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Assessing the impact of COVID-19 on HIV Outcomes in the United States: A modeling study

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Abstract

Background: The COVID-19 pandemic impacted sexual behaviors and the HIV continuum-of-care in the United States, reducing HIV testing and diagnosis, and use of pre-exposure prophylaxis (PrEP) and antiretroviral therapy (ART). We aim to understand the future implications of these effects through a modeling study.

Methods: We first ran our compartmental model of HIV transmission in the US accounting for pandemic-related short-term changes in transmission behavior and HIV prevention and care provision in 2020–2021 only. We then ran a comparison scenario that did not apply pandemic effects but assumed a continuation of past HIV prevention and care trends. We compared results from the two scenarios through 2024.

Results: HIV incidence was 4.4% lower in 2020–21 for the pandemic scenario compared with the no-pandemic scenario due to reduced levels of transmission behavior, despite reductions in HIV prevention and care caused by the pandemic. However, reduced care led to less viral load suppression among people with HIV (PWH) in 2020 and, in turn, our model resulted in a slightly greater incidence of 2.0% from 2022–24 in the COVID-19 scenario, as compared to the non-COVID scenario.

Discussion: Disruptions in HIV prevention and care services during COVID-19 may lead to somewhat higher post-pandemic HIV incidence, than assuming pre-pandemic trends in HIV care and prevention continued. These results underscore the importance of continuing to increase HIV prevention and care efforts in the coming years.

Short summary:

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A modeling study of the effect of COVID-19 on HIV in the US, incorporating recent data. Analysis shows a likely decrease in 2020–21 incidence, but absent additional prevention efforts, a possible increase in 2023–24 incidence.

Keywords

HIV; COVID-19; mathematical modeling; Ending the HIV Epidemic (EHE)

Introduction

The emergence of COVID-19 in December 2019, which became a global pandemic, had an unprecedented global impact on all aspects of human life, health, and mortality (hereafter, the term “pandemic” will refer exclusively to the COVID-19 pandemic). In the United States, age-adjusted mortality in the general population increased by 16·8% in 2020.¹ Because of the pandemic’s impact on health behaviors and clinical prevention and management of disease, a portion of the increase in mortality was due to increases in deaths from non-COVID-19 causes, including diabetes, heart disease, and unintentional injuries.¹ The COVID-19 pandemic affected nearly all aspects of life in the United States, with HIV being no exception.

A year before the pandemic began, in February 2019, the U.S. Department of Health and Human Services announced the Ending the HIV Epidemic in the U.S. (EHE) initiative, with a goal of achieving a 75% reduction in annual HIV incidence by 2025 and a 90% decrease in annual incidence by 2030.^{2,3} At the time of the EHE announcement, substantial improvements were observed in all stages of the HIV continuum of care,⁴ and HIV incidence showed steady annual declines beginning around 2015.⁵

If, and to what degree, the COVID-19 pandemic interrupted EHE progress is an open question. Current research shows that COVID-19 and the associated responses led to disruptions in several aspects of the HIV continuum of care. Decreases were observed in HIV testing and care provision,^{6,7} as well as statistically significant reductions in uptake and adherence for both pre-exposure prophylaxis (PrEP) and antiretroviral therapy (ART).^{8,9} Additionally, HIV diagnoses decreased 17% in 2020 from 2019 levels, in part due to observed decreases in HIV testing.^{10,11} The COVID-19 pandemic also caused a significant increase in mortality among persons with HIV (PWH) similar to that observed in the general population.^{12,13}

Considering the disruptions of the COVID-19 pandemic in 2020, with some lasting into 2021 and 2022, the long-term impact of the pandemic on the future course of HIV incidence in the United States is not clear. During the period of disruption caused by the pandemic, we might expect to observe an increase in HIV incidence, as it is well-known that reductions in PrEP use, increased delays in time-to-diagnosis after acquiring infection, and reductions in ART adherence are associated with increased HIV incidence.^{14,15} Longer delays in time-to-diagnosis are also associated with a lower probability of achieving and maintaining viral suppression (VLS), as well as increased mortality risk.¹⁶ On the other hand, there is evidence that the pandemic led to reductions in sexual risk behaviors, including reductions

in the number of sexual partners among people who have multiple risk factors for HIV, presumably offsetting the negative effects of the care disruptions, though it is not clear to what extent.^{17–19}

The inherent difficulty in measuring the effects of the COVID-19 pandemic on HIV prevention, care and transmission has led many researchers to address these questions through mathematical modeling. Several simulation studies for specific localities in the United States have analyzed the pandemic's impact.^{20–23} These studies concluded that the long-term effects of the COVID-19 pandemic on future HIV transmission remain uncertain and depend on the magnitude and duration of reductions in HIV prevention and care provision (if such reductions continue) compared to any possible changes in behaviors among PWH. Modeled scenarios in which levels of transmission behavior dropped sharply due to the pandemic, while HIV testing, ART use, and other prevention and care efforts remained at pre-pandemic levels generally showed large, lasting declines in incidence. However, other model scenarios, in which transmission behaviors dropped only slightly, or only for a brief period of time, while care and prevention efforts were severely curtailed, showed increases in HIV incidence.

In this study, we aim to re-examine the possible impact of the COVID-19 pandemic on HIV outcomes in the United States, both during the pandemic and in the subsequent years through 2024. Our study differs from previous studies in the following important respects. First, we used a national-level model, the HIV Optimization and Prevention Economics (HOPE) model, whereas other published studies employed city-specific models. Second, we use more recent data on how the pandemic affected PrEP and ART prescriptions, HIV testing, HIV diagnosis, transmission behaviors, and mortality among both the general and PWH populations during 2020.^{20–23}

Methods

We employed the HOPE model, a dynamic, national-level compartmental model of HIV in the United States, for our analyses. HOPE simulates HIV disease progression and continuum-of-care stages, incorporating population stratification by transmission group, age, assigned sex at birth, number of HIV transmission risk factors, circumcision status, and race/ethnicity. HIV disease stage is defined by CD4 count, and the continuum-of-care for PWH includes five stages: undiagnosed, diagnosed but not engaged in care, engaged in care but not on ART, on ART but not VLS, and VLS. Including demographic characteristics (transmission group, race/ethnicity, sex assigned at birth, age group), disease stage (stratified by CD4 count), and care level, HOPE has 273 populations in total.

The model is parameterized through a combination of literature values and calibration. The model is calibrated by comparing model outputs to surveillance targets, which consist of incidence, prevalence, mortality, continuum-of-care, and other important data over a range of years. The surveillance targets are regularly updated as new data becomes available. The calibration procedure allows parameters to vary within acceptable ranges informed by literature values and is terminated when the surveillance targets are within acceptable levels. Further details, including information regarding model calibration, validation, and

sensitivity/uncertainty analyses have been previously published and are also provided in the technical report.²⁴

We used the HOPE model to simulate the effects of the COVID-19 pandemic on factors affecting HIV transmission in the United States.^{6,8,9,11,12} The model is initialized in the year 2010 and run for several years to reduce the dependence of model behavior on initial conditions during the study period. Outcomes for the years 2018–19 were validated against HIV surveillance data. To incorporate the effects of COVID-19, we introduced changes to the model inputs during the years 2020–22, before returning all inputs to their pre-COVID-19 values from 2023–24 (Table 1). We then obtained a counterfactual, no COVID-19 pandemic scenario by running the calibrated model through the year 2024 with no pandemic-related effects. Hence the COVID-19 pandemic and no COVID-19 pandemic scenarios have identical input values through 2019, and in 2023–24.

We note that the simulated post-COVID-19 pandemic time period (2023–24) does not consider any additional increases to prevention efforts other than continuing the progress that was already being made pre-COVID, such as the *Ending the HIV Epidemic in the U.S.* (EHE) Initiative and National HIV/AIDS Strategy, which are currently in progress.^{3,25} This analytic approach was chosen to isolate the potential COVID-19 effects on future HIV incidence and to understand the extent to which COVID-19 may have set back progress towards reaching EHE goals, independently of any newly increased prevention efforts.

To estimate the impact of the COVID-19 pandemic on sexual behaviors, we used data collected during the iSTAMP study,¹⁹ which showed sexual partnerships among Black and Hispanic/Latino MSM without previously diagnosed HIV, but with multiple risk factors, decreased 20% in 2020. This estimate is consistent with other analyses of MSM in the United States during 2020^{17–18}. We assumed the same decrease in partnerships occurred among MSM of all other races and ethnicities with multiple risk factors, heterosexuals with multiple risk factors, and all persons who inject drugs (PWID) in 2020. Available surveys on PWID suggest that injection behaviors did not change, or perhaps increased slightly, during the COVID-19 pandemic^{26,27}. Accordingly, we did not make any COVID-19 related adjustments to PWID injection behaviors.

Among PWH, we assumed decreases in diagnosis rates of 17%, 22%, and 16% among Black/African Americans, Hispanic/Latino persons, and all other racial/ethnic groups, corresponding to an 18% decrease in diagnosis rates overall.¹¹ We assumed a 25% decrease in PrEP initiation rates among all groups of persons without HIV with multiple risk factors in 2020.⁸ We assumed ART prescriptions for PWH decreased 4·5% in 2020.⁹ A summary of the pandemic effects is provided in Table 1.

Most of the data and studies we used only examined the effects in 2020, requiring us to make additional assumptions on pandemic-related effects in 2021 (Table 1). As a base assumption, we assumed that the pandemic effects on diagnosis rate and ART use (i.e., HIV care effects) continued at 25% of their 2020 value during 2021 (i.e., ART use in 2021 was assumed 1·125% lower than 2019 levels, compared to 4·5% lower in 2020). Pandemic-related decreases in numbers of sexual partners (i.e., behavioral effects) during 2021 were

assumed to be 50% of the 2020 reductions. We note that, as surveillance data showed a strong rebound in PrEP initiation in 2021, we did not consider COVID-19 pandemic effects on PrEP after 2020.⁴

We considered constant increases in pandemic-related mortality rates for both the general and PWH populations in 2020 and 2021, with these increases varying by age group and defined according to HIV surveillance data.^{1,12} We assumed 25% of these increases in 2022, and a return to pre-pandemic rates in 2023 and beyond (Table 1).

To evaluate the robustness of our results, and account for uncertainty, we ran both the pandemic and pandemic-free scenarios for ten distinct calibration sets. These results were used to derive credible ranges for our outputs of interest in our results. To account for the additional uncertainty around pandemic effects in 2021, we performed a sensitivity analysis examining additional COVID-19 pandemic scenarios that varied the 2021 COVID-19 pandemic impact assumptions. Specifically, we varied the 2021 decreases in HIV care effects in 2021 to 0%, 25% and 50% of their 2020 effects. We also varied the behavioral effects in 2021 to 0%, 50%, and 100% of the 2020 effects. We simulated each combination of the alternative care and behavioral effects, leading to 9 additional scenarios. These analyses were considered in the credible ranges reported for our pandemic-scenario results. Further details are provided in Supplement A.

Results

Our COVID-19 simulation scenario resulted in a 17.4% drop in diagnoses of HIV (37,757 to 31,180) from 2019 to 2020, followed by a 16.2% increase (31,180 to 36,254) in 2021 (Figure 1, Table 2). Simulated incidence showed a similar trend, decreasing nine percent (37,106 to 33,725) from 2019 to 2020, then increasing 4.8% (33,725 to 35,328) from 2020 to 2021. Simulation results are generally consistent with available surveillance data in 2020 and 2021. For completeness, we also report the agreement between surveillance data and model outcomes for the years 2018–19 (Table 2). The simulated values for the percent of diagnosed PWH who have viral suppression and who are on ART and for the number of people on PrEP also show agreement with surveillance data in terms of both absolute numbers and the magnitude of the changes observed during the COVID-19 pandemic.

Compared to the no-COVID-19 pandemic scenario, the COVID-19 pandemic simulation scenario resulted in reduced viral suppression, higher percentages of PWH undiagnosed, and lower use of PrEP and ART in 2020–24 (Table 3). We report simulation results for the years 2020–2021 and 2022–24 to reflect the pandemic onset and late/post-pandemic periods, respectively (Table 3). From 2020 to 2021, simulated incidence was 4.4% lower (1,575 fewer new infections per year) in the COVID-19 pandemic scenario compared to the no-COVID-19 pandemic scenario. However, from 2022 to 2024, simulated incidence was two percent higher in the COVID-19 pandemic scenario compared to the no-COVID-19 pandemic scenario, with an average of 713 more new infections per year (Figure 1, Table 3). This difference in incidence between the two simulation scenarios declined from 889 new infections in 2022 (a 2.5% increase in the pandemic scenario) to 562 (a 1.6% increase)

in 2024. Over the entire simulation period from 2020–24, cumulative incidence in the two scenarios differed by less than one percent.

For other important indicators, including viral suppression, awareness of status, and ART use, the COVID-19 pandemic scenario consistently showed small differences compared to the no-pandemic scenario (Table 3).

Our sensitivity analysis (Supplement A) results showed large variations in incidence in 2021 (ranging from 33,395 to 37,313; blue lines in Figure A1), with the variation primarily determined by the effect of the pandemic on behavioral effects in 2021. In contrast, the effects of pandemic-related HIV care disruptions in 2021 on HIV incidence were most apparent from 2022 onward, suggesting that the effect of service disruptions may not be immediately apparent. In addition, we conclude that HIV diagnoses in 2021 were impacted primarily by the effects of the COVID-19 pandemic on HIV care in 2021 and were largely unrelated to any changes in behaviors. We note that certain scenarios with pronounced differences in 2021 incidence (12%) nonetheless produced very similar levels of 2021 HIV diagnosis (less than one percent difference). Due to reductions in testing, this suggests large differences in incidence could result in similar numbers of diagnoses over the short-term. In 2022 and beyond, this simulation suggests HIV diagnoses to be affected more so by the pandemic-related disruptions in HIV care than by the corresponding changes in behaviors.

The uncertainty analyses consistently produced similar results to our reported values and are reported as credible ranges in Tables 2 and 3. COVID-19 effects produced similar changes in our key outcomes for all our examined calibrations sets. Further, the difference between the pandemic and no-pandemic scenarios remained similar across calibration sets. This suggests that our findings are robust, particularly regarding the effects of COVID-19 on HIV incidence, new diagnoses, and the continuum of care. We provide more information in supplementary Appendix A.

Discussion

In this simulation analysis, we examined potential changes in HIV incidence, diagnosis, viral suppression, awareness of status, and PrEP use both during the COVID-19 pandemic onset, and in the following years. Our results showed relatively small but notable COVID-19 pandemic-related effects on HIV incidence and diagnoses both during and following the pandemic onset. Compared to the no COVID-19 pandemic scenario, simulated incidence in the pandemic scenario was lower during the years 2020–21, and higher in 2022–24. The difference in incidence in 2022–24 declines over time to a difference of 1–6% in 2023. Other important HIV indicators resulted in small shifts due to the pandemic during 2020–21, with differences of less than one percentage point in most cases; by 2024, these differences largely disappear.

The work shown here includes some limitations. In some instances, data were uncertain, or specific to narrowly defined transmission populations. Additionally, while our study incorporated updated data-driven parameterizations for key model inputs, in some instances these were based on data from the year 2020 and were less reliable for 2021. Specifically,

COVID-19 effects regarding PrEP use/adherence and mortality were based on data sources up to and including 2022. In contrast, COVID-19 effects concerning behavior, ART use/adherence and HIV testing/diagnosis were primarily based on data from 2020; data for 2021 were incomplete and less certain. Additionally, our assumptions regarding changes to transmission behaviors were based on survey data for MSM. As similar data were less readily available for heterosexual persons, we assumed that similar patterns held among heterosexual persons and PWID with comparable numbers of sexual partners; however, we acknowledge that this may be an oversimplification.

To account for this uncertainty, we performed a sensitivity analysis related to COVID-19 effect assumptions (full details in Supplement A). This analysis suggests that simulated incidence in 2021 was mainly dependent on pandemic-related effects on behavior that same year. However, simulated incidence in 2022 and later was impacted by the care-related disruptions in 2021. Our model analyses demonstrated that the effect of any pandemic-related changes in behavior on HIV incidence, diagnoses, and care outcomes was likely transient, while the effect of reduced HIV care services may persist for several years. Continued efforts towards collecting data to better understand behavioral changes during the COVID-19 pandemic are important, particularly if the pandemic affected behaviors differently by demographic sub-groups.

We further note that, in addition to the uncertainty regarding model inputs, there is also some uncertainty in the HIV incidence estimates based on the HIV surveillance data from recent years. While our simulations show good agreement with 2020–21 incidence estimates (see e.g. Fig. A2 in the supplementary materials), uncertainty in those estimates necessarily limits the precision with which we can compare our model against reality. In turn, this may limit our ability to interpret and contextualize our findings to some extent.

This study does not address important health equity issues. The available data did not always reflect disparities among different racial/ethnic groups, transmission categories, or other population stratifications, and hence the current study can only provide overall population-level analyses. However, such information is important, particularly for the implementation of interventions that may better serve populations disproportionately affected by both HIV and COVID.

Our simulation results focused on COVID-19 pandemic disruptions during the years 2020 and 2021 and assumed that HIV prevention and care provisions returned to pre-pandemic trends in 2022. As the primary goal of the current analysis was to study the effects of the COVID-19 pandemic on HIV outcomes in isolation, this analysis did not include other confounding contextual changes, such as the 2022 M-pox epidemic, or changes in future prevention efforts.

Given the unprecedented level of public resources required to address the COVID-19 pandemic, several key EHE initiatives were postponed or scaled back in 2020–21.²⁸ As the current analysis does not explore the hypothetical benefits of such interventions as if they were not scaled back, it does not necessarily reflect the true impact of the COVID-19 pandemic on reaching EHE goals. Nonetheless, there is value in quantifying the explicit

effects of COVID-19 on HIV incidence and other key outcomes. These findings can be used in other modeling studies examining the effects of other changes that could either mitigate or exacerbate the predicted differences presented in this analysis. For example, a follow up analysis could explore the necessary acceleration of HIV prevention efforts or additional funding needed to eliminate these COVID-19 effects and move towards reaching EHE goals.

The acceleration of HIV prevention efforts to meet EHE goals is currently underway.²⁵ Several lines of research show that the COVID-19 pandemic caused substantial disruptions to HIV prevention and care programs.^{6,8,9,11,12,17,29,30} Our findings showed these disruptions resulted in a notable, but small, setback with respect to several EHE-relevant outcomes, most notably simulated incidence in 2022–24. However, in terms of reaching EHE goals, our results suggest that COVID-19 may have had less impact overall than previously anticipated. While a possible pandemic-related two percent increase in incidence in 2022–24 is important to note and incorporate in programmatic and funding decisions, it may be relatively negligible as we are working towards the EHE goal of 90% reduction in HIV incidence by 2030. Even before considering the effects of COVID-19, reaching this goal would require significant effort and investment.²⁴

Continued efforts to increase HIV prevention and care to offset any COVID-19 pandemic-related setbacks are important and necessary.²⁵ As our results suggest, the effect of changes to HIV care and prevention efforts can last for several years. Expanding such efforts, as soon as possible, can help mitigate the effects of COVID-19 on HIV incidence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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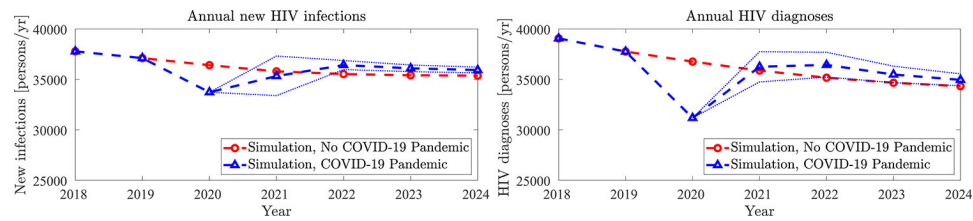


Figure 1: Comparison between COVID-19 pandemic scenario (blue) and no-COVID pandemic scenario (red) for: annual new HIV infections (left) and annual HIV diagnoses (right), 2018–24. *Note: Upper and lower bounds for the COVID-19 pandemic simulations were obtained through sensitivity analysis to COVID-19 effects (Supplement A).*

Table 1:

Summary of the modeled COVID-19 pandemic effects by time period

Year(s)	Behavior change	Diagnosis rate	ART initiation rate	ART drop-off rate + loss of VLS rate	PrEP initiation rate	Mortality rates
2020	20% decrease from 2019 in partnerships among MSM with multiple risk factors, HET with multiple risk factors, and all PWID ¹⁹	18% decrease from 2019 rates among all PWH. Stratifications by race/ethnicity ¹¹	4.5% decrease from 2019 rate ⁹	Increases in rates to match 2.5% drop in ART ⁹	25% decrease from 2019 rate ⁸	Group-specific Increases varying by age, race/ethnicity, sex-at-birth ¹²
2021	10% decrease from 2019 in partnerships among MSM with multiple risk factors, HET with multiple risk factors, and all PWID(50% of 2020 effect)	4.5% decrease from 2019 rates (25% of 2020 effects)	1.125% decrease from 2019 rate (25% of 2020 effect)	25% of increases from 2020 (25% of 2020 effect)	Return to 2019 rates ⁴	Group-specific Increases varying by age, race/ethnicity, sex-at-birth (100% of 2020 effect) ¹²
2022	No effect	No effect	No effect	No effect	No effect	25% of 2020 increases
2023–24	No effect	No effect	No effect	No effect	No effect	No effect

Table 2:

Comparison of simulation values and surveillance data over the immediate pre-COVID-19 (2018–19) and COVID-19 (2020–21) time periods for several relevant indicators. Credible range for simulated values obtained through uncertainty analysis (2018–20) and combined uncertainty analysis and sensitivity analysis to COVID-19 effects (2021).

Time period	2018		2019		2020		2021	
Data type	Simulated	Surveillance	Simulated	Surveillance	Simulated	Surveillance	Simulated	Surveillance
Estimates of New HIV infections	37,778 (32,142-37,778)	36,100 (34,600–37,700) ⁵	37,107 (31,106-37,107)	34,800 (33,100–36,600) ⁵	33,725 (27,360-33,725)	33,600 (31,600–35,700) ⁵	35,328 (26,526-37,313)	32,100 (29,900–34,300) ⁵
HIV diagnoses	39,063 (33,924-39,178)	37,299 ⁴	37,757 (32,118-37,836)	36,421 ⁴	31,180 (25,986-31,180)	30,275 ⁴	36,254 (28,332-37,745)	35,716 ⁴
% VLS among diagnosed PWH	63.4% (61.8%-65.9%)	64.7% ⁴	64.2% (62.4%-66.6%)	65.5% ⁴	63.4% (61.5%-65.9%)	64.6% ⁴	64.1% (61.5%-66.7%)	65.9% ⁴
% of diagnosed PWH on ART	77.8% (76.9%-83.8%)	75.7% ⁴	78.5% (77.7%-84.5%)	76.0% ⁴	76.8% (75.5%-83.8%)	73.2%-75.2% ⁴	77.8% (75.9%-84.2%)	Not reported
Number of people on PrEP	263,243 (258,666-267–512)	219,954 ⁴	278,663 (273,616-285,543)	274,922 ⁴	291,903 (286,352-297,528)	300,887 ⁴	354,243 (347,319-361,492)	365,919 ⁴

Table 3:

Comparison of the no COVID-19 and COVID-19 simulation results over the COVID-19 onset period (2020–21), and late COVID-19 pandemic/post COVID-19 pandemic period (2022–24). *Note: the sum over the indicated period is reported for new HIV infections and HIV diagnoses. For % of diagnosed PWH who are on ART and VLS, % of PWH unaware of infection, and number of PWH on PrEP, the value in the last year of that time period is reported. Credible range for simulated values obtained through uncertainty analysis (2018–20) and combined uncertainty analysis and sensitivity analysis to COVID-19 effects (2021).*

Time period	2020–21		2022–2024	
Simulation scenario	No-COVID	COVID	No-COVID	COVID
New HIV infections (total)	72,204 (58,878–72,204)	69,053 (53,886–71,038)	106,303 (83,454–106,303)	108,442 (83,756–109,579)
New HIV infections (cumulative)	72,204 (58,878–72,204)	69,053 (53,886–71,038)	178,507 (142,332–178,507)	177,495 (137,642–180,617)
New HIV infections (annual avg.)	36,102 (29,439–72,204)	34,526 (26,943–35,519)	35,434 (27,818–35,434)	36,147 (27,918–36,526)
HIV diagnoses (total)	72,640 (59,739–72,640)	67,434 (54,308–68,925)	104,154 (83,083–104,154)	106,872 (82,520–109,548)
HIV diagnoses (annual avg.)	36,320 (29,690–36,320)	33,717 (27,154–34,462)	34,718 (27,694–37,718)	35,624 (27,506–36,516)
% VLS among diagnosed PWH	65.4% (63.3%–67.7%)	64.1% (61.5%–66.1%)	66.7% (64.1%–68.7%)	66.1% (63.3%–68.0%)
% of diagnosed PWH on ART	79.7% (78.7%–85.7%)	77.8% (75.9%–84.2%)	80.8% (79.6%–86.7%)	80.0% (78.5%–86.2%)
% of PWH undiagnosed	7.3% (4.7%–8.2)	7.5% (4.9%–8.6%)	6.8% (4.3%–7.5%)	7.0% (4.3%–7.6%)
Number of PWH on PrEP	370,242 (362,969–377,889)	354,243 (347,319–361,492)	387,465 (379,463–396,863)	387,430 (379,417–396,656)