Published in final edited form as:

AIDS. 2015 May 15; 29(8): 947–954. doi:10.1097/QAD.0000000000000640.

Time above 1500 copies: a viral load measure for assessing transmission risk of HIV-positive patients in care

Gary Marks^a, Lytt I. Gardner^a, Charles E. Rose^a, Anne Zinski^b, Richard D. Moore^c, Susan Holman^d, Allan E. Rodriguez^e, Meg Sullivan^f, and Thomas P. Giordano^g

^aDivision of HIV/AIDS Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia

^bDepartment of Medicine, Division of Infectious Diseases, University of Alabama at Birmingham, Birmingham, Alabama

^cDepartment of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland

^dState University of New York, Downstate Medical Center, Brooklyn, New York

^eDivision of Infectious Diseases, Miller School of Medicine, University of Miami, Florida

^fDepartment of Medicine, Boston University School of Medicine, Boston, Massachusetts

^gDepartment of Medicine, Baylor College of Medicine, and the Center for Innovations in Quality, Effectiveness and Safety, Michael E DeBakey Veterans Affairs Medical Center, Houston, Texas, USA

Abstract

Objective—We examined HIV transmission potential of patients in care by analyzing the amount of person-time spent above a viral load threshold that increases risk for transmission.

Design—Observational cohort and supplemental data.

Methods—The cohort included HIV patients who received care at six HIV clinics in the United States, from 1 April 2009 to 31 March 2013, and had two or more viral load tests during this interval. Person-time (in days) above a viral load of 1500 copies/ml out of the total observation time was determined by inspecting consecutive pairs of viral load results and the time intervals between those pairs. The person-time rate ratios comparing demographic and clinical subgroups were estimated with Poisson regression.

Results—The cohort included 14 532 patients observed for a median of 1073 days with a median of nine viral load records. Ninety percent of the patients had been prescribed antiretroviral therapy. On average, viral load exceeded 1500 copies/ml during 23% of the patients' observation time (average of 84 days per year, per patient). Percentage of person-time above the threshold was higher among patients who had more than a fourth of their viral load pairs exceeding a 6-month interval (34% of observation time), patients not on antiretroviral therapy (58% of time), new/re-engaging patients (34% of time), patients 16–39 years of age (32% of time), and patients of black race (26% of time).

Correspondence to Gary Marks, Centers for Disease Control and Prevention, Division of HIV/AIDS Prevention, 1600 Clifton Road, MS: E-45, Atlanta, GA 30333, USA. gmarks@cdc.gov.

Conflicts of interest

There are no conflicts of interest for any of the authors.

Conclusion—HIV patients in care spent an average of nearly a quarter of their time with viral loads above 1500 copies/ml, higher among some subgroups, placing them at risk for potentially transmitting HIV to others.

Keywords

cohort study; HIV; person-time; transmission; viral load

Introduction

In the United States, HIV-infected people who are aware of their seropositive status – approximately 85% of the infected population [1] – account for over 50% of HIV transmissions [2,3]. As HIV-testing initiatives expand, the relative proportion of transmission from HIV-diagnosed persons may increase, because they will comprise a larger segment of the HIV-infected population. And as programs that facilitate entry and retention in care improve, proportionally more transmissions may stem from HIV patients in care.

We examined the HIV transmission potential of patients in care by analyzing the amount of person-time they spent above a viral load threshold that increases risk for transmission. Several studies have examined ‘blips’ in HIV RNA levels, which are transient small increases (e.g. blips to above 50 or to above 400 copies/ml) in viral load occurring after a patient had previously had a viral load below the limit of detection of the assay [4,5]. These studies were not intended to characterize the transmission potential of patients, because the temporary increases in viral load may not reach a level that heightens that risk. Although studies have found isolated instances of HIV transmission occurring between serodiscordant heterosexual couples when viral load was less than 1000 copies/ml [6], for the overwhelming majority of couples, risk for transmission increased when viral load was above 1500 copies/ml [7–9].

Using data from HIV patients in care at six clinics in the United States, we characterized the proportion of time in which patients had a viral load exceeding 1500 copies/ml relative to the total amount of time their viral load results were observed. We present findings on person-time above this threshold for the entire cohort and stratified by several demographic and clinical subgroups, such as patients who had few or many viral load tests with intervals longer than 6 months, patients who were on antiretroviral therapy (ART) or not, and patients who had undetectable viral loads followed by their next viral loads being above 1500 copies/ml.

Methods

The cohort included HIV patients who received medical care from 1 April 2009 to 31 March 2013 at HIV clinics located in Baltimore, Maryland; Birmingham, Alabama; Boston, Massachusetts; Brooklyn, New York; Houston, Texas, and Miami, Florida. All patients who had two or more viral load tests as part of routine medical care in this 4-year period were included, with the stipulation that patients had to have at least 30 days between their first and last viral load test, and new and re-engaging patients had to have at least one viral load result

by the end of March 2012, thus increasing the opportunity to observe multiple viral loads during the final 12-month period.

The cohort dataset did not contain patient-level information about whether patients were on ART. Thus, we conducted a supplemental analysis using another dataset to examine person-time above 1500 copies/ml stratified by whether patients had been prescribed ART (on the basis of medical chart reviews). This supplemental dataset included HIV patients enrolled in a retention-in-care intervention trial at the same six clinics. Enrollees were not part of the observational cohort. Patients were eligible for the trial if they had missed any primary care appointments in the past 12 months, had a gap in care greater than 6 months, or were new to the clinic (first or second visit or re-engaging after a 3-year lapse). Enrollees were randomized to one of the two intervention arms or to a standard-of-care (control) arm (see Gardner *et al.* [10] for details of the interventions). The interventions improved clinic attendance [10], but not patients' viral loads. Enrollment began on 1 June 2010, and viral load results from routine medical care (not study visits) were observed for 24–30 months per enrollee. We restricted our analysis to enrollees (97% of total) who had a viral load result within ± 6 months of enrollment (which served as a baseline) and had at least one subsequent viral load result at least 30 days after baseline.

Calculation of person-time with viral load above 1500 copies/ml

The date of the first and the last viral load result reflects the total observation time (in days) for a patient. To determine the amount of time spent above a viral load of 1500 copies/ml, we inspected all consecutive pairs of viral load results and the time intervals between those results. If two consecutive results each had a viral load that exceeded 1500 copies/ml, we assumed that the entire time period between those results was above the threshold. If two consecutive results each had a viral load equal to or less than 1500 copies/ml, we assumed that the entire time between those results was below the threshold. If two consecutive results went from below the threshold to above the threshold, or *vice versa*, we estimated the amount of time above the threshold by first looking at the range of the viral load results and determining the relative position of the 1500 threshold within that range. For example, if a patient's first viral load was 50 copies/ml and the next was 2200 copies/ml, the range is 2150. The viral load of 2200 copies/ml exceeds 1500 by 700, which is 0.33 of the range (700/2150). The same proportion would be obtained had this patient's first viral load result been 2200 copies/ml and his next was 50 copies/ml. We used this proportion to estimate the amount of time spent above 1500. If the date of the first viral load was 20 May 2012 and the next was 20 October 2012 (154 days), then we estimated that 0.33 of 154 days was spent above 1500, which is 51 days during the time between these two consecutive viral load results. The number of estimated days above the threshold during consecutive pairs of viral load results was summed, yielding a single value per patient.

Statistical analysis

We used Poisson regression models with robust standard errors (SEs) to estimate a rate reflecting the number of days above the threshold relative to the total number of days of observation and 95% confidence interval (CI). The rate was expressed as a percentage of observation time spent above a viral load of 1500 copies/ml.

In the cohort dataset, we examined several stratification variables obtained from clinics' electronic medical records (EMRs). Patients were grouped according to the percentage of their viral load pairs that had intervals longer than 6 months: 0–9.99% of viral load pairs, 10–25%, and above 25–100%. Intervals longer than 6 months are generally not recommended [11,12]. These three subgroups were chosen to reduce the skew in the distribution, as the majority of patients had few viral load pairs with intervals exceeding 6 months. Other stratification variables included year of entry into the analytic cohort (2009–2010, 2010–2011, 2011–2012), whether patient's viral load at time of entry was above 1500 copies/ml, CD4⁺ cell count at entry, age, race/ethnicity, sex/sexual orientation (MSM, heterosexual men, women), whether injection drug use was an exposure factor for acquiring HIV infection, health insurance status, and clinic site. Subgroups were compared with univariate and multivariable rate ratios from the Poisson models.

For the analysis of the supplemental data, we created a three-group ART status variable: prescribed ART prior to enrollment, had not been prescribed ART prior to enrollment, but started ART during the next 12 months, and had not been prescribed ART prior to enrollment and did not start during the next 12 months. Three other variables were included in the analysis: trial arm, patient type (new to clinic vs. established patient), and clinic site. Subgroups were compared with univariate and multivariable Poisson models. All analyses were performed with SAS, version 9.2, SAS Institute, (Cary, North Carolina, USA).

Results

Findings from observational cohort

The cohort included 14 532 patients with two or more viral load records, of whom 10 735 (74%) had their initial viral load for analysis between 1 April 2009 and 31 March 2010. Approximately 85% of these 10 735 patients were established patients as opposed to new patients (new to care or transfers) or re-engaging patients [13]. Cohort patients who had their initial viral load for analysis between 1 April 2010 and 31 March 2011, or between 1 April 2011 and 31 March 2012 were primarily new or re-engaging patients. Among the full cohort, the median length of time between the first and the last viral load result (observation time) was 1073 days (range 30–1459 days), and the median number of viral load records was 9 (range 2–40).

Demographic and clinical characteristics of the cohort are displayed in Table 1. The cohort included approximately equal thirds of MSM, heterosexual men, and women. Sixty-four per cent were black, 70% were aged 40 years and older, 15% had private health insurance, and the remaining had other forms of insurance (Medicaid, Medicare) or payment (Ryan White, charitable contributions). Fifty-four per cent of the cohort had at least one viral load result above 1500 copies/ml during their observation time. Using all records above 1500 copies/ml, the geometric mean viral load was 29 427 copies/ml [interquartile range (IQR) 7232–99 903].

Although we did not have patient-level data on ART status for cohort members, clinic-level metrics indicated that 90.5% (range 88–93%) of patients, averaged across clinics, had received an ART prescription during the 3 years of 2010 through 2012.

Analysis of the person-time outcome indicated that, on average, viral load exceeded 1500 copies/ml during 23% of patients' observation time, which equates to an average of 84 days per year (0.23×365 days) per patient. Table 2 displays the stratified results. In univariate analysis, person-time above viral load of 1500 copies/ml was lower among patients who had their initial viral load for analysis in 2009–2010 than in 2010–2011 or 2011–2012. This difference diminished considerably in the full multivariable model, and was accounted for primarily by confounding due to differences in proportion of patients whose initial viral load was above 1500 copies/ml (less likely among patients who entered the cohort in 2009–2010, the vast majority of whom were established patients).

We found several significant multivariable effects. The percentage of person-time above the 1500 threshold was higher among patients whose initial viral load exceeded 1500 copies/ml (51% of time), patients who had more than 25% of their viral load pairs exceeding a 6-month interval (34% of time) compared with patients who had fewer than 10% exceeding that interval (16% of time), and patients who had a CD4⁺ cell count less than 350 cells/ml at entry (33% of time). Person-time above the threshold was higher among patients 16–39 years of age (32% of time) compared with those who were aged 50–85 years (16% of time), patients of black race (26% of time) versus those of white race (16% of time), patients who had injection drug use as an exposure factor for acquiring HIV infection (26% of time), and those on Medicaid (25% of time) or other healthcare assistance programs (28% of time) compared with patients who had private health insurance (13% of time). Person-time above the threshold was lower among MSM (20% of time) than among heterosexual men (24% of time) or women (25% of time). There was substantial variation in the person-time outcome among the six HIV clinics.

We conducted a sub-analysis of patients who had one or more instances of having an undetectable viral load (below limit of detection of assay) during their observation time ($n = 11\,550$). Seventeen percent of these patients had an instance of having an undetectable viral load followed by their next viral load result being above 1500 copies/ml (a 'spike'). Aggregating all such instances of these spikes indicated that they accounted for only an average of 2.9% of person-time above 1500 copies/ml. This suggests that these spikes were short in duration and contributed minimally to the overall person-time above 1500 copies/ml.

Findings from supplemental analysis

Recall, the supplemental analysis was performed primarily to examine the association of patients' ART status with the person-time outcome. This analysis used noncohort patients who had enrolled in a retention-in-care trial at the six clinics. The analytic sample size was 1779 patients. Their clinical (e.g. viral load and CD4⁺ cell count at baseline) and demographic (e.g. age, race/ethnicity, sex/sexual orientation) characteristics closely matched the characteristics of the cohort, with the exception that African Americans comprised 72% of the trial, compared with 64% in the cohort. Trial participants were observed for a median of 1032 days (range 41–1456 days) with a median of 11 (range 2–33) viral load records.

Viral load exceeded 1500 copies/ml during 26% of trial patients' observation time (average of 95 days per year, per patient). Univariate and multivariable findings are displayed in Table

3. There were strong differences by ART status. The percentage of person-time above the 1500 threshold was higher among patients who were not on ART at enrollment or during the next 12 months (58% of time) than patients who started ART during the first 12 months of follow-up (45% of time) or patients on ART at enrollment (21% of time). Person-time was higher among new patients (34% of time) than established patients (24% of time), but not significant in the adjusted analysis. Differences by clinic were similar to the findings in the cohort analysis. There were no significant differences by trial arm.

Discussion

The present analysis of more than 14 500 HIV patients from six US clinics found that a considerable number of patients were at risk of transmitting HIV infection by virtue of their viral load being above 1500 copies/ml. In the context of 90% of cohort patients being on ART, they were above that threshold approximately a quarter of the time under observation. Person-time above the threshold was considerably higher among patients who were not on ART (58% of time) and among patients who were new to the clinic (34% of time), many of whom may not have been on ART during a portion of the observation time.

We also found large differences in person-time above 1500 copies/ml according to the percentage of viral load pairs that had intervals longer than 6 months. Person-time was lower among patients who had fewer than 10% of such pairs (16% of time) than patients who had 10–25% of such pairs (25% of time) or more than 25% of such pairs (34% of time). Thus, having a larger percentage of viral load tests greater than 6 months apart was a risk factor for having a longer period with a viral load above 1500 copies/ml. Clinical care that strives to minimize the number of viral load tests with intervals greater than 6 months may reduce person-time above the threshold, lower transmission risk, and benefit patients' health.

Our analysis did not take into account disengaging patients (e.g. those who provided two or three viral load results and then disappeared from clinic). Approximately 10–15% of HIV patients disappeared from their regular place of HIV care for 12 months or more [13]. If not in care elsewhere, these persons are likely to have a viral load greater than 1500 copies/ml during the disengagement period. Thus, our findings may underestimate the amount of person-time in which HIV patients, in general, have a viral load above 1500 copies/ml.

The person-time metric presented here offers a dynamic, longitudinal view of viral load patterns that place patients at risk of transmitting HIV by virtue of the amount of time spent above a transmission threshold. Knowing the amount of time HIV patients spend above the threshold may improve the accuracy of estimates of sexual transmission, for example, with respect to how many sex partners are placed at high risk of infection during a window of time. A clinic-based study [14] found that 68 of 496 HIV-positive MSM in care (13.7%) self-reported that they engaged in insertive anal intercourse or vaginal intercourse without using condoms with a total of 225 receptive partners who were HIV-negative or of unknown serostatus in a 3-month period. Not all of these partners are at high risk of becoming infected, because, on the basis of our person-time findings, HIV-positive MSM in care spent, on average, only 20% of their time above a transmission threshold of 1500 copies/ml. If we assume that numbers of partners are equally distributed across time, then 20% of the 225

partners (45) were at high risk of becoming infected during a 3-month period. Granted, some MSM may spend more time than other MSM above a viral load of 1500 copies/ml. If highly sexually active MSM spend more time than less sexually active MSM above that threshold, then more partners would be at risk.

Further insights about HIV transmission are gleaned from our stratified results. Person-time above a viral load of 1500 copies/ml was higher among younger patients (16–39 years of age) and patients of black race. If HIV patients of these two demographic subgroups engage in unprotected sex with at-risk partners, and they engage in assortative partnering (young with young; black with black), this may partially explain the higher incidence of HIV infection observed among young, black persons in the United States [15].

In estimating person-time above a viral load of 1500 copies/ml, we used a linear approach that equated increments in viral load level with increments in time. This approach was used in calculating person-time between consecutive viral load results when, for example, the first viral load was below 1500 copies/ml and the next viral load was above that value. During the interval of time between these two viral load results, it is possible that a patient may have spiked up quickly and then plateaued; thus, this patient may have spent more time above the threshold than estimated by our linear approach. Another patient with the same two viral load results may have remained below the threshold for most of the time interval and then suddenly spiked up toward the end; thus, this patient may have spent less time above the threshold than estimated by our approach. In the absence of having more detailed viral load profiles than we had, with viral load results closer together in time than available in our clinic data, our method for estimating person-time may counterbalance these two opposing errors and, thus, provide a relatively accurate estimate when averaging across a large number of patients. Caution is warranted, though. The data were from only six HIV clinics in the United States, and the clinics were not selected in any probabilistic manner. The vast majority of the patients were of black race, and approximately a third were heterosexual men. Our findings should not be generalized to the entire US population of HIV patients in care. Finally, while our viral load person-time findings provide a context for understanding possible transmission risk, since we did not collect data on patients' sexual behaviors, we were not able to examine transmission risk in greater detail.

In conclusion, we observed that some HIV patients in care spent a considerable amount of time with their viral loads above 1500 copies/ml, which increases the risk for potentially transmitting HIV to others. As HIV diagnosis and linkage to care continue to improve [16,17], a larger proportion of HIV transmission may stem from behaviors of HIV-diagnosed persons in care, relative to undiagnosed HIV-infected persons. Analyses such as the ones presented here, combined with sexual behavior data, will help characterize the fraction of potential transmission from HIV patients in care going forward. To achieve the goals of 'treatment as prevention', efforts by HIV providers and patients to minimize the duration of time with viral load above 1500 copies/ml may help reduce transmission risk.

Acknowledgments

G.M. conceived idea and method, contributed to conceptualization of statistical analyses, and wrote the manuscript. L.I.G. contributed to idea and method, conducted statistical analyses, and edited manuscript. C.E.R. consulted on

statistical analysis and edited manuscript. A. Z., R.D.M., S. H., A.E.R., M.S., and T.P.G. were site investigators for the retention-in-care trial and edited the manuscript.

References

- Bradley H, Hall I, Wolitski RJ, Van Handel MM, Stone AE, LaFlam M, et al. Vital signs: HIV diagnosis, care, and treatment among persons living with HIV: United States, 2011. *MMWR Morb Mortal Wkly Rep*. 2014; 63:1113–1117. [PubMed: 25426654]
- Hall HI, Holtgrave DR, Maulsby C. HIV transmission rates from persons living with HIV who are aware and unaware of their infection. *AIDS*. 2012; 26:893–895. [PubMed: 22313960]
- Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. *AIDS*. 2006; 20:1447–1450. [PubMed: 16791020]
- Fung ICH, Gambhir M, Sighem AV, Wolf FD, Garnett GP. The clinical interpretation of viral blips in HIV patients receiving antiviral treatment: are we ready to infer poor adherence? *J Acquir Immune Defic Syndr*. 2012; 60:5–11. [PubMed: 22267019]
- Grennan JT, Loutfy MR, Su D, Harrigan PR, Cooper C, Klein M, et al. Magnitude of virologic blips in associated with a higher risk for virologic rebound in HIV-infected individuals: a recurrent events analysis. *J Infect Dis*. 2012; 205:1230–1238. [PubMed: 22438396]
- Murray JM, Zaunders JJ, Koelsch KK, Natarajan V, Badralmaa Y, McBride K, et al. Short communication: HIV blips while on antiretroviral therapy can indicate consistently detectable viral levels dues to assay underreporting. *AIDS Res Hum Retroviruses*. 2013; 29:1621–1625. [PubMed: 23844947]
- Attia S, Egger M, Muller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. *AIDS*. 2009; 23:1397–1404. [PubMed: 19381076]
- Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. *N Engl J Med*. 2000; 342:921–929. [PubMed: 10738050]
- Tovanabutra S, Robison V, Wongtrakul J, Sennum S, Suriyanon V, Kingkeow D, et al. Male viral load and Heterosexual transmission of HIV-1 subtype E in Northern Thailand. *J Acquir Immune Defic Syndr*. 2002; 29:275–283. [PubMed: 11873077]
- Gardner LI, Giordano TP, Marks G, Wilson TE, Craw JA, Drainoni M, et al. Enhanced personal contact with HIV patients across time improves retention in primary care: a randomized trial in six U.S. HIV clinics. *Clin Infect Dis*. 2014; 59:725–734. [PubMed: 24837481]
- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services; Nov. 2014 <http://aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>
- Gunthard HF, Aberg JA, Eron JJ, Hoy JF, Telenti A, Benson CA, et al. Antiretroviral treatment of adult HIV infection 2014 recommendations of the International Antiviral Society-USA panel. *JAMA*. 2014; 312:410–425. [PubMed: 25038359]
- Gardner LI, Marks G, Craw J, Wilson T, Drainoni ML, Moore R, et al. A low-effort clinic-wide intervention improves attendance for HIV primary care. *Clin Infect Dis*. 2012; 55:1124–1134. [PubMed: 22828593]
- Golin C, Marks G, Wright J, Gerkovich M, Tien HC, Patel SN, et al. Psychosocial characteristics and sexual behaviors of people in care for HIV infection: an examination of men who have sex with men, heterosexual men, and women. *AIDS Behav*. 2009; 13:1129–1142. [PubMed: 19763810]
- CDC. Increase in newly diagnosed HIV infections among young black men who have sex with men: Milwaukee County, Wisconsin, 1999–2008. *MMWR Morb Mortal Wkly Rep*. 2011; 60:99–102. [PubMed: 21293324]
- CDC. Vital signs: HIV prevention through care and treatment: United States. *MMWR Morb Mortal Wkly Rep*. 2011; 60:1618–1623. [PubMed: 22129997]

17. Marks G, Gardner LI, Craw J, Crepaz N. Entry and retention in care among HIV-diagnosed persons: a meta-analysis. *AIDS*. 2010; 24:2665–2678. [PubMed: 20841990]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1

Demographic and clinical characteristics of HIV patients in the observational cohort.

Subgroups	Subgroup [N (%)]	% With VL result above 1500 copies/ml during observation time	95% CI
Overall	14 532	54.36	53.55, 55.17
Year of initial VL in analysis			
4-1-2011 to 3-31-2012	1828 (12.6)	68.65	66.56, 70.81
4-1-2010 to 3-31-2011	1969 (13.6)	71.66	69.70, 73.68
4-1-2009 to 3-31-2010	10735 (73.9)	48.75	47.81, 49.70
Initial VL in analysis above 1500 copies/ml			
Yes	5479 (37.7)	100.00	100.0, 100.0
No	9053 (62.3)	26.73	25.84, 27.66
Percentage of VL pairs with intervals longer than 6 months ^a			
>25–100%	3509 (24.2)	56.28	54.67, 57.95
10–25%	3665 (25.2)	56.70	55.12, 58.33
0–9.99%	7358 (50.6)	52.27	51.14, 53.42
CD4 ⁺ cell count <350 cells/μl at time of initial VL in analysis			
Yes	6533 (45.0)	72.71	71.64, 73.80
No	7999 (55.0)	39.37	38.31, 40.45
Age at time of initial VL in analysis (years)			
16–39	4415 (30.4)	66.09	64.71, 67.50
40–49	5228 (36.0)	53.54	52.20, 54.91
50–85	4889 (33.6)	44.63	43.26, 46.05
Race/ethnicity			
Black	9246 (63.6)	57.92	56.92, 58.93
Hispanic	2640 (18.2)	52.01	50.14, 53.95
Other	220 (1.5)	44.55	38.44, 51.62
White	2426 (16.7)	44.23	42.30, 46.25
Sex/sexual orientation			
MSM	4460 (30.7)	52.38	50.93, 53.86
Women	4983 (34.3)	55.59	54.23, 56.99
Heterosexual men	5089 (35.0)	54.88	53.53, 56.27
Injection drug use as exposure for acquiring HIV infection ^b			
Yes	1933 (13.3)	54.58	52.40, 56.84
No	12599 (86.7)	54.32	53.46, 55.20
Health insurance at time of initial VL in analysis			
Medicare	2198 (15.1)	41.17	39.17, 43.28
Medicaid	3608 (24.8)	54.68	53.08, 56.33
Ryan White/Charity	6603 (45.4)	63.49	62.34, 64.66
Private	2123 (14.6)	39.05	37.03, 41.18
Clinic			
A	966 (6.7)	51.04	47.98, 54.29

Subgroups	Subgroup [N (%)]	% With VL result above 1500 copies/ml during observation time	95% CI
B	2897 (19.9)	51.36	49.58, 53.22
C	2540 (17.5)	56.18	54.28, 58.14
D	1870 (12.9)	47.22	45.01, 49.54
E	5119 (35.2)	61.93	60.61, 63.27
F	1140 (7.6)	38.42	35.70, 41.35

CI, confidence interval; VL, viral load.

^aIn the full cohort, the median interval of time between VL pairs was 114 days (IQR 91–150). In the above 25–100% group, the n-weighted mean was 52.9% of VL pairs with intervals longer than 6 months. In the 10–25% group, the n-weighted mean was 17.4% of VL pairs exceeding 6 months, and in the 0–9.99% group, the n-weighted mean was 1.6% of VL pairs.

^bThis variable does not reflect current injection drug use.

Table 2

Percentage of person-time with viral load above 1500 copies/ml among HIV patients in the observational cohort, by demographic and clinical subgroups.

Subgroups	% Of observation time VL above 1500 copies/ml	95% CI	Unadjusted rate ratio	95% CI	P	Adjusted rate ratio	95% CI	P
Overall	23.08	22.51, 23.66						
Year of initial VL in analysis								
4-1-2011 to 3-31-2012	34.52	32.73, 36.40	1.64	1.54, 1.74	<0.001	1.08	1.02, 1.13	0.004
4-1-2010 to 3-31-2011	34.13	32.39, 35.97	1.62	1.52, 1.72	<0.001	0.95	0.91, 1.00	0.065
4-1-2009 to 3-31-2010	21.11	20.49, 21.75	Ref			Ref		
Initial VL in analysis above 1500 copies/ml								
Yes	50.81	49.72, 51.92	4.85	4.60, 5.11	<0.001	4.03	3.80, 4.28	<0.001
No	10.48	10.00, 10.98	Ref			Ref		
Percentage of VL pairs with intervals longer than 6 months								
>25-100%	34.33	32.94, 35.77	2.18	2.06, 2.31	<0.001	2.04	1.94, 2.14	<0.001
10-25%	25.49	24.40, 26.62	1.62	1.53, 1.72	<0.001	1.52	1.45, 1.60	<0.001
0-9.99%	15.73	15.10, 16.39	Ref			Ref		
CD4 ⁺ cell count <350 cells/ μ l at time of initial VL in analysis								
Yes	32.80	31.84, 33.78	2.01	1.91, 2.12	<0.001	1.15	1.10, 1.20	<0.001
No	16.28	15.63, 16.96	Ref			Ref		
Age at time of initial VL in analysis (years)								
16-39	32.12	30.93, 33.36	1.95	1.83, 2.08	<0.001	1.38	1.30, 1.46	<0.001
40-49	22.77	21.85, 23.74	1.38	1.30, 1.48	<0.001	1.18	1.12, 1.25	<0.001
50-85	16.47	15.66, 17.32	Ref			Ref		
Race/ethnicity								
Black	26.08	25.34, 26.85	1.63	1.50, 1.76	<0.001	1.24	1.16, 1.32	<0.001
Hispanic	19.65	18.44, 20.93	1.22	1.11, 1.35	<0.001	0.98	0.90, 1.06	0.610
Other	12.39	9.27, 16.57	0.77	0.57, 1.04	0.092	0.72	0.55, 0.93	0.011
White	16.04	14.88, 17.31	Ref			Ref		
Sex/sexual orientation								
MSM	20.09	19.14, 21.08	0.85	0.80, 0.91	<0.001	0.94	0.89, 0.99	0.024
Women	25.09	24.10, 26.13	1.06	1.00, 1.13	0.044	1.01	0.97, 1.06	0.588

Subgroups	% Of observation time VL above 1500 copies/ml	95% CI	Unadjusted rate ratio	95% CI	P	Adjusted rate ratio	95% CI	P
Heterosexual men	23.64	22.67, 24.65	Ref			Ref		
Injection drug use as exposure for acquiring HIV infection ^a								
Yes	25.63	24.04, 27.33	1.13	1.05, 1.21	0.0006	1.21	1.15, 1.29	<0.001
No	22.69	22.08, 23.31	Ref			Ref		
Health insurance at time of initial VL in analysis								
Medicare	16.13	14.95, 17.41	1.23	1.10, 1.39	<0.0001	1.29	1.17, 1.43	<0.001
Medicaid	25.47	24.29, 26.70	1.95	1.77, 2.15	<0.0001	1.40	1.28, 1.54	<0.001
Ryan White/Charity	28.44	27.52, 29.39	2.18	1.98, 2.39	<0.0001	1.33	1.22, 1.45	<0.001
Private	13.06	11.98, 14.24	Ref			Ref		
Clinic								
A	18.84	16.96, 20.94	1.30	1.11, 1.52	0.0010	1.36	1.20, 1.54	<0.001
B	21.51	20.30, 22.79	1.48	1.30, 1.69	<0.0001	1.16	1.05, 1.29	0.004
C	26.84	25.38, 28.38	1.85	1.63, 2.11	<0.0001	1.42	1.28, 1.58	<0.001
D	16.34	15.05, 17.73	1.13	0.98, 1.30	0.0967	0.99	0.88, 1.12	0.885
E	27.83	26.81, 28.90	1.92	1.70, 2.17	<0.0001	1.28	1.16, 1.42	<0.001
F	14.49	12.91, 16.26	Ref			Ref		

CI, confidence interval; VL, viral load.

^aThis variable does not reflect current injection drug use.

Table 3

Percentage of person-time with viral load above 1500 copies/ml among HIV patients in the supplemental (trial) analysis, by strata.

Subgroups (N)	% Of observation time VL above 1500 copies/ml	95% CI	Unadjusted rate ratio	95% CI	P	Adjusted rate ratio	95% CI	P
Overall (1779)	26.28	24.75, 27.90						
ART status								
Not on ART before enrollment or during next 12 months (112)	57.59	50.00, 66.38	2.69	2.29, 3.16	<0.001	2.70	2.28, 3.21	<0.001
Not on ART before enrollment, started in next 12 months (263)	45.37	41.42, 49.70	2.12	1.88, 2.39	<0.001	2.09	1.83, 2.38	<0.001
On ART prior to enrollment (1404)	21.40	19.85, 23.07	Ref			Ref		
Patient type								
New patients ^a (478)	34.22	30.96, 37.81	1.40	1.24, 1.58	<0.001	0.98	0.86, 1.12	0.802
Established patients (1301)	24.46	22.77, 26.28	Ref			Ref		
Clinic								
A (297)	23.20	19.89, 27.06	1.15	0.90, 1.46	0.259	1.23	0.98, 1.54	0.076
B (296)	27.08	23.45, 31.27	1.34	1.06, 1.69	0.014	1.20	0.98, 1.48	0.077
C (285)	23.67	20.22, 27.71	1.17	0.92, 1.49	0.199	1.29	1.03, 1.62	0.029
D (295)	28.78	25.19, 32.88	1.42	1.14, 1.79	0.002	1.36	1.10, 1.67	0.005
E (317)	35.22	31.30, 39.64	1.74	1.40, 2.17	<0.001	1.68	1.37, 2.05	<0.001
F (289)	20.21	16.83, 24.27	Ref			Ref		
Intervention arm								
Enhanced contact + skills ^b (590)	27.93	25.29, 30.83	1.12	0.97, 1.30	0.114	1.14	0.98, 1.30	0.071
Enhanced contact ^b (597)	26.10	23.48, 29.01	1.05	0.90, 1.22	0.516	1.04	0.90, 1.20	0.582
Standard of care (592)	24.84	22.34, 27.62	Ref			Ref		

ART, antiretroviral therapy; CI, confidence interval; VL, viral load.

^aFirst or second visit to the clinic or re-engaging after 3-year lapse.

^bSee Gardner *et al.* [10] for details of the intervention.