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Trends in time from HIV diagnosis to first viral suppression following revised U.S. HIV treatment guidelines, 2012–2017

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Abstract

Background: Since 2012, treatment guidelines have recommended initiating antiretroviral therapy for all persons as soon as possible after HIV diagnosis, irrespective of CD4 counts. If clinicians adopted the treatment guidelines, a shortened interval between diagnosis and first viral suppression (Dx-to-VS) would be expected, with greater declines among those with CD4 counts ≥500 cells/μL at diagnosis.

Methods: Using the National HIV Surveillance System data, we examined Dx-to-VS intervals among persons aged ≥13 years with HIV infection diagnosed during 2012–2017. Analyses were stratified by the first CD4 count: CD4 ≥500 cells/μL, 200–499 cells/μL, <200 cells/μL, and no CD4 value reported within 3 months after diagnosis.

Results: During 2012–2017 in the 27 US jurisdictions with complete laboratory reporting, 138,759 HIV diagnoses occurred. The median Dx-to-VS interval shortened overall for persons with HIV diagnosed in 2012 vs. 2017 from 9 to 5 months, a 12.3% annual decrease ($P < 0.001$) and in all CD4 groups. In 2012, the Dx-to-VS interval was longer for persons with CD4 ≥500 cells/μL than 200–499 cells/μL and <200 cells/μL (median, 9, 7, and 6 months, respectively). By 2017, the median interval was 4 months for these groups, compared with 25 months for those without a CD4 value within 3 months after diagnosis.

Conclusion: Decreases in Dx-to-VS intervals across all CD4 groups with a greater decrease among those with CD4 ≥500 cells/μL are consistent with the implementation of treatment recommendations. The Dx-to-VS interval was longest among persons not linked to care within 3 months after diagnosis, underscoring the importance of addressing barriers to linkage to care for ending the HIV epidemic.

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Disclaimer. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Keywords

HIV treatment guidelines; time from diagnosis to viral suppression; persons with diagnosed HIV infection

Introduction

Treating HIV infection promptly after diagnosis and helping people with HIV to achieve and sustain viral suppression is one of the four key pillars of ending the HIV epidemic (EHE) in the United States.[1] HIV treatment guidelines have evolved over the years.[2] Changes in recommendations for specific antiretroviral therapy (ART) regimens have been based on enhanced durable virologic efficacy, improved tolerability and toxicity profiles, and convenience of use. A primary criterion for determining when to initiate ART had been CD4 cell count. Over the course of time, the CD4 threshold for treatment initiation increased with recognition of the benefits of starting ART at higher CD4 counts to preserve immunologic function, improve clinical outcomes for persons with HIV, and to reduce onward transmission.[3,4] Since 2012, treatment guidelines have recommended ART initiation as soon as possible after HIV diagnosis irrespective of CD4 count.[5,6]

If clinicians have adopted revised ART recommendations, we would expect a shortened interval between HIV diagnosis and ART initiation, with greater declines in the interval among those with CD4 ≥500 cells/μL at the time of diagnosis, since, prior to 2012, some persons in this group might not have been eligible for ART. Date of ART initiation is not well captured in the National HIV Surveillance System (NHSS). However, viral suppression is routinely monitored in NHSS and is an important clinical and public health outcome. In this report, we examined the diagnosis and first viral suppression (Dx-to-VS) interval by CD4 status at HIV diagnosis among persons with HIV infection diagnosed during 2012–2017 to assess the implementation of revised U.S. HIV treatment guidelines. We also examined the Dx-to-VS interval by sex, age, race/ethnicity and transmission category to identify factors associated with improvement in time to viral suppression.

Methods

HIV infection is reportable in all 50 states, the District of Columbia, and 6 U.S. dependent areas. However, not all jurisdictions have mandatory reporting of HIV-related laboratory tests, including CD4 cell counts (or percentages) and viral load tests. We analyzed cumulative data reported to NHSS from 27 jurisdictions with complete laboratory reporting during 2012–2017. The 27 jurisdictions include Alabama, Alaska, California, the District of Columbia, Hawaii, Illinois, Indiana, Iowa, Louisiana, Maine, Maryland, Michigan, Missouri, Nebraska, New Hampshire, New York, North Dakota, Oregon, South Carolina, South Dakota, Tennessee, Texas, Utah, Virginia, Washington, West Virginia, and Wisconsin. Complete laboratory reporting requires meeting all of the three criteria: The jurisdiction's laws/regulations required the reporting of all CD4 and viral load results to the state or local health department; laboratories that perform HIV-related testing for the jurisdictions had reported a minimum of 95% of HIV-related test results to the state or local health department; By December 31, the jurisdiction had reported to CDC at least 95% of all

CD4 and viral load test results received from January through September of the calendar year.[7] The 27 jurisdictions accounted for 58.5% of all persons with HIV infection diagnosed during 2012–2017 in the United States.

Analyses included HIV diagnoses occurring during 2012–2017 among persons aged ≥13 years who resided at diagnosis in one of the 27 jurisdictions. We analyzed data reported to NHSS through June 2019, which allowed for at least 18 months after HIV diagnosis to observe viral suppression. We classified persons with diagnosed HIV infection into 4 groups based on the first CD4 test result within 3 months after diagnosis: ≥500 cells/μL, between 200–499 cells/μL, <200 cells/μL, and no reported CD4 value (i.e., CD4 count or percentage). CD4 percentages were converted to CD4 counts for those whose first reported value was a percentage without a count.[8]

The main outcome, Dx-to-VS interval, was calculated by using the dates of HIV diagnosis and of first viral suppression (<200 copies/μL) reported to NHSS. We adopted a Kaplan-Meier estimation procedure to account for persons who were censored.[9] More specifically, when estimating the distribution of Dx-to-VS interval, we used weights to account for persons who, by June 30, 2019, had died (2.6%); had had no viral load test reported (6.4%); or had reported viral load results but had not achieved viral suppression (8.7%). The median month of the D-to-VS interval was then derived from the estimated distribution. We examined the trends in Dx-to-VS intervals during 2012–2017 by CD4 counts at diagnosis, sex, age, race/ethnicity, and transmission category. CD4 counts were classified according to the four groups described above. The other variables were classified based on the standard categories used for HIV surveillance.[7] Trends were examined using estimated annual percentage change (EAPC) which was calculated using a log-linear regression assuming that annual percentage change is constant during the time period under consideration.[10]

We also examined two secondary outcomes: interval from HIV diagnosis to linkage to HIV medical care (Dx-to-LtCare) and interval from linkage to care to first viral suppression (LtCare-to-VS). According to standard HIV surveillance practices, the date of first reported CD4 or viral load result after diagnosis was considered to be the date of linkage to care.[7] Persons not linked to care prior to death or by June 30, 2019, were excluded from the LtCare-to-VS analysis. For both secondary analyses, persons who did not achieve the outcome prior to death or by June 30, 2019 were censored from analysis, and the Kaplan-Meier procedure was applied.[9]

Results

During 2012–2017, a total of 138,759 diagnoses occurred among persons aged ≥13 years in the 27 jurisdictions (study cohort). Within 3 months after HIV diagnosis, 35,155 (25.3%) persons had a first CD4 result that was ≥500 cells/μL, 37,915 (27.3%) persons had a first CD4 result that was between 200 and 499 cells/μL, 35,667 (25.7%) persons had a first CD4 result that was <200 cells/μL, and 30,022 (21.7%) persons had no CD4 result reported (Table 1). From 2012 to 2017, the proportion of diagnoses with first CD4 ≥500 cells/μL and of diagnoses with first CD4 between 200 and 400 cells/μL increased within 3 months after diagnosis. The proportion of diagnoses with first CD4 <200 cells/μL and of diagnoses

with no reported CD4 value decreased within 3 months after diagnosis (Table 1). Within 6 months after HIV diagnosis, 69,633 (50.2% of the cohort) persons were alive and virally suppressed, and the proportion of this group increased from 39.8% in 2012 to 59.2% in 2017 (Table 1).

Overall, the median Dx-to-VS interval shortened from 9 months for persons with HIV diagnosed in 2012 to 5 months for persons with HIV diagnosed in 2017 (Table 2). From 2012 to 2017, the Dx-to-VS interval decreased 12.3% per year (95% confidence interval [CI], −13.5% to −11.0%, P <0.001). In analyses stratified by CD4 group, in 2012, Dx-to-VS interval was longer for persons with CD4 ≥500 cells/μL than with CD4 between 200 and 499 cells/μL and CD4 <200 cells/μL (median, 9, 7, 6 months, respectively) and was longest for persons without a CD4 value within 3 months after diagnosis (median, 38 months) (Table 2). The median Dx-to-VS intervals shortened during 2012–2017 in all four CD4 groups and the greatest proportional decrease was among those with CD4 ≥500 cells/μL (16.5% decrease per year). By 2017, the median Dx-to-VS interval was 4 months for persons from three CD4 groups (i.e., CD4 ≥500 cells/μL, CD4 between 200 and 499 cells/μL, and CD4 <200 cells/μL) and 25 months for those without a reported CD4 value with 3 months of diagnosis. Of the 108,737 persons with a CD4 test result within 3 months after HIV diagnosis, 7,630 persons had viral suppression reported prior to or at the same time as the first CD4 test, a possible indication of previous HIV treatment. In sensitivity analyses in which these 7,630 persons were excluded when estimating Dx-to-VS intervals, the annual percentage changes of median Dx-to-VS intervals were similar (data not shown).

During 2012–2017, median Dx-to-VS intervals shortened significantly for all sex, age, race/ethnicity, and transmission groups and was 4–7 months in 2017 for all groups (Table 2). Although males had a longer Dx-to-VS interval than females in 2012 (median, 10 vs. 8 months), by 2017, the interval was 5 months for both males and females. In 2012, Dx-to-VS intervals were longest among those aged 13–24 years (median, 14 months) and shortest among those aged 55 years and older (median, 7 months). However, annual percentage decreases were greatest among the younger age groups. By 2017, median Dx-to-VS intervals were 6 months for those aged 13–24 years and 5 months for all other age groups. Among racial/ethnic groups, Blacks had the longest Dx-to-VS interval in 2012 (median, 12 months), but also showed the greatest annual percentage decrease (15.4% decrease per year). In 2017, the Dx-to-VS interval was 4 months for Whites and 5 months for Blacks, Hispanic/Latinos, and other races. By transmission category, the greatest proportional decline during 2012–2017 was among men with infection attributed to male heterosexual contact (14.3% decrease per year). In 2017, the longest Dx-to-VS interval was for women with infection attributed to injection drug use (median, 7 months).

Overall, the median Dx-to-LtCare interval was 1 month (interquartile range [IQR]: 0 to 2 months) for persons with HIV diagnosed in 2012 and less than 1 month (IQR: 0 to 1 months) for persons with HIV diagnosed in 2017 (data not shown). The same values and declining pattern were seen in all sex, age, race/ethnicity, and transmission risk groups. Among the 114,914 with a reported CD4 or viral load result within 3 months after diagnosis, the median Dx-to-LtCare interval was less than 1 month in 2012 and 2017 and did not differ by CD4 groups, sex, age, race/ethnicity, or transmission category. Among 23,845 (17.2% of

the cohort) persons who had neither a CD4 nor viral load result reported within 3 months after diagnosis, the median Dx-to-LtCare interval was 20 months (IQR: 8 to 64 months) for persons with HIV diagnosed in 2012 and 15 months (IQR: 7 to 28 months) for persons with HIV diagnosed in 2017.

Among 131,517 (94.8% of the cohort) who had one or more CD4 or viral load test results reported by June 30, 2019, the median LtCare-to-VS interval shortened from 6 months (IQR: 3 to 20 months) for persons with HIV diagnosed in 2012 to 3 months (IQR: 2 to 9 months) for persons with HIV diagnosed in 2017 (EAPC −11.3%; 95% CI, −13.6% to −8.9%, P <0.001). The median LtCare-to-VS intervals shortened in all CD4 groups, sex, age, race/ethnicity, or transmission category. Among the CD4 groups, the greatest absolute and proportional declines among those with CD4 ≥500 cells/μL. In 2012, the LtCare-to-VS interval was 8 months for persons with CD4 ≥500 cells/μL compared to 6 months for persons with CD4 <500 cells/μL, 5 months for persons with CD4 between 200 and 499 cells/μL, and 7 months for persons without a CD4 value. During 2012–2017, persons with CD4 ≥500 cells/μL had a substantially greater annual percentage decline in the LtCare-to-VS interval (EAPC: −17.6%. 95%CI, −20.2% to −14.9%, P <0.001) compared to persons with CD4 between 200 and 499 cells/μL (EAPC: −11.5%, 95%CI, −14.6% to −8.4%, P <0.001), persons with CD4 <200 cells/μL (EAPC: −5.3%, 95%CI, −7.9% to −2.6%, P <0.001), and persons without a CD4 value within 3 months after HIV diagnosis (−4.7%, 95%CI, −6.9% to −2.4%, P <0.001). By 2017, the median LtCare-to-VS interval was 3 months (IQR: 2 to 8 months) for persons with CD4 ≥500 cells/μL and persons with CD4 between 200 and 499 cells/μL, 4 months (IQR: 2 to 8 months) for persons with CD4 <200 cells/μL; and 5 months (IQR: 2 to 19 months) for persons without a CD4 value within 3 months after HIV diagnosis.

Discussion

During 2012–2017, the median Dx-to-VS interval shortened and the proportion of persons who achieved virally suppression within 6 months after HIV diagnosis increased, suggesting that patients are receiving treatment and achieving viral suppression more quickly with more potent, convenient, and tolerable regimens, particularly with integrase inhibitors which rapidly reduce viral load.[11] Elimination of CD4 thresholds for ART eligibility may, in part, explain (1) the significantly greater declines in Dx-to-VS and LtCare-to-VS intervals in those with CD4 ≥500 cells/μL at diagnosis compared with those with CD4 between 200 and 499 cells/μL and those with CD4<200 cells/μL and (2) the equivalent Dx-to-VS and LtCare-to-VS intervals in those CD4 groups in 2017. These findings are consistent with the uptake and implementation of revised U.S. HIV treatment guidelines.

Dx-to-VS intervals shortened in all CD4, sex, age, race/ethnicity, and transmission groups during 2012–2017, suggesting that all of these groups have benefitted from revisions to treatment guidelines regarding timing of initiation of and recommended regimens for antiretroviral treatment. Two groups of particular concern include those with late diagnosis (i.e., those with CD4 <200 cells/μL at the time of HIV diagnosis) and those who are not rapidly linked to care. For persons whose HIV infection was diagnosed late, the median time from diagnosis to first viral suppression was 6 months in 2012 and 4 months in 2017.

In addition, the median time from diagnosis to linkage to care was less than 1 month in 2012 and remained the same in 2017. The median time from linkage to care to first viral suppression decreased from 5 months in 2012 to 4 months in 2017, suggesting that persons whose HIV infection was diagnosed late may have also benefitted from implementation of the revised treatment guidelines. On the other hand, the group of persons not linked to care within 3 months after diagnosis (i.e., without a reported CD4 value within 3 months after diagnosis) had the longest median time from HIV diagnosis to viral suppression (median of 25 months in 2017). Delays in linking to HIV care prevent many persons from this group fully benefitted from effective regimens. Nonetheless, during 2012–2017, persons not linked to care within 3 months after diagnosis demonstrated improvements in Dx-to-LtCare, LtCare-VS, and Dx-to-VS intervals, suggesting that the implementation of the revised guidelines is also benefitting persons with delays in linking to care. In fact, once linked to HIV care, this group achieved viral suppression in a similar time frame (median: 5 months) as those who were linked to care soon after diagnosis.

Four limitations warrant consideration. First, our findings were based on data from 27 jurisdictions with complete laboratory reporting and may not be generalizable to the entire United States. Second, ART initiation dates and specific ART regimens, both of which affect the Dx-to-VS interval, are incompletely reported to the NHSS and therefore could not be used for this analysis. Third, findings were presented in median months. Caution is warranted as medians do not provide the whole picture of the Dx-to-VS distribution that was asymmetrical with a long tail to the right. Finally, our analyses focused on individual-level characteristics associated with Dx-to-VS intervals that are captured in the NHSS. Jurisdictional characteristics such as ability to meet complete laboratory reporting requirements, HIV case burden on a health system, expansion of Medicaid under the Affordable Care Act, and the AIDS Drug Assistance Program waiting lists, as well as individual insurance coverage might impact Dx-to-VS intervals but are not captured in the NHSS. However, one recent study from Alabama shows that larger municipalities with more resources did not necessarily have shorter Dx-to-VS intervals.[12] Associations between jurisdictional characteristics and time to first viral suppression on the jurisdictional level could be further explored in future ecological analyses.

In summary, our finding of a decrease in time from diagnosis to first viral suppression across all CD4 groups with greatest reduction among persons with CD4 ≥500 cells/μL at diagnosis is consistent with an uptake and implementation of the revised treatment recommendations. Despite progress reducing the Dx-to-VS interval, the finding that the Dx-to-VS interval was longest among those with delayed linkage to care underscores the critical importance of addressing barriers to linkage to and retention in care for achieving viral suppression and ending the HIV epidemic.

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Table 1.

Number and percentage of persons with HIV infection diagnosed at age ≥13 years during 2012–2017, 27 U.S. jurisdictions, by year of HIV diagnosis and characteristics

	2012	2013	2014	2015	2016	2017	Total
Total	**N = 24032**	**N = 23069**	**N = 23642**	**N = 23275**	**N = 22903**	**N = 21838**	**N = 138759**
CD4 within 3 months of HIV diagnosis							
	n (Column %)	n (Column %)	n (Column %)	n (Column %)	n (Column %)	n (Column %)	n (Column %)
CD4 ≥500 cells/μL	5455 (22.7)	5477 (23.7)	5847 (24.7)	6105 (26.2)	6235 (27.2)	6036 (27.6)	35155 (25.3)
CD4 between 200 and 499 cells/μL	6146 (25.6)	6175 (26.8)	6347 (26.8)	6442 (27.7)	6441 (28.1)	6364 (29.1)	37915 (27.3)
CD4 <200 cells/μL	6431 (26.8)	6049 (26.2)	6038 (25.5)	5881 (25.3)	5779 (25.2)	5489 (25.1)	35667 (25.7)
No reported CD4 value	6000 (25.0)	5368 (23.3)	5410 (22.9)	4847 (20.8)	4448 (19.4)	3949 (18.1)	30022 (21.6)
Within 6 months after HIV diagnosis							
	n (Column %)	n (Column %)	n (Column %)	n (Column %)	n (Column %)	n (Column %)	n (Column %)
Died	355 (1.5)	271 (1.2)	192 (0.8)	158 (0.7)	126 (0.6)	54 (0.3)	1156 (0.8)
Alive, not virally suppressed	14102 (58.7)	12559 (54.4)	11754 (49.7)	10737 (46.1)	9968 (43.5)	8850 (40.5)	67970 (49.0)
Alive, virally suppressed	9575 (39.8)	10239 (44.4)	11696 (49.5)	12380 (53.2)	12809 (55.9)	12934 (59.2)	69633 (50.2)

Table 2.

Median months from HIV diagnosis to first viral suppression among persons with HIV infection diagnosed at age ≥ 13 years during 2012–2017, by selected characteristics, 27 U.S. jurisdictions

Characteristics	2012	2013	2014	2015	2016	2017	2012 to 2017
	Median months (IQR) No.	Median months (IQR) No.	Median months (IQR) No.	Median months (IQR) No.	Median months (IQR) No.	Median months (IQR) No.	EAPC (95% CI) P value
All	9 (4 to 37) *n = 24032*	8 (4 to 32) *n = 23069*	7 (3 to 25) *n = 23642*	6 (3 to 23) *n = 23275*	5 (3 to 21) *n = 22903*	5 (3 to 15) *n = 21838*	−12.3 (−13.5, −11.0) P < 0.001
CD4 within 3 months of diagnosis							
CD4 ≥500 cells/μL	9 (4 to 28) *n = 5455*	7 (3 to 24) *n = 5477*	6 (3 to 18) *n = 5847*	5 (2 to 13) *n = 6105*	4 (2 to 12) *n = 6235*	4 (2 to 9) *n = 6036*	−16.5 (−18.5, −14.5) P < 0.001
CD4 between 200 and 499 cells/μL	7 (4 to 17) *n = 6146*	6 (3 to 15) *n = 6175*	5 (3 to 13) *n = 6347*	5 (3 to 11) *n = 6442*	4 (3 to 11) *n = 6441*	4 (2 to 9) *n = 6364*	−11.3 (−13.3, −9.3) P < 0.001
CD4 <200 cells/μL	6 (4 to 12) *n = 6431*	6 (3 to 12) *n = 6049*	5 (3 to 10) *n = 6038*	5 (3 to 9) *n = 5881*	4 (3 to 9) *n = 5779*	4 (2 to 9) *n = 5489*	−8.7 (−10.8, −6.5) P < 0.001
No reported CD4 value	38 (14 to 87) *n = 6000*	36 (13 to 77) *n = 5368*	30 (11 to 65) *n = 5410*	32 (11 to 53) *n = 4847*	32 (11 to 41) *n = 4448*	25 (9 to 29) *n = 3949*	−6.4 (−9.1, −3.5) P < 0.001
Sex							
Male	10 (5 to 37) *n = 19495*	8 (4 to 32) *n = 18863*	7 (3 to 26) *n = 19369*	6 (3 to 23) *n = 19187*	6 (3 to 21) *n = 18779*	5 (3 to 15) *n = 17948*	−13.0 (−13.4, −12.6) P < 0.001
Famale	8 (4 to 38) *n = 4537*	7 (3 to 31) *n = 4206*	6 (3 to 24) *n = 4273*	6 (3 to 22) *n = 4088*	5 (2 to 20) *n = 4124*	5 (2 to 15) *n = 3890*	−11.4 (−11.6, −11.2) P < 0.001
Age at diagnosis (years)							
13–24	14 (6 to 45) *n = 5483*	11 (5 to 38) *n = 5257*	9 (4 to 32) *n = 5534*	7 (3 to 27) *n = 5355*	6 (3 to 22) *n = 5065*	6 (3 to 18) *n = 4838*	−17.7 (−18.3, −17.1) P < 0.001
25–34	10 (4 to 40) *n = 7269*	9 (4 to 34) *n = 7218*	7 (4 to 26) *n = 7631*	6 (3 to 24) *n = 7848*	6 (3 to 21) *n = 7953*	5 (3 to 16) *n = 7772*	−13.3 (−13.6, −12.9) P < 0.001
35–44	8 (4 to 31) *n = 5038*	7 (4 to 28) *n = 4635*	6 (3 to 22) *n = 4796*	6 (3 to 22) *n = 4492*	5 (3 to 21) *n = 4336*	5 (2 to 14) *n = 4147*	−11.2 (−11.7, −10.8) P < 0.001

Characteristics	2012	2013	2014	2015	2016	2017	2012 to 2017
	Median months (IQR) No.	Median months (IQR) No.	Median months (IQR) No.	Median months (IQR) No.	Median months (IQR) No.	Median months (IQR) No.	EAPC (95% CI) P value
45–54	8 (4 to 26) *n = 4134*	7 (4 to 24) *n = 3809*	6 (3 to 20) *n = 3626*	5 (3 to 17) *n = 3554*	5 (3 to 18) *n = 3425*	5 (2 to 14) *n = 3066*	−10.3 (−10.7, −9.9) P < 0.001
55 and older	7 (4 to 31) *n = 2108*	7 (4 to 30) *n = 2150*	6 (3 to 23) *n = 2055*	5 (3 to 19) *n = 2026*	5 (3 to 19) *n = 2124*	5 (2 to 15) *n = 2015*	−9.0 (−9.4, −8.6) P < 0.001
Race/ethnicity							
Black	12 (5 to 50) *n = 9772*	10 (4 to 41) *n = 9393*	8 (4 to 33) *n = 9542*	7 (3 to 30) *n = 9304*	6 (3 to 26) *n = 9313*	5 (3 to 19) *n = 8809*	−15.4 (−15.8, −15.1) P < 0.001
Hispanic/Latino	9 (4 to 35) *n = 6134*	8 (4 to 32) *n = 5939*	7 (3 to 26) *n = 6291*	6 (3 to 25) *n = 6320*	6 (3 to 20) *n = 6329*	5 (3 to 15) *n = 6141*	−11.7 (−12.0, −11.4) P < 0.001
White	8 (4 to 23) *n = 6202*	7 (4 to 22) *n = 5867*	6 (3 to 16) *n = 5997*	5 (3 to 15) *n = 5872*	5 (3 to 14) *n = 5556*	4 (2 to 12) *n = 5316*	−11.2 (−11.6, −10.8) P < 0.001
Other[a]	9 (4 to 30) *n = 1924*	7 (4 to 28) *n = 1870*	6 (3 to 20) *n = 1812*	5 (3 to 17) *n = 1779*	5 (3 to 19) *n = 1705*	5 (2 to 13) *n = 1572*	−13.5 (−14.2, −12.7) P < 0.001
Transmission Category [b]							
Male-to-male sexual contact	9 (4 to 35) *n = 15971*	8 (4 to 31) *n = 15519*	7 (3 to 25) *n = 16183*	6 (3 to 23) *n = 15933*	5 (3 to 20) *n = 15682*	5 (3 to 15) *n = 15149*	−12.9 (−13.3, −12.5) P < 0.001
Male injection drug user	11 (4 to 51) *n = 789*	13 (5 to 59) *n = 739*	9 (4 to 41) *n = 720*	8 (4 to 32) *n = 804*	8 (3 to 36) *n = 864*	6 (3 to 27) *n = 678*	−11.6 (−13.2, −9.9) P < 0.001
Male-to-male sexual contact and injection drug use	12 (5 to 39) *n = 1005*	11 (5 to 34) *n = 907*	8 (4 to 27) *n = 861*	8 (3 to 25) *n = 832*	7 (3 to 26) *n = 827*	6 (3 to 17) *n = 796*	−13.8 (−14.6, −13.0) P < 0.001
Male heterosexual contact	11 (5 to 49) *n = 1709*	9 (4 to 37) *n = 1678*	7 (4 to 33) *n = 1590*	6 (3 to 25) *n = 1600*	6 (3 to 24) *n = 1571*	5 (3 to 17) *n = 1309*	−14.3 (−15.0, −13.7) P < 0.001
Female heterosexual contact	8 (4 to 35) *n = 3884*	7 (3 to 29) *n = 3625*	6 (3 to 23) *n = 3718*	5 (3 to 21) *n = 3441*	5 (2 to 18) *n = 3536*	4 (2 to 14) *n = 3319*	−11.5 (−11.7, −11.3) P < 0.001
Female injection drug use	11 (4 to 51) *n = 638*	11 (4 to 37) *n = 564*	9 (4 to 39) *n = 546*	8 (3 to 32) *n = 637*	7 (3 to 37) *n = 575*	7 (3 to 27) *n = 553*	−10.1 (−11.1, −9.1) P < 0.001

[a] Other includes American Indians/Alaska Natives, Asians, Native Hawaiians/other Pacific Islanders and persons reporting multiple races.

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[b] Data have been statistically adjusted to account for missing transmission category.

EAPC = estimated annual percentage change; CI = confidence interval