrEP trials specific to each risk group, as reported above.[8,9] We selected, as the upper bounds, the efficacy among participants with detectable levels of drugs in the PrEP trials specific to each risk group.[8,9]

Coverage

We assumed a portion of the eligible population initiated PrEP in 2016, and no new initiation occurred after that time. We set the coverage for the year 2016 and then allowed the coverage level to change according to any PrEP dropout, and aging, death, and HIV infection. Based on expert recommendations, we assumed the following coverage levels by transmission group: 40% of high-risk MSM, 10% of HRH, and 10% of PWID (Table 1). We varied the coverage levels by ±50% in the scenario analysis (Table 1).

Dropout

Given the lack of data on PrEP dropout, we assumed in the base-case analysis that no one who started PrEP discontinued using it. However, we investigated the effect of varying the annual probability of dropping off of PrEP in our scenario analysis. In that analysis, we assumed that a fixed portion of PrEP users discontinued its use entirely each year (including the year in which PrEP was initiated), and we examined the effect of dropout on the total number of new infections from 2016 to 2020 and the marginal benefit of PrEP.

Sensitivity and Uncertainty Analysis

Given the significant nonlinear effects in the model (ie, changes in model inputs affected outputs in unpredictable ways), we used the elementary effects method to screen all model parameters for inclusion in further sensitivity analysis. In our application of the method, we first selected 52 inputs

TABLE 1. Values of PrEP Efficacy and Coverage for Each Transmission Group

	High-Risk MSM	HRH	PWID
PrEP efficacy (reduction in incidence)			
Base case	73%	75%	49%
Range	44%–92%*	55%–90%†	9.6%–70%‡
PrEP coverage			
Base case	40%	10%	10%
Range	20%–60%	5%–15%	5%–15%

*Grant RM, Lama JR, Anderson PL, et al. Pre-exposure Chemoprophylaxis for HIV prevention in MSM. *N Engl J Med*. 2010;363:2587–2599.

†Baeten JM, Donnell D, Ndase P, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med*. 2012;367:399–410.

‡Choopanya K, Martin M, Suntharasamai P, et al. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomized, double-blind, placebo-controlled phase 3 trial. *Lancet*. 2013;381:2083–2090.

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whose values were uncertain. The 20 parameters with the greatest effect on the key outcome (total US HIV incidence in 2020) were selected for inclusion in the 1-way sensitivity analysis where we varied the inputs by ±20% of their base-case values. Further details of the elementary effects analysis are described in Section 12.1, Supplemental Digital Content, http://links.lww.com/QAI/B158. We also describe the uncertainty analysis and the generation of uncertainty ranges in Section 12.3, Supplemental Digital Content, http://links.lww.com/QAI/B158.

RESULTS

Our model predicted 162,254 new infections nationally from 2016 to 2020 in the base case with the current continuum-of-care levels without PrEP (Table 2). Introducing PrEP in 2016 for persons at high risk of acquiring HIV reduced the total number of HIV infections from 2016 to 2020 by 18.1% (29,371 cases) under the current continuum-of-care levels. Compared with the base case with no PrEP, achieving the national goals alone resulted in a 34.4% (55,828 cases) reduction in new infections. Implementing PrEP along with the national goals achievement resulted in a 11.1% (17,950 cases prevented) marginal benefit compared with reaching the national goals alone. Implementing PrEP when national goals were achieved partially resulted in 14.8% (24,010 cases prevented) marginal benefit of PrEP (see Table 9.2, Supplemental Digital Content, http://links.lww.com/QAI/B158).

We estimated the total number of new infections from 2016 to 2020 separately for MSM, HET, and PWID (Table 2). In the base case, our model predicted 102,410 new infections among MSM; 43,167 new infections among HET; and 16,676 new infections among PWID. Introducing PrEP at the current continuum-of-care levels resulted in a marginal benefit of 25.2% for MSM, compared with 6.2% for HRH, and 5.0% for PWID. Compared with the base case, achieving national goals led to a reduction in new infections from 2016 to 2020 of 36.5%, 34.4%, and 21.6% for MSM, HET, and PWID, respectively. Implementing PrEP along with the achievement of national goals provided a marginal benefit of 15.2%, 3.9%, and 3.8% for MSM, HET, and PWID, respectively.

Scenario Analyses: Varying PrEP Parameters

The marginal benefit of PrEP increased with its increasing efficacy and coverage (Table 3). For example, when national goals were achieved 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 7.2%, 11.1%, and 13.6%, respectively. When national goals were achieved and the proportion covered among those eligible was set at the lower bound, base case, and upper bound, the marginal benefit of PrEP was 5.7%, 11.1%, and 16.3%, respectively.

The marginal benefit of PrEP decreased as the annual rate of dropping off of PrEP increased. When the national goals were achieved and PrEP dropout probabilities were 5%, 20%, and 50%, the marginal benefit of PrEP was 10.1%, 7.8%, and 4.5%, respectively, in contrast with the 11.1% 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 15.2% to 6.2% for MSM as the dropout probability increased from zero to 50%. The corresponding decrease in marginal benefit of PrEP was from 3.9% to 1.6% for HETs and from 3.8% to 1.4% for PWID.

Sensitivity and Uncertainty Analysis

We found that mixing between transmission groups: percentage of sexual partners of HET men with HET women (versus female PWID) and percentage of sexual partners of HET women with HET men (versus MSM and male PWID) had the largest effect on HIV incidence in 2020 (see Figure 12.2, Supplemental Digital Content, http://links.lww.com/QAI/B158). Further details on results from the elementary effects method and 1-way sensitivity analysis are presented in the Appendix.

The uncertainty analysis results indicated that the cumulative HIV incidence (from 2016 to 2020) across multiple calibration sets stayed within 25% of the base-case outcome (see Table 12.3, Supplemental Digital Content, http://links.lww.com/QAI/B158).

TABLE 2. Cumulative Number of New Infections 2016–2020 for Different Scenarios. *

Scenario	MSM	HET	PWID	Total
Current care-continuum levels—no PrEP (base case)	102,410	43,167	16,676	162,254
Current care-continuum levels—with PrEP	76,562	40,473	15,849	132,883
HIV infections prevented because of PrEP/marginal benefit of PrEP (%)	25,848 (25.2)	2694 (6.2)	827 (5.0)	29,371 (18.1)
National goals achieved—no PrEP	65,059	28,302	13,075	106,426
HIV infections prevented (%)	37,351 (36.5)	14,865 (34.4)	3601 (21.6)	55,828 (34.4)
National goals achieved—with PrEP	49,444	26,599	12,434	88,476
HIV infections prevented (%)	52,966 (51.7)	16,569 (38.4)	4242 (25.4)	73,778 (45.5)
HIV infections prevented because of PrEP/marginal benefit of PrEP (%)	15,615 (15.2)	1704 (3.9)	641 (3.8)	17,950 (11.1)

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

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TABLE 3. Cumulative Number of New HIV Infections From 2016 to 2020 and the Marginal Benefit of Delivering PrEP as PrEP Parameters are Varied.*†‡

	MSM (%)	HET (%)	PWID (%)	Total (%)
Varying efficacy: coverage and dropout rate set to base-case values				
Efficacy				
Lower bound	54,912 (9.9)	27,016 (3.0)	12,900 (1.0)	94,828 (7.2)
Base case	49,444 (15.2)	26,599 (3.9)	12,434 (3.8)	88,476 (11.1)
Upper bound	45,909 (18.7)	26,292 (4.7)	12,181 (5.4)	84,381 (13.6)
Varying coverage: efficacy and dropout rate set to base-case values				
Coverage				
Lower bound	57,069 (7.8)	27,444 (2.0)	12,754 (1.9)	97,267 (5.7)
Base case	49,444 (15.2)	26,599 (3.9)	12,434 (3.8)	88,476 (11.1)
Upper bound	42,111 (22.4)	25,770 (5.9)	12,116 (5.7)	79,998 (16.3)
Varying dropout rate: efficacy and coverage set to base-case values				
Dropout rate				
0% Base case	49,444 (15.2)	26,599 (3.9)	12,434 (3.8)	88,476 (11.1)
5%	50,736 (13.9)	26,745 (3.6)	12,495 (3.5)	89,980 (10.1)
20%	54,073 (10.7)	27,123 (2.7)	12,649 (2.6)	93,845 (7.8)
50%	58,715 (6.2)	27,636 (1.6)	12,849 (1.4)	99,200 (4.5)

*Efficacy, coverage, and dropout rate of PrEP are independently varied for the scenario when national goals have been achieved.

†In the Appendix, we report the marginal benefit of PrEP as efficacy, coverage, and dropout rates vary, in the context of maintaining current levels of the HIV care continuum, not when national goals are achieved by 2020 (see Table 9.1, Supplemental Digital Content, http://links.lww.com/QAI/B158).

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

DISCUSSION

In this study, we used a dynamic, compartmental model that simulates the sexually active US population aged 13 to 64 years to analyze the effects of reaching national goals and implementing PrEP. Our results show that scaling up these strategies in combination can prevent 45.5% of infections by 2020. Reaching the health services national goals alone can reduce the number of new HIV infections by 34.4% by 2020. This highlights the importance of access to HIV care and treatment.

The marginal benefits of PrEP, compared with care and treatment of people living with HIV, vary depending on the scope of care and treatment and characteristics of the PrEP program. When care and treatment are expanded to reach ambitious national goals by 2020, our estimates suggest that PrEP will prevent 11.1% more cases compared with care and treatment alone over 5 years. When care and treatment are expanded but national goals are not fully achieved by 2020, our results show that PrEP will prevent 14.8% more cases compared with treatment alone. If the current scope of treatment was maintained through 2020, PrEP would have a larger contribution, preventing 18.1% more cases than treatment alone.

The marginal benefits of PrEP accrue unevenly across risk groups. With expanded treatment, we estimate that PrEP will prevent 15.2% more cases among MSM, compared with 3.9% and 3.8% more among HET and PWID, respectively. The marginal benefit of PrEP can be diminished if program implementation is weak. Assuming PrEP efficacy at the base-case level, PrEP coverage at half the base-case value prevented 5.7% more cases than when national care and treatment goals alone are reached (Table 3) and 9.2% more cases than current levels of treatment (see Table 9.1, Supplemental Digital Content, http://links.lww.com/QAI/B158). If coverage goals are reached, but a 50% annual dropout rate occurs, PrEP will prevent 4.5% more cases than achievement of national goals alone (Table 3) and 6.4% more than current levels of treatment (see Table 9.1, Supplemental Digital Content, http://links.lww.com/QAI/B158). These findings indicate that, in addition to supporting strong adherence, PrEP programs will yield the best results if recommended coverage levels are reached and sustained.

Previous studies have explored the individual roles of achieving key national goals. Shah et al[19] used a dynamic transmission model to study the effect of reaching national goals (90% awareness of serostatus, 85% linkage within 1 month of diagnosis, and 90% of diagnosed individuals in care) in the United States. Their results show that achieving these goals can decrease the cumulative incidence of HIV in the period 2016–2025 by 58%. Their results are comparable with the estimate provided by our model, that is, a 34% reduction compared with the base case in cumulative infections in a 5-year period when the national goals have been achieved.

The impact of delivering PrEP in the United States has also been examined.[20–28] However, most of those studies focus on initiating PrEP either among specific

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transmission groups[20–22,24–28] or into specific geographical areas.[23,27] Juusola et al[20] used a dynamic model that estimated that initiating PrEP in 50% of high-risk MSM in the US would reduce the number of new HIV infections by 29% over a period of 20 years. Paltiel et al[21] used a state transition, Monte Carlo simulation model to show that, in a cohort with a mean age of 34, PrEP can reduce the lifetime infection risk of MSM who are at high risk of getting HIV from 44% to 25%. Jenness et al[28] used a network-based model to estimate that implementing CDC PrEP guidelines at 40% coverage of indicated MSM and 62% high adherence among those covered would avert 33% of new infections among MSM in the United States over a period of 10 years. The effect of combining prevention strategies (initiating PrEP and expanded HIV testing combined with enhanced ART provision) in the United States has also been examined.[26,27] These studies focused on specific transmission groups[26,27] or geographical areas.[27] Bernard et al[26] investigated the effect of initiating PrEP and frequent screening and enhanced ART provision among PWID in the United States. Drabo et al[27] used a mathematical model to investigate the cost effectiveness of test-and-treat (expanded HIV testing combined with immediate treatment) and initiation of PrEP among MSM aged 15–65 years, who reside in Los Angeles County, California. Our work investigates the impact on the incidence of HIV in the United States of achieving national goals and delivering PrEP to all transmission groups at high risk of acquiring HIV.

Our study has several limitations. Our model simulates the sexually active population in the United States, and therefore, a large amount of data is required to inform the model inputs. Uncertainty in model inputs can lead to uncertainty in our estimates of the cumulative number of new HIV infections. Therefore, we conducted sensitivity analysis. We also varied the values of PrEP efficacy, PrEP coverage, and PrEP dropout rates to understand their effect on our outcomes. Another limitation of our study is that sexual risk behaviors are assumed to be constant over time. However, in reality, people might reduce their risk behaviors if they stop taking PrEP. We also did not include drug resistance associated with PrEP in our model because the iPreX study for MSM and the Bangkok Tenofovir study for PWID did not find any development of drug resistance.[7,9] Finally, models are always a limited representation of reality. Our model simulates HIV in the United States at the national level, and we have taken multiple steps to ensure its validity. Our model type cannot answer questions related to the details of network structures. Agent-based and network models are better suited for those questions.

In conclusion, increasing diagnosis, and care and treatment of PLWH resulted in a large decrease in HIV incidence by 2020. The marginal benefit of PrEP decreased as diagnosis, care, and treatment improved. However, even at high levels of viral suppression, PrEP continued to achieve reductions in HIV incidence over 5 years.

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