Time From HIV Diagnosis to Viral Load Suppression: 2007–2013

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Abstract

Background—US guidelines now recommend that all HIV-infected persons receive antiretroviral therapy). HIV prevention is increasingly focused on ensuring that infected persons are diagnosed soon after HIV acquisition and quickly link to care and initiate antiretroviral therapy. We examined trends in time from HIV diagnosis to viral load suppression in King County, WA, to gauge improvement in our HIV care continuum over time.

Methods—We used HIV surveillance data and Cox proportional hazards to evaluate how the time from diagnosis to viral suppression changed among persons newly diagnosed as having HIV in King County, WA, between 2007 and 2013.

Results—A total of 1490 (84%) of 1766 newly diagnosed persons achieved viral suppression in a median time of 213 days (95% confidence interval, 203–229). Thirty-six percent of all persons diagnosed in 2007 and 77% in 2013 were virally suppressed within 12 months of HIV diagnosis ($P < 0.0001$). Differences in time to suppression by calendar year persisted when stratifying by CD4 count at diagnosis. Race was not significantly associated with time to viral suppression.

Conclusions—Time from HIV diagnosis to viral suppression dramatically declined between 2007 and 2013, and more than three quarters of recently HIV-diagnosed individuals in King County, WA, now achieve viral suppression within a year of diagnosis. This improvement was evident among all persons newly diagnosed as having HIV, regardless of race/ethnicity or CD4 count at time of diagnosis.

In 2012, US Health Resources and Service Administration recommended that all persons with human immunodeficiency virus (HIV) infection receive antiretroviral treatment (ART), regardless of their CD4 lymphocyte count (Table 1).[5] That change in treatment guidelines was adopted in the face of new evidence that early ART improves patients' health and has the potential to diminish HIV transmission.[6,7] The emphasis on early treatment codified in

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the guidelines is also evident in the US National HIV/AIDS Strategy, and the more recent HIV Care Continuum Initiative.[8] All of these documents focus on the HIV care continuum —the sequential steps from HIV diagnosis, to linkage and retention in care, ART initiation, and viral suppression[9–12]—and all emphasize the importance of identifying persons with HIV infection shortly after HIV acquisition and rapidly achieving the goal of viral suppression.

We previously published data on the HIV care continuum in King County, WA, demonstrating that 67% to 75% of all diagnosed persons with HIV infection are virally suppressed.[13,14] This cross-sectional evaluation is a measure of the success of the HIV prevention and care system in King County, but provides relatively little insight into the system's success in meeting the needs of persons with recently diagnosed HIV infection, and accelerating progress along the HIV care continuum. Here we present data on trends in the time from diagnosis to viral suppression among persons diagnosed as having HIV infection in King County, WA, from 2007 to 2013, demonstrating that our local care system has rapidly responded to new scientific evidence, treatment guidelines, and public health initiatives that emphasize early linkage to care and initiation of ART.

MATERIALS AND METHODS

We examined the time from HIV diagnosis to viral suppression among persons diagnosed as having HIV infection in King County, WA, from 2007 to 2013. The work was conducted at the Public Health–Seattle & King County HIV/AIDS Epidemiology section and included the period after all CD4 and viral loads became legally reportable (mid-2006). Participants included all HIV-infected individuals older than 14 years diagnosed between 2007 and 2013 who resided in King County at the time of diagnosis and were reported to Public Health–Seattle & King County as of June 4, 2015. Individuals known to be enrolled in research studies were not included in this analysis because WA State law excludes research studies from HIV laboratory reporting requirements. Study status is ascertained through provider and patient contact either during surveillance and partner services investigations undertaken when cases are first reported or, if the individual has not had a laboratory in a 12-month period, through an investigation undertaken of persons thought to be out of care. Public Health does not collect data on the period of study involvement, so we excluded individuals enrolled in a study at any point.

This study is a secondary data analysis of data collected through public health HIV surveillance, including HIV Incidence and Core HIV Surveillance data sources. HIV Incidence and Core HIV Surveillance comprise the Washington State HIV data system called eHARS. HIV Incidence collects testing data, whereas Core contains demographic and transmission characteristics and laboratory tests. Both sources contain data from medical record abstractions, provider reports, and patient interviews. HIV core surveillance and partner services investigations are substantially integrated in King County, and Public Health attempts to interview all persons with newly diagnosed HIV infection. We defined first HIV diagnosis as the earliest positive HIV diagnostic test result or date of self-reported HIV diagnosis. In the event that these differed by more than 40 days, Public Health staff investigated cases to establish which date was likely to be the more accurate. The date of

initial viral suppression was defined as the date of first reported plasma quantitative real-time HIV-1 RNA polymerase chain reaction test result showing an HIV viral load of 200 copies/mL or less. This assay is consistently used for viral load quantification in King County. The following variables were assessed for associations with time to viral suppression: age group at time of diagnosis (15–24, 25–34, 35–44, 45–54, 55+ years), sex, race/ethnicity (non-Hispanic white, foreign-born black, non-Hispanic US born black, Hispanic, and other), HIV exposure category (men who have sex with men [MSM], injection drug user [IDU], MSM-IDU, unknown exposure, or heterosexual exposure as indicated by the National HIV Surveillance System), CD4 lymphocyte count within the first 6 months of diagnosis (defined in groups <350, 350–500, >500 per mm^3), and year of diagnosis (2007 through 2013). CD4 counts more than 6 months after diagnosis were changed to missing due to concern that such values might not be representative of CD4 counts at time of diagnosis.

We calculated estimates of time taken for 50% and 75% of the population to reach viral suppression and created Kaplan-Meier survival plots to visually present time from HIV diagnosis to viral suppression. Individuals contributed time from their date of HIV diagnosis to the date of initial viral suppression (event). Persons with no laboratory results demonstrating HIV viral suppression who were not known to have left the area or died were censored on the date the analytic dataset was created (June 5, 2015). Persons who died were censored on the date of their death. Patient deaths are updated in eHARS from the Washington state and King County death certificates, the National Death Index, and the Social Security Death Master File. Persons who migrated out of WA State were censored on the date of their last laboratory test result reported to Public Heath HIV surveillance. We have previously reported our procedures for identifying persons who migrate out of the area.[15] We used log rank testing and Cox proportional hazard regression to evaluate the association of independent variables with time to viral suppression. We decide a priori to include age, sex, exposure category, race/ethnicity, CD4 count at diagnosis, and year of diagnosis in the multivariable model of the association of independent variables with time to viral suppression. To address the lack of laboratory completeness validation 2007–2009, we repeated analysis for the 3 years with greater than 90% laboratory completeness (2011–2013). We also conducted a secondary multivariable analysis excluding elite controllers (viral loads <50 copies/mL) to examine whether they were skewing results. People missing a CD4 count or with CD4 counts more than 6 month after diagnosis were removed from multivariable models. A secondary multivariable analysis and Kaplan-Meier plots were done for those without CD4 counts within 6 months of diagnosis and for alternative groupings of CD4 counts (0–200, 200–350, 350, 500, >500 per mm^3).

RESULTS

Between 2007 and 2013, 1841 persons were newly diagnosed as having HIV infection in King County, WA. We excluded 56 persons who were enrolled in research studies and 19 persons younger than 14 years from further analysis, leaving a study population of 1766 persons (96% of persons newly diagnosed as having HIV during the study period). A total of 140 (8%) people did not have a CD4 lymphocyte count reported to Public Health in the first 6 months after HIV diagnoses; these persons were excluded from analyses that included CD4 count as an independent variable.

The population was predominantly non-Hispanic white (59%), 25 to 44 years of age (59%), and composed of MSM (76% including 8% MSM-IDU; Table 2). Of those with CD4 lymphocyte counts done within 6 months of diagnosis, 45% had less than 350 cells/mm^3. Although some demographic, clinical, and risk characteristics varied year-to-year, we did not observe significant changes in trends of the characteristics of the newly HIV-diagnosed population.

The 1766 newly diagnosed persons included in the study population achieved viral suppression or were censored in a median time of 258 days (0–3063 days) with an average of 3 viral loads per year before suppression. Of the 276 (16%) who were censored without achieving viral suppression, 36 (13%) died, 86 (31%) moved out of the state, 56 (20%) were still in care with laboratory results reported to surveillance in the final year of study observation (June 2014 or later), and 98 (36%) had no laboratory test results reported in surveillance in the final year of study observation and were not known to have moved out of state or died. This indicates roughly 9% (154 persons) of our initial population never achieved viral suppression, including those who seemed to be out of care as of June 2015 (i.e., no laboratory results reported in the 12 months before the end of observation).

A total of 1490 (84%) persons achieved viral suppression in a median time of 213 days (95% confidence interval [CI], 203–229) after HIV diagnosis. In 2007, half of newly diagnosed persons had achieved viral suppression by 685 days after diagnosis. In contrast, by 2013, half of all newly diagnosed persons were virally suppressed 142 days after diagnosis. In 2007, 36% of all persons diagnosed were virally suppressed within the first 12 months after HIV diagnosis, whereas in 2013, 77% were suppressed 12 months after HIV diagnosis ($P < 0.0001$).

Trends in time from HIV diagnosis to viral suppression varied by initial CD4 lymphocyte count, although all groups did see a significant decrease in time to suppression over this period (Fig. 1A–C [also see Figure, Supplemental Digital Content 1, http://links.lww.com/OLQ/A120, trends for those with CD4 count 200–350 cells/mm^3]). A similar pattern persisted when looking at those without CD4 counts within 6 months, although significance was lost due to small number size (see Figure, Supplemental Digital Content 2, http://links.lww.com/OLQ/A121, trends for those without CD4 counts). Persons with initial CD4 counts less than 350 cells/mm^3 rapidly achieved viral suppression throughout the period of observation (median, 157 days; 95% CI, 151–167). Among persons with CD4 counts greater than 500, the time from diagnosis to when 50% of persons were virally suppressed decreased 87%, from 1112 days in 2007 to 142 days in 2013. This decrease was only slightly smaller (83%) among persons with initial CD4 lymphocyte counts of 350 to 500 cells/mm^3 (717 days in 2007 vs. 120 days in 2013).

On univariate analysis, more rapid viral suppression was significantly associated with unknown HIV risk, IDU, or heterosexual transmission categories, female sex, CD4 lymphocyte count less than 500 cells/mm^3, older age, being a foreign-born black, and later year of HIV diagnosis (Table 3 and Fig. 2). On multivariable analysis, lower CD4 count, older age, female sex, and more recent year of diagnosis were all significantly associated with more rapid viral suppression (Table 4 [also see Table, Supplemental Digital Content 3,

http://links.lww.com/OLQ/A122, multivariable analysis with alternative CD4 groupings]). Similar associations were seen when restricting the analysis to those without CD4 counts at diagnosis (see Table, Supplemental Digital Content 4, http://links.lww.com/OLQ/A123, multivariate analysis for those without CD4 counts). Multivariable analysis restricted to 2011, 2012, and 2013 showed minimal differences in variables associated with time to viral suppression (see Table, Supplemental Digital Content 5, http://links.lww.com/OLQ/A124, multivariable analysis restricted to 2011–2013). An analysis excluding 19 elite controllers with viral loads less than 50 copies/mL did not significantly change the multivariable adjusted hazard ratio (HR_{adj}) findings (data not shown).

DISCUSSION

Evaluating King County, WA, HIV surveillance data, we found that the median time from diagnosis to viral load suppression declined 79% for individuals diagnosed between 2007 and 2013, and the decline was most pronounced among persons diagnosed as having higher CD4 counts. We observed no significant indication of racial disparities in time to suppression. These findings highlight the success of one US urban area in instituting early initiation of ART. Further studies are needed to elucidate whether provider prescribing practices or other local implementation factors (funding, political climate, patient awareness, access to medication and the health care system, etc) are primarily responsible for early ART initiation. Our findings have favorable implications related to the clinical outcomes among persons living with HIV/AIDS and HIV transmission.[16]

Although much of the change in time to viral suppression is likely a consequence of changes in clinical practice prompted by changes in US national ART guidelines, our findings suggest that guideline changes alone do not entirely explain the dramatic increase in how quickly patients became virally suppressed. Stratifying by CD4 count, we found that the time to viral suppression among persons with the highest CD4 counts clearly declined before the 2012 change in HIV treatment guidelines recommending that all persons with HIV receive ART. This finding demonstrates that clinical practice favoring earlier initiation of ART, at least in King County, WA, changed well in advance of national treatment guidelines.

Prior studies from San Francisco and New York City (NYC) evaluated trends in time from diagnosis to viral load suppression. Investigators in San Francisco found that the median time to virologic suppression decreased roughly 69% between 2004 and 2009, from 32 months (~960 days) to 10 months (~300 days).[17] In NYC, persons suppressed (defined as viral load <400 copies/mL) 12 months after diagnoses increased from 36% in 2006 to 45% in 2009, with the most rapid viral suppression occurring among persons with the lowest CD4 lymphocyte counts (0–199 cells/mm^3).[18] The pattern of viral suppression in King County in 2009 was very similar to that reported in NYC and San Francisco; in 2009, the median time to viral suppression in King County was 363 days, and 50% of persons suppressed within the first 12 months after diagnosis. Our more recent data demonstrate that viral suppression now occurs much more quickly after HIV diagnosis. That older data from King County are so similar to findings in other cities suggests that our more recent data may be reflective of patterns of viral suppression occurring in at least some other US cities.

After adjusting for calendar year and CD4 count at time of HIV diagnosis, the only factor significantly associated with a lower likelihood of viral suppression was younger age. This finding highlights the need to focus particular attention on young persons with HIV, but also demonstrates our area's success in avoiding significant racial or ethnic disparities in ensuring that persons with HIV receive the care they need after HIV diagnosis. Nationally, blacks are less likely to be virally suppressed than whites, and reducing HIV-related disparities is a critical component of the National HIV/AIDS Strategy.[19,20] Our findings are good evidence that such disparities can be mitigated, at least in the initial period after HIV diagnosis.

Our study has several limitations. Laboratory reporting improved over the study period, and more complete ascertainment of viral suppression, rather than a true change in virologic outcomes, may have contributed to our findings. Although this change in surveillance data quality could have affected data from earlier years of observation, we believe that changes in data completeness are unlikely to have affected our more recent data. Viral load reporting completeness increased from 86% in 2010 to 93% in 2011 and has subsequently stayed high.[21] Because of an administrative censoring date of June 5, 2015, it is also possible that very recent laboratories were missed, although this impact should be small due to high levels of suppression before this date. Surveillance data could also be limited by missing or inaccurate dates of HIV diagnosis. However, all new HIV diagnoses in King County are investigated through medical record reviews and, when possible, interviews with patients conducted as part of HIV partner services, and date of HIV diagnosis reflects the results of these comprehensive efforts. We may also be unaware of individuals enrolled in studies, although through initial interviews and follow-up with providers when laboratories are missing, missing study information should be minimized. Our team would not have ascertained viral suppression among persons who left WA State after HIV diagnosis. When looking at the total population of persons living with HIV/AIDS, migration leads to substantial underestimates of population-level viral suppression.[11] This limitation is likely less important when evaluating outcomes in the period immediately after HIV diagnosis, but could have led to an underestimate of viral suppression in our data. We defined time to viral suppression using the date of first HIV RNA test demonstrating viral suppression. The true time to viral suppression is clearly somewhat shorter than this date. Thus, our findings are conservative. Finally, because it was not possible to include specific drug regimen used as an independent variable in our analysis, we cannot assess the extent to which more rapid viral suppression may have been a consequence of use of drug regimens that more quickly achieve viral suppression.

In summary, we found that the time from HIV diagnosis to viral suppression dramatically declined between 2007 and 2013; that the median time from diagnosis to documented viral suppression in King County, WA, in 2013 was 142 days; and that 77% persons in the area in 2013 were virally suppressed within 1 year of HIV diagnosis. Although additional efforts to further shorten this period between diagnosis and effective treatment may be worthwhile, our findings demonstrate that most persons with HIV in our area rapidly achieve the goals of HIV treatment after initial diagnosis. In areas like ours, efforts to minimize the morbidity associated with HIV and diminish transmission should focus on ensuring that HIV diagnoses

occur as quickly as possible after infection and promoting the effective treatment for the minority of persons who fail to achieve viral suppression.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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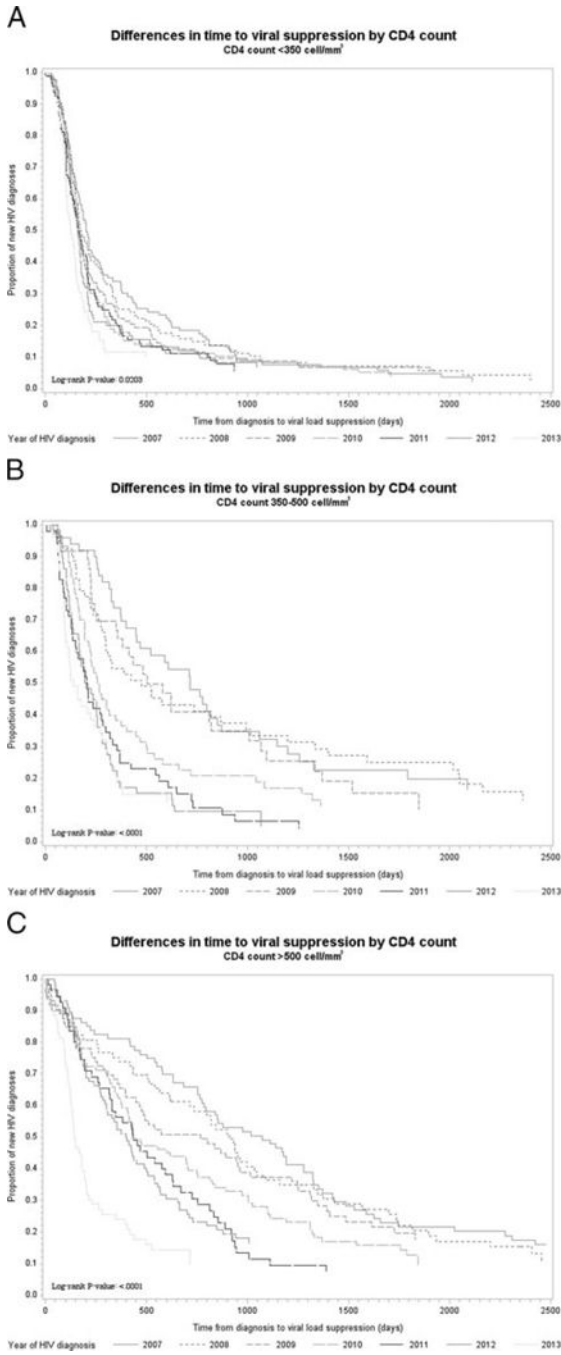
FIGURE 1.
A–C, Kaplan-Meier curves depicting time to viral load suppression by diagnosis year, among those with CD4 counts less than 350 cells/mm^3, 350–500 cells/mm^3, and greater than 500 cells/mm^3 in King County, WA (2007–2013).
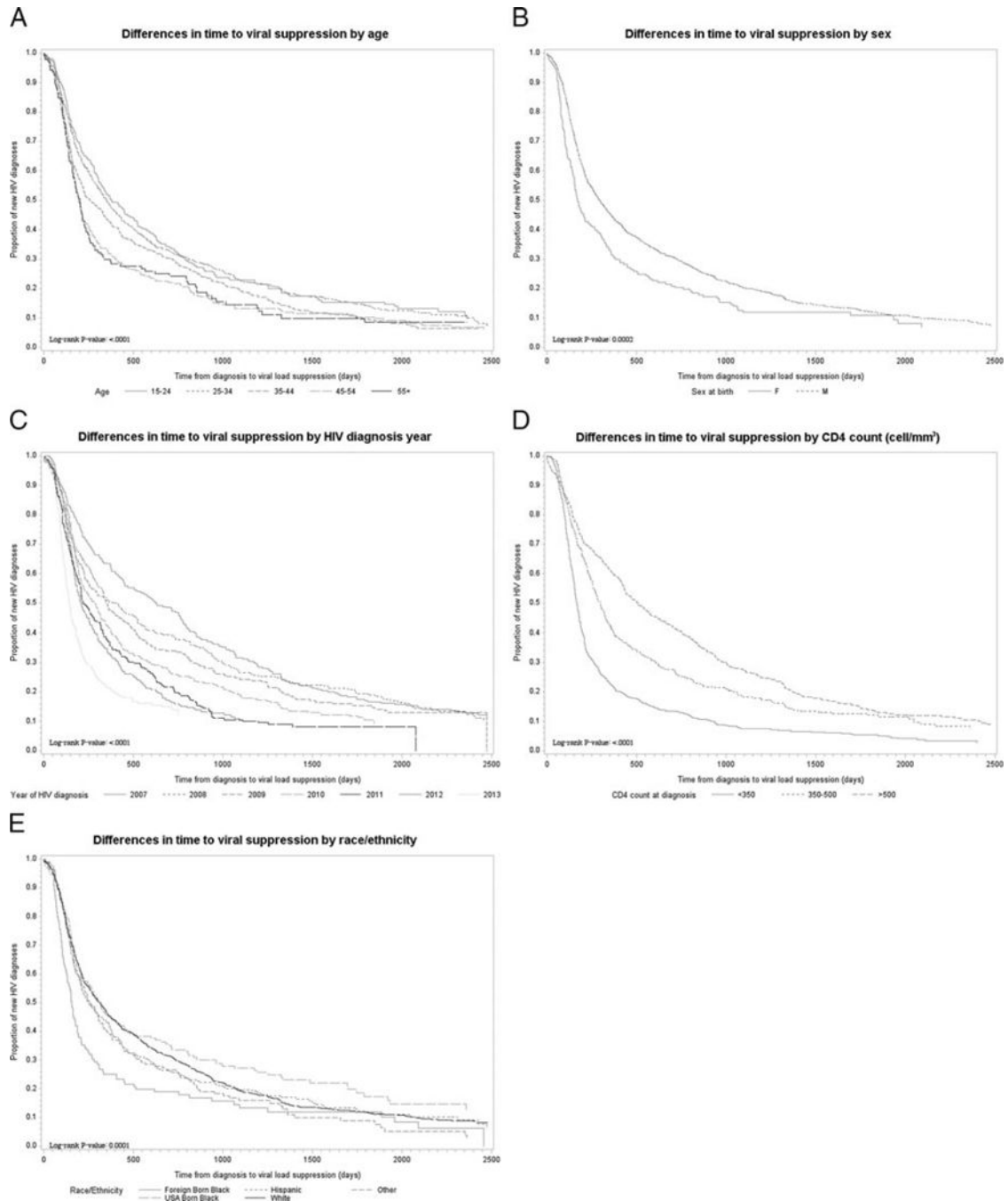
FIGURES 2.

A–F, Kaplan-Meier curves depicting time to viral load suppression among newly diagnosed cases by age, sex, year of diagnosis, CD4 count, race/ethnicity, and transmission category in King County, WA (2007–2013). HETERO indicates heterosexuals.

TABLE 1

ART Initiation Recommendation Issued by "Department of Health & Human Services" (2006–2012)[1–4]

2006	After CD4 count <350/mm^3 and before 200/mm^3
2008	Before CD4 count <350/mm^3 with individualized initiation decisions >350/mm^3
2009	CD4 count 500/mm^3
2012	ART to all patients regardless of CD4 count

TABLE 2

Demographic and Transmission Characteristics Among Those Newly Diagnosed With HIV in King County, WA (2007–2013)

	2007	2008	2009	2010	2011	2012	2013	Total No. (%)
				No. (%)				
Risk								
MSM	181 (64.9)	172 (62.6)	170 (68.3)	205 (73.0)	156 (69.6)	156 (63.9)	147 (68.7)	1187 (67.2)
MSM/IDU	27 (9.7)	16 (5.8)	19 (7.6)	20 (7.1)	26 (11.6)	24 (9.8)	17 (7.9)	149 (8.4)
IDU	7 (2.5)	8 (2.9)	11 (4.4)	12 (4.3)	8 (3.6)	10 (4.1)	4 (1.9)	60 (3.4)
Heterosexual	30 (10.8)	35 (12.7)	21 (8.4)	23 (8.2)	9 (4.0)	16 (6.6)	15 (7.0)	149 (8.4)
Unknown	34 (12.2)	44 (16.0)	28 (11.2)	21 (7.5)	25 (11.2)	38 (15.6)	31 (14.5)	221 (12.5)
Race/ethnicity								
Foreign-born black	22 (7.9)	26 (9.5)	14 (5.6)	7 (2.5)	16 (7.1)	18 (7.4)	17 (7.9)	120 (6.8)
US-born black	32 (11.5)	28 (10.2)	25 (10.0)	19 (6.8)	24 (10.7)	25 (10.3)	22 (10.3)	175 (9.9)
Non-Hispanic white	157 (56.3)	150 (54.6)	152 (61.0)	181 (64.4)	135 (60.3)	147 (60.3)	116 (54.2)	1038 (58.8)
Hispanic	47 (16.9)	40 (14.6)	40 (16.1)	46 (16.4)	34 (15.2)	28 (11.5)	35 (16.4)	270 (15.3)
Other	21 (7.5)	31 (11.3)	18 (7.2)	28 (10.0)	15 (6.7)	26 (10.7)	24 (11.2)	163 (9.2)
Age at diagnosis, y								
15–24	41 (14.7)	42 (15.3)	36 (14.5)	44 (15.7)	38 (17.0)	34 (13.9)	31 (14.5)	266 (15.1)
25–34	81 (29.0)	88 (32.0)	78 (31.3)	94 (33.5)	70 (31.2)	86 (35.3)	65 (30.4)	562 (31.8)
35–44	81 (29.0)	75 (27.3)	64 (25.7)	76 (27.1)	53 (23.7)	69 (28.3)	63 (29.4)	481 (27.2)
45–54	46 (16.5)	45 (16.4)	52 (20.9)	53 (18.9)	40 (17.9)	38 (15.6)	41 (19.2)	315 (17.8)
55+	30 (10.6)	25 (9.1)	19 (7.6)	14 (5.0)	23 (10.3)	17 (7.0)	14 (6.5)	142 (8.0)
Sex								
Female	33 (11.8)	35 (12.7)	24 (9.6)	29 (10.3)	21 (9.4)	33 (13.5)	26 (12.2)	201 (11.4)
Male	246 (88.2)	240 (87.3)	225 (90.4)	252 (89.7)	203 (90.6)	211 (86.5)	188 (87.9)	1565 (88.6)
CD4, cells/mm^3 [*]								
< 350	106 (44.7)	121 (48.8)	117 (51.5)	110 (41.4)	98 (47.6)	91 (38.1)	84 (41.4)	727 (44.7)
350–500	50 (21.1)	54 (21.8)	37 (16.3)	61 (22.9)	53 (25.7)	60 (25.1)	49 (24.1)	364 (22.4)
>500	81 (34.2)	73 (29.4)	73 (32.2)	95 (35.7)	55 (26.7)	88 (36.8)	70 (34.5)	535 (32.9)
Viral load, copies/mL†								
<50	4 (1.6)	4 (1.6)	2 (0.9)	2 (0.8)	4 (1.9)	1 (0.4)	2 (1.0)	19

	2007	2008	2009	2010	2011	2012	2013	Total No. (%)
				No. (%)				
50–1000	23 (9.2)	19 (7.6)	22 (9.6)	17 (6.4)	11 (5.3)	16 (6.8)	13 (6.4)	121
>1000	224 (89.2)	228 (90.8)	205 (89.5)	247 (92.9)	194 (92.8)	220 (92.8)	187 (92.6)	1505
Total	279 (100)	275 (100)	249 (100)	281 (100)	224 (100)	244 (100)	214 (100)	1766

*
CD4 counts done later than 6 months after initial diagnosis have been removed (140 missing).

†
Viral loads done later than 6 months after initial diagnosis have been removed (121 missing).

TABLE 3

Univariate Proportional Cox Analysis of Variables Associated With Viral Suppression After HIV Diagnosis in King County, WA (2007–2013)

	Time for 50% of Persons to Be Suppressed, d	Time for 75% of Persons to Be Suppressed, d	HR	95% CI	P
Race/ethnicity					
Foreign-born black	155	406	1.52	1.24–1.86	<0.0001
US-born black	322	2358	0.87	0.72–1.04	0.13
Hispanic	269	980	1.06	0.91–1.22	0.45
Other	286	842	1.15	0.97–1.38	0.11
Non-Hispanic white	322	1004	Reference		
CD4, cells/mm³					
<350	169	358	2.14	1.89–2.42	<0.0001
350–500	300	868	1.27	1.10–1.47	<0.01
>500	524	1350	Reference		
Sex					
Female	176	620	1.36	1.16–1.60	<0.001
Male	308	1034	Reference		
Age at diagnosis, y					
15–24	413	1192	0.68	0.54–0.85	<0.001
25–34	364	1223	0.72	0.59–0.88	<0.01
35–44	281	995	0.84	0.69–1.04	0.11
45–54	198	621	0.98	0.79–1.21	0.82
55+	204	855	Reference		
Risk					
Unknown	188	980	0.94	0.75–1.17	0.56
IDU	279	962	0.75	0.54–1.05	0.09
MSM	317	952	0.72	0.60–0.87	<0.001
MSM/IDU	610	—	0.51	0.40–0.66	<0.0001
Heterosexual	189	482	Reference		
Year of diagnosis					
2007	685	1502	0.37	0.31–0.46	<0.0001
2008	433	1739	0.42	0.34–0.51	<0.0001

	Time for 50% of Persons to Be Suppressed, d	Time for 75% of Persons to Be Suppressed, d	HR	95% CI	P
2009	363	1325	0.47	0.38–0.58	<0.0001
2010	291	894	0.56	0.46–0.68	<0.0001
2011	230	630	0.68	0.55–0.83	<0.001
2012	211	543	0.71	0.58–0.87	<0.001
2013	142	327	Reference		

TABLE 4

Multivariable Proportional Cox Analysis of Variables Associated With Viral Suppression After HIV Diagnosis in King County, WA (2007–2013)

	HR$_{adj}$	95% CI	P
Race/ethnicity			
Foreign-born black	1.05	0.82–1.33	0.72
US-born black	0.87	0.72–1.06	0.17
Hispanic	0.96	0.82–1.12	0.60
Other	0.97	0.81–1.17	0.77
Non-Hispanic white	Reference		
CD4, cells/mm^3			
<350	2.07	1.82–2.35	<0.0001
350–500	1.27	1.10–1.47	<0.01
>500	Reference		
Sex			
Female	1.31	1.02–1.69	0.04
Male	Reference		
Age at diagnosis, y			
15–24	0.80	0.63–1.01	0.06
25–34	0.79	0.64–0.98	0.03
35–44	0.93	0.75–1.15	0.48
45–54	1.09	0.87–1.36	0.48
55+	Reference		
Risk			
Unknown	1.05	0.80–1.37	0.73
IDU	0.75	0.53–1.08	0.12
MSM	1.03	0.78–1.36	0.81
MSM/IDU	0.72	0.52–1.01	0.06
Heterosexual	Reference		
Year of diagnosis			
2007	0.39	0.32–0.48	<0.0001
2008	0.43	0.35–0.52	<0.0001
2009	0.49	0.39–0.60	<0.0001
2010	0.58	0.47–0.70	<0.0001
2011	0.71	0.58–0.87	<0.01
2012	0.70	0.57–0.86	<0.001
2013	Reference		