Single Viral Load Measurements Overestimate Stable Viral Suppression Among HIV Patients in Care: Clinical and Public Health Implications

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Background: The HIV continuum of care paradigm uses a single viral load test per patient to estimate the prevalence of viral suppression. We compared this single-value approach with approaches that used multiple viral load tests to examine the stability of suppression.

Methods: The retrospective analysis included HIV patients who had at least 2 viral load tests during a 12-month observation period. We assessed the (1) percent with suppressed viral load (<200 copies/mL) based on a single test during observation, (2) percent with suppressed viral loads on all tests during observation, (3) percent who maintained viral suppression among patients whose first observed viral load was suppressed, and (4) change in viral suppression status comparing first with last measurement occasions. Prevalence ratios compared demographic and clinical subgroups.

Results: Of 10,942 patients, 78.5% had a suppressed viral load based on a single test, whereas 65.9% were virally suppressed on all tests during observation. Of patients whose first observed viral load was suppressed, 87.5% were suppressed on all subsequent tests in the next 12 months. More patients exhibited improving status (13.3% went from unsuppressed to suppressed) than worsening status (5.6% went from suppressed to unsuppressed). Stable suppression was less likely among women, younger patients, black patients, those recently diagnosed with HIV, and those who missed ≥1 scheduled clinic visits.

Conclusions: Using single viral load measurements overestimated the percent of HIV patients with stable suppressed viral load by 16% (relative difference). Targeted clinical interventions are needed to increase the percent of patients with stable suppression.

Key Words: HIV, viral suppression, viral load, care

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INTRODUCTION

The HIV continuum of care paradigm includes parameters on the diagnosis, care, and health status of HIV-infected persons. The continuum begins with the estimated number of people living with HIV infection, followed by the number of infected persons who are diagnosed, linked to care, retained in care, prescribed antiretroviral therapy (ART), and virally suppressed.[1] Viral suppression, a key end point, has been defined in recent surveillance and continuum of care analyses[2–6] as HIV RNA less than 200 copies per milliliter; this threshold is also a key indicator for monitoring the progress of the US National HIV/AIDS strategy.[7]

In the care continuum paradigm, estimates of the percentage of HIV-infected persons with suppressed plasma viremia are typically based on a single viral load test result per patient in care, usually the latest test in the past 12 months. Using this single-value approach, national surveillance data collected in 2011[2] and 2012[4] indicated that 30% of the estimated 1.2 million people living with HIV infection in the United States were virally suppressed (<200 copies/mL).

However, rates of suppression were higher when focusing on HIV-diagnosed persons engaged in care. Among HIV patients who had evidence of a care visit between January and April of the respective year, their latest viral load result indicated that 75.6% were virally suppressed in 2011[2] and 77.3% in 2012.[4] Large clinical cohort studies,[6,8,9] and many state and city health departments that monitor continuum of care parameters locally have also used the single-value method to estimate the prevalence of viral suppression on a population level.

The results of a single test may not accurately reflect the dynamic nature of HIV viral load suppression or the extent to which a patient is stably suppressed across time. Because viral load is such a pivotal variable for epidemiologic assessment, patient care, and transmission risk, it would be informative to compare the single-value method against methods that use multiple test results per patient to estimate the percentage who have stable suppressed viral load in a clinic population. Herein, we compared these different methods for characterizing viral suppression among patients engaged in care and examined clinical and demographic subgroup differences in the outcomes.

METHODS

Adult HIV patients in this analysis received medical care between June 30, 2012 and December 31, 2013 at 6 academically affiliated HIV clinics located in Birmingham, Boston, Houston, Miami, San Diego, and Seattle. The analytic cohort comprised patients who had at least 1 viral load test at these clinics during a 6-month window from June 30, 2012 to December 31, 2012 and at least 1 subsequent viral load test within 12 months of their cohort entry date, which was the date of the first viral load result during the 6-month window. Each cohort member was observed for 12 months from entry, during which time all available viral loads at the clinics, including the entry viral load, were captured for analysis. Patients were identified by unique study codes generated at the clinics. Institutional review board approval was obtained at each participating site.

This cohort of patients with 2 or more viral load tests served as a common denominator for the single-value and multiple-values methods. Following the procedures used by other investigators[2–4] and US National HIV/AIDS strategy,[7] in the single-value method, we selected a patient's latest viral load in the 12-month follow-up period (ie, the viral load closest to the 12-month end date) and coded it as suppressed ($<$200 copies/mL) or not. In a sensitivity analysis, we repeated the single-value method selecting, instead, the patient's earliest viral load in the 12-month period (ie, the patient's entry viral load).

In the multiple-values method, we calculated the following end points: (1) Stability of viral suppression using 3 mutually exclusive and exhaustive categories: (a) all viral load results for a patient were less than 200 copies per milliliter during the 12 months of observation (ie, patients with stable suppression); (b) some but not all viral load results were suppressed; and (c) no suppressed results. (2) Maintenance of viral suppression using as the denominator only those patients whose cohort entry viral load was suppressed and calculating the percentage of those patients who had all subsequent viral loads suppressed during observation. (3) Change in viral suppression status using a matched-pairs method that included only a patient's first and last viral load test results during the observation period. This matched-pairs approach generated 4 groups: (a) first and last viral loads were suppressed, (b) first and last unsuppressed, (c) first unsuppressed and last suppressed, and (d) first suppressed and last unsuppressed. We were particularly interested in determining the percentage of the cohort patients who were in the 2 discordant viral suppression groups ("c" and "d") and estimating the matched-pair (McNemar) odds ratio of group "c" (percent of patients who exhibited improved viral suppression status) relative to group "d" (percent of patients who exhibited worsening viral suppression status).

Chi-square tests examined demographic and clinical correlates of patients who had suppressed viral loads on all, some, or none of their tests. The stratification variables, obtained from the electronic medical records of the clinics, included sex, age, race/ethnicity, HIV acquisition (exposure) risk category, time since testing HIV positive, number of viral load records in the observation period, number of scheduled HIV primary care visits missed (no-show without prior cancellation) during observation, CD4 cell count at the time of entry in cohort, and clinic site.

Univariate and multivariable prevalence ratios (PR) and 95% confidence intervals derived from Poisson regression models (with robust standard errors), compared patient subgroups on the following 3 binary outcomes: (1) Stable suppression among all patients in the cohort (1 = all viral load results suppressed; 0 = not all suppressed). (2) Maintenance of suppression among the subgroup of patients whose cohort entry viral load was suppressed (1 = all subsequent viral loads suppressed; 0 = not all subsequent results suppressed). (3) Change in viral suppression status from first to last measurement occasions among patients with discordant viral suppression status (groups "c" and "d"), where patients exhibiting improvement (going from unsuppressed to suppressed) were coded 1 and patients with worsening status (going from suppressed to unsuppressed) were coded 0. All analyses were conducted with SAS (version 9.3; SAS Institute, Cary, NC).

RESULTS

A total of 12,202 patients from the 6 clinics had a viral load test during the 6-month entry window. Ten percent (n = 1260) of whom had only 1 viral load test during this window and no subsequent viral load tests in the next 12 months at these clinics and, thus, were excluded from the analytic cohort because there was no opportunity to examine the stability of viral suppression across time. Of these excluded patients, 62.9% (792 of 1260) of their single viral load results were less than 200 copies per milliliter.

The analytic cohort included 10,942 patients; of whom, 72.2% were male, 34.6% white, 38.8% black, and 23.5% Hispanic. Median age was 51 years (18–91 years) at the time of entry into the cohort. The main risk factor for acquiring HIV infection was male-to-male sexual exposure in 40.2% and heterosexual exposure in 42.2%.

Cohort patients had a median of 4 [interquartile range (IQR), 3–5] viral load results, including the entry viral load, during the 12 months of observation. There was a median of 200 days (IQR, 123–280 days) between the first and last viral load tests. The HIV RNA assays had a lower limit of detection of 20 copies per milliliter at each participating clinic. The median entry viral load was 48 copies per milliliter (IQR, 20–186 copies/mL) in the 10,942 cohort members, 14,321 copies per milliliter (IQR 1290–76,661 copies/mL) among the subgroup of 2704 patients whose entry value was not suppressed (≥200 copies/mL), and 40 copies per milliliter (IQR, 20–48 copies/mL) among the 8238 patients whose entry value was suppressed (<200 copies/mL).

Prevalence of Viral Load Suppression

Table 1 displays the findings on the prevalence of viral suppression among cohort patients according to the method of assessment. In the single-value method, 83.0% of cohort members had a suppressed viral load on their latest test during the 12 months of observation. In the sensitivity analysis, 75.3% of cohort members were virally suppressed on their first (entry) viral load test. When we include the 1260 patients who were omitted from the cohort because they only had an entry viral load and no subsequent tests during observation, then 74.0% had a suppressed viral load at entry.

In the multiple-values method, 65.9% of cohort members had a suppressed viral load on all test results during observation, with an additional 24.9% having suppressed viral load on some but not all tests (among patients in this latter group, an average of 54.7% of viral load tests were suppressed) and 9.3% not having any suppressed viral load results during observation. Turning to the outcome on maintenance of viral suppression, among patients whose cohort entry viral load was suppressed (n = 8238), 87.5% had suppressed viral loads on all subsequent tests. Finally, in the matched-pairs analysis of change in viral suppression status from first to last measurement occasions, we found that a significantly larger percentage of patients exhibited improvement in viral suppression status (13.3% of the cohort went from unsuppressed to suppressed) compared with the percentage who exhibited worsening viral suppression status (5.6% went from suppressed to unsuppressed; McNemar's odds ratio, 2.37; 95% confidence intervals, 2.15 to 2.61).

TABLE 1. Percentage of Patients With Suppressed Viral Load According to Method of Measurement, 2012–2013*

Method of Measurement During 12-Month Observation Period	% (n/N)
Single-value method	
% patients who had suppressed viral load on their latest assessment during observation	83.0 (9083/10,942)
% patients who had suppressed viral load on their first (entry) assessment during observation	75.3 (8238/10,942)
Using all viral loads during observation	
% patients who had all viral loads suppressed (stable suppression)	65.9 (7206/10,942)
% who had some, but not all, viral loads suppressed	24.9 (2722/10,942)
% who had no viral loads suppressed	9.3 (1014/10,942)
Maintenance of suppressed viral load	
Among patients whose cohort entry viral load was suppressed, % who had all subsequent viral loads suppressed during observation	87.5 (7206/8238)
Change in status from first to last viral load during observation	
First suppressed/last suppressed	69.7 (7628/10,942)
First unsuppressed/last unsuppressed	11.4 (1249/10,942)
First unsuppressed/last suppressed	13.3 (1455/10,942)
First suppressed/last unsuppressed	5.6 (610/10,942)

*Cohort patients had at least 2 viral load records during 12 months of observation. There were 69 patients in the cohort who were transgender. These 69 patients were included in the denominators of the outcomes reported in this table.

Viral Suppression by Demographic and Clinical Subgroups

Table 2 displays the percentage of patients who were virally suppressed on all, some, or none of their viral load tests during the observation period, by demographic and clinical subgroups. Each stratification variable was significantly associated with this 3-category outcome measure. Table 3 pinpoints subgroup differences in the percentage of patients who had suppressed viral load on all tests (stable suppression) versus less than all tests suppressed (the "some" and "none" groups combined). The multivariable model, which included all of the variables listed in Table 3, showed that the proportion of patients with stable viral suppression was higher among males (vs. females), patients aged 40 years and older (vs. 18–39 years), patients of Hispanic or "other" race/ethnicity (vs. white), those who had a CD4 count of ≥ 200 cells per microliter at the time they entered the cohort (vs. <200 cells/μL), and those who had been diagnosed with HIV infection 3 months or more before entry (vs. <3 months before entering cohort). Stable viral suppression was proportionally lower among patients of black race (vs. white), patients whose HIV acquisition risk was men who have sex with men (MSM) and were injection drug users (IDU) (vs. heterosexual risk), and patients who had 4 or more viral load tests (vs. 2 tests) during the 12-month observation period. Stable viral suppression was also proportionally lower among patients who had missed 1 or more scheduled HIV primary care visits during observation (vs. no missed visits); the PRs declined with increasing number of missed visits. Finally, the PRs varied by clinic site; 5 clinics had higher PRs compared with the referent clinic (selected solely because it had the lowest prevalence of stable viral suppression among the 6 clinics).

Table 4 displays the findings for the (1) maintenance of viral suppression (among patients whose cohort entry viral load was suppressed) and (2) improvement in viral suppression status (among patients who had discordant viral suppression status on first and last measurement occasions). In the multivariable analysis, maintenance of suppression was proportionally higher among patients aged 40 years and older (vs. 18–39 years), Hispanic patients (vs. white), and patients whose cohort entry CD4 count was ≥200 cells per microliter (vs. <200 cells/μL), and lower among patients who had 3 or

TABLE 2. Percentage of Patients Who Had All, Some, or No Viral Loads Suppressed During 12 Months of Observation, by Demographic and Clinical Subgroups, 2012–2013*

Subgroups	All Viral Load Results Suppressed, % (n)	Some Viral Load Results Suppressed, % (n)	No Viral Load Results Suppressed, % (n)	χ^2 Result (*P*)
Sex†				
Female (n = 2973)	60.7 (1805)	27.9 (831)	11.3 (337)	49.27 (<0.001)
Male (n = 7896)	67.8 (5350)	23.7 (1873)	8.5 (673)	
Age at the time of entry in cohort, yr				
18–39 (n = 2147)	52.2 (1120)	32.6 (699)	15.3 (328)	286.83 (<0.001)
40–49 (n = 2830)	64.8 (1834)	24.8 (702)	10.4 (294)	
50–91 (n = 5894)	71.3 (4201)	22.1 (1304)	6.6 (389)	
Race/ethnicity				
White non-Hispanic (n = 3766)	68.3 (2571)	24.4 (918)	7.4 (277)	113.35 (<0.001)
Black non-Hispanic (n = 4229)	61.1 (2584)	26.2 (1109)	12.7 (536)	
Hispanic (n = 2537)	69.0 (1751)	23.9 (606)	7.1 (180)	
Other (n = 291)	71.5 (208)	23.0 (67)	5.5 (16)	
HIV acquisition (exposure) risk category				
Heterosexual (n = 4611)	62.5 (2881)	26.9 (1242)	10.6 (488)	
MSM (n = 4355)	70.6 (3077)	22.0 (959)	7.3 (319)	79.60 (<0.001)
MSM + IDU (n = 614)	64.0 (393)	25.4 (156)	10.6 (65)	
IDU (n = 591)	62.1 (367)	28.1 (166)	9.8 (58)	
Undetermined/unknown/other/ missing (n = 702)‡	62.4 (438)	25.9 (182)	11.7 (82)	
Recency of testing HIV positive (from the time of entry viral load), mo				
<3 (n = 1042)	45.4 (473)	41.1 (428)	13.5 (141)	
3–12 (n = 382)	47.1 (180)	39.5 (151)	13.4 (51)	287.78 (<0.001)
13–24 (n = 516)	71.5 (369)	20.2 (104)	8.3 (43)	
25–48 (n = 1053)	66.1 (696)	23.5 (248)	10.4 (109)	
49+ (n = 7880)	69.0 (5438)	22.5 (1774)	8.5 (668)	
No. viral load results during observation				
2 (n = 2723)	71.8 (1954)	13.4 (365)	14.8 (404)	
3 (n = 3765)	73.9 (2782)	18.5 (697)	7.6 (286)	913.16 (<0.001)
4 (n = 2646)	65.0 (1720)	28.5 (755)	6.5 (171)	
5 (n = 1019)	47.4 (483)	43.8 (446)	8.8 (90)	
6–10 (n = 720)	30.1 (217)	61.4 (442)	8.5 (61)	
Missed scheduled HIV primary care visit§				
0 (n = 7642)	71.5 (5461)	21.5 (1644)	7.0 (537)	
1 (n = 2517)	56.2 (1415)	30.3 (763)	13.5 (339)	438.32 (<0.001)
2 (n = 591)	42.5 (251)	38.8 (229)	18.8 (111)	
3+ (n = 123)	23.6 (29)	56.1 (69)	20.3 (25)	
CD4 count at the time of entry in cohort, cells/μL				
<200 (n = 1448)	29.3 (424)	44.3 (641)	26.4 (383)	1297.34 (<0.001)
200–500 (n = 4208)	62.9 (2649)	27.9 (1176)	9.1 (383)	
>500 (n = 5216)	78.3 (4083)	17.0 (888)	4.7 (245)	
Clinic				
A (n = 1333)	53.1 (708)	38.6 (514)	8.3 (111)	
B (n = 1096)	70.4 (771)	22.3 (244)	7.4 (81)	
C (n = 2064)	73.0 (1507)	20.2 (416)	6.8 (141)	337.75 (<0.001)
D (n = 1607)	74.1 (1190)	18.9 (304)	7.0 (113)	
E (n = 1108)	71.9 (797)	20.1 (223)	7.9 (88)	
F (n = 3665)	59.6 (2183)	27.4 (1004)	13.0 (478)	

Some variables have a few cases of missing data.

*Cohort patients had at least 2 viral load tests during 12 months of observation.

†The 69 transgender patients were not included as a separate subgroup because of small numbers, and they were not included in the denominators of the other stratification variables in this table.

‡The HIV acquisition (exposure) variable included 170 cases of missing data.

§No-show without prior cancellation during 12-month observation period.

TABLE 3. PRs of Subgroup Differences in Patients Who Had All (vs. Less Than All) Viral Loads Suppressed During 12 Months of Observation, 2012–2013*

Subgroups	Univariate PR and 95% Confidence Interval	Multivariable† PR and 95% Confidence Interval
Sex‡		
Female	Ref	Ref
Male	1.12 (1.08 to 1.15)§	1.05 (1.02 to 1.09)§
Age at the time of entry in cohort, yr		
18–39	Ref	Ref
40–49	1.24 (1.18 to 1.30)§	1.22 (1.17 to 1.28)§
50–91	1.36 (1.31 to 1.43)§	1.35 (1.29 to 1.40)§
Race/ethnicity		
White non-Hispanic	Ref	Ref
Black non-Hispanic	0.89 (0.86 to 0.92)§	0.96 (0.93 to 0.99)‖
Hispanic	1.01 (0.97 to 1.05)	1.12 (1.08 to 1.15)§
Other	1.04 (0.97 to 1.13)	1.07 (1.01 to 1.15)‖
HIV acquisition (exposure) risk category		
Heterosexual	Ref	Ref
MSM	1.13 (1.09 to 1.16)§	0.98 (0.95 to 1.02)
MSM + IDU	1.02 (0.96 to 1.09)	0.88 (0.83 to 0.94)§
IDU	0.99 (0.93 to 1.06)	0.95 (0.90 to 1.01)
Undetermined/ unknown/other/ missing¶	0.99 (0.94 to 1.06)	1.03 (0.97 to 1.10)
Recency of testing HIV positive (from the time of entry viral load), mo		
<3	Ref	Ref
3–12	1.04 (0.92 to 1.18)	1.18 (1.04 to 1.33)§
13–24	1.57 (1.45 to 1.72)§	1.59 (1.47 to 1.73)§
25–48	1.46 (1.35 to 1.58)§	1.44 (1.34 to 1.56)§
49+	1.52 (1.42 to 1.63)§	1.38 (1.29 to 1.47)§
No. viral load results during observation		
2	Ref	Ref
3	1.03 (0.99 to 1.06)	1.02 (0.99 to 1.05)
4	0.91 (0.87 to 0.94)§	0.93 (0.90 to 0.97)§
5	0.66 (0.62 to 0.71)§	0.76 (0.71 to 0.81)§
6–10	0.42 (0.37 to 0.47)§	0.55 (0.49 to 0.61)§
Missed scheduled HIV primary care visit#		
0	Ref	Ref
1	0.78 (0.76 to 0.82)§	0.85 (0.82 to 0.88)§
2	0.59 (0.54 to 0.65)§	0.70 (0.65 to 0.77)§
3+	0.33 (0.24 to 0.45)§	0.48 (0.36 to 0.65)§
CD4 count at the time of entry in cohort, (cells/μL)		
<200	Ref	Ref
200–500	2.15 (1.98 to 2.33)§	1.89 (1.74 to 2.04)§
>500	2.67 (2.46 to 2.89)§	2.26 (2.10 to 2.45)§
Clinic		
A	Ref	Ref
B	1.32 (1.24 to 1.41)§	1.42 (1.33 to 1.51)§
C	1.37 (1.29 to 1.45)§	1.27 (1.20 to 1.35)§
D	1.39 (1.31 to 1.47)§	1.43 (1.35 to 1.51)§
E	1.35 (1.27 to 1.44)§	1.28 (1.21 to 1.36)§
F	1.12 (1.06 to 1.18)§	1.11 (1.05 to 1.18)§

*Cohort patients had at least 2 viral load tests during 12 months of observation.
†The multivariable model (n = 10,820) included all variables listed in the table.
‡The 69 transgender patients were not included as a separate subgroup because of small numbers, and they were not included in the denominators of the other stratification variables in this table.
§$P < 0.01$.
‖$P < 0.05$.
¶The HIV acquisition (exposure) variable included 170 cases of missing data.
#No-show without prior cancellation during 12-month observation period.

more viral load tests (vs. 2 tests) during the observation period and patients who missed 1 or more scheduled HIV primary care visits during that period (vs. no missed visits). Comparison by clinic site showed that 5 of the 6 clinics had similar PRs, each significantly higher than the referent clinic. Turning to the multivariable analysis of improvement (vs. worsening) in viral suppression status, improvement was proportionally higher among patients in the MSM + IDU risk group (vs. heterosexual risk) and patients who had 4 or more viral load tests (vs. 2 tests) during the observation period, and lower among patients who had been diagnosed with HIV infection more than 12 months before entering the cohort (vs. < 3 months prior) and those whose cohort entry CD4 was ≥200 cells per microliter (vs. <200 cells/μL). Finally, there were significant differences by clinic.

DISCUSSION

The continuum of care paradigm has become a powerful public health and policy tool to monitor the US HIV epidemic and evaluate successive steps from HIV diagnosis, to entry into care, and achievement of viral suppression. The continuum provides a snapshot at a moment in time, basing estimates of the prevalence of viral suppression on a single viral load test result per patient, even though most HIV patients engaged in medical care have multiple viral load tests. Estimates based on a single viral load result may fail to capture the dynamic nature of viral load control across time and, thus, may not reflect the extent to which patients are stably suppressed. Our findings clearly support this perspective.

Based on the single-value method, we found that 75.3% of cohort members were suppressed on their first (entry) viral load test; this percentage decreased slightly to 74.0% when we included the 1260 noncohort members who only had an entry viral load and no other viral load tests in the subsequent 12 months. A total of 83.0% of cohort members were suppressed on their latest test during observation. Although we do not have any direct data, part of this increase in

TABLE 4. PRs of Subgroup Differences in Patients Who Exhibited Maintenance of Viral Suppression and Improvement in Viral Suppression Status During 12 Months of Observation, 2012–2013*

	Maintenance of Viral Suppression†			Improvement in Viral Suppression Status‡		
Subgroups	**% (n/N)**	**Univariate PR and 95% CI**	**Multivariable§ PR and 95% CI**	**% (n/N)**	**Univariate PR and 95% CI**	**Multivariable§ PR and 95% CI**
Sex‖						
Female	84.8 (1805/2128)	Ref	Ref	68.9 (422/612)	Ref	Ref
Male	88.4 (5350/6054)	1.04 (1.02 to 1.06)¶	1.00 (0.98 to 1.03)	70.9 (1022/1441)	1.03 (0.96 to 1.09)	0.96 (0.89 to 1.03)
Age at the time of entry in cohort, yr						
18–39	84.6 (1129/1334)	Ref	Ref	74.1 (421/568)	Ref	Ref
40–49	87.3 (1847/2115)	1.03 (1.00 to 1.06)	1.04 (1.02 to 1.08)¶	70.4 (385/547)	0.95 (0.88 to 1.06)	0.99 (0.93 to 1.07)
50–91	88.3 (4179/4734)	1.04 (1.01 to 1.07)¶	1.08 (1.05 to 1.11)¶	68.0 (638/938)	0.92 (0.86 to 0.98)#	1.00 (0.94 to 1.07)
Race/ethnicity						
White non-Hispanic	87.3 (2571/2945)	Ref	Ref	68.0 (470/691)	Ref	Ref
Black non-Hispanic	86.3 (2584/2993)	0.98 (0.96 to 1.00)	0.98 (0.96 to 1.01)	71.0 (589/829)	1.04 (0.98 to 1.12)	0.96 (0.89 to 1.03)
Hispanic	88.9 (1751/1969)	1.02 (0.99 to 1.04)	1.05 (1.02 to 1.07)¶	72.4 (343/474)	1.06 (0.99 to 1.15)	0.97 (0.89 to 1.04)
Other	89.3 (208/233)	1.02 (0.97 to 1.07)	1.00 (0.96 to 1.05)	70.9 (39/55)	1.04 (0.87 to 1.24)	0.88 (0.75 to 1.04)
HIV acquisition (exposure) risk category						
Heterosexual	85.6 (2881/3366)	Ref	Ref	68.9 (634/920)	Ref	Ref
MSM	89.5 (3077/3439)	1.04 (1.02 to 1.06)¶	1.00 (0.97 to 1.02)	71.1 (535/752)	1.03 (0.97 to 1.10)	1.03 (0.96 to 1.11)
MSM + IDU	89.9 (393/437)	1.05 (1.01 to 1.08)¶	0.99 (0.95 to 1.03)	79.7 (98/123)	1.15 (1.05 to 1.27)¶	1.14 (1.02 to 1.27)#
IDU	84.9 (367/432)	0.99 (0.95 to 1.03)	0.98 (0.94 to 1.02)	65.8 (81/123)	0.95 (0.83 to 1.09)	0.96 (0.84 to 1.09)
Undetermined/unknown/other/missing**	85.9 (438/510)	1.00 (0.96 to 1.04)	0.97 (0.93 to 1.01)	71.1 (96/135)	1.03 (0.92 to 1.16)	0.95 (0.84 to 1.06)
Recency of testing HIV positive (from the time of entry viral load), mo						
<3	88.3 (473/536)	Ref	Ref	89.5 (325/363)	Ref	Ref
3–12	88.2 (180/204)	0.99 (0.94 to 1.06)	1.03 (0.96 to 1.09)	89.4 (110/123)	0.99 (0.93 to 1.07)	0.99 (0.92 to 1.07)
13–24	90.2 (369/409)	1.02 (0.97 to 1.07)	1.03 (0.98 to 1.08)	69.8 (60/86)	0.78 (0.67 to 0.90)¶	0.81 (0.71 to 0.94)¶
25–48	88.6 (696/786)	1.00 (0.96 to 1.04)	1.00 (0.96 to 1.05)	69.8 (134/192)	0.78 (0.70 to 0.86)¶	0.86 (0.79 to 0.95)¶
49+	87.0 (5438/6249)	0.98 (0.95 to 1.02)	0.97 (0.93 to 1.00)	63.2 (815/1289)	0.70 (0.67 to 0.74)¶	0.76 (0.72 to 0.81)¶
No. viral load results during observation						
2	92.3 (1954/2116)	Ref	Ref	55.6 (203/365)	Ref	Ref
3	90.0 (2782/3091)	0.97 (0.96 to 0.99)¶	0.97 (0.96 to 0.99)¶	62.2 (330/531)	1.11 (0.99 to 1.26)#	1.10 (0.99 to 1.23)
4	85.2 (1720/2019)	0.92 (0.90 to 0.94)¶	0.93 (0.91 to 0.95)¶	73.4 (398/542)	1.32 (1.19 to 1.46)¶	1.26 (1.14 to 1.39)¶
5	76.6 (483/631)	0.83 (0.79 to 0.87)¶	0.84 (0.81 to 0.88)¶	82.2 (249/303)	1.48 (1.33 to 1.64)¶	1.33 (1.20 to 1.48)¶
6-10	66.4 (217/327)	0.72 (0.66 to 0.78)¶	0.77 (0.71 to 0.83)¶	84.6 (264/312)	1.52 (1.37 to 1.69)¶	1.36 (1.22 to 1.50)¶
Missed scheduled HIV primary care visit††						
0	89.9 (5461/6069)	Ref	Ref	72.4 (922/1274)	Ref	Ref
1	81.9 (1415/1728)	0.91 (0.88 to 0.93)¶	0.93 (0.91 to 0.95)¶	66.4 (384/578)	0.92 (0.85 to 0.98)#	0.96 (0.90 to 1.02)
2	75.8 (251/331)	0.84 (0.79 to 0.93)¶	0.88 (0.83 to 0.94)¶	69.2 (110/159)	0.96 (0.86 to 1.06)	0.96 (0.87 to 1.07)
3+	51.8 (29/56)	0.57 (0.45 to 0.74)¶	0.65 (0.51 to 0.84)¶	66.7 (28/42)	0.92 (0.74 to 1.14)	0.86 (0.70 to 1.05)
CD4 count at the time of entry in cohort, cells/μL						
<200	79.1 (424/536)	Ref	Ref	85.9 (429/499)	Ref	Ref
200–500	86.2 (2649/3073)	1.09 (1.04 to 1.14)¶	1.07 (1.03 to 1.12)¶	72.1 (662/918)	0.83 (0.79 to 0.88)¶	0.86 (0.82 to 0.91)¶
>500	89.3 (4083/4575)	1.13 (1.08 to 1.18)¶	1.11 (1.06 to 1.16)¶	55.5 (353/636)	0.64 (0.59 to 0.69)¶	0.69 (0.64 to 0.75)¶
Clinic						
A	74.4 (708/952)	Ref	Ref	56.8 (218/384)	Ref	Ref
B	89.3 (771/863)	1.20 (1.15 to 1.25)¶	1.21 (1.16 to 1.27)¶	71.6 (116/162)	1.26 (1.11 to 1.43)¶	1.16 (1.01 to 1.33)#
C	90.6 (1507/1663)	1.21 (1.17 to 1.27)¶	1.18 (1.14 to 1.23)¶	71.6 (237/331)	1.26 (1.13 to 1.41)¶	1.17 (1.04 to 1.31)¶
D	92.6 (1190/1285)	1.25 (1.20 to 1.30)¶	1.23 (1.18 to 1.28)¶	77.8 (189/243)	1.37 (1.22 to 1.53)¶	1.19 (1.05 to 1.33)¶

TABLE 4. (*Continued*) PRs of Subgroup Differences in Patients Who Exhibited Maintenance of Viral Suppression and Improvement in Viral Suppression Status During 12 Months of Observation, 2012–2013*

	Maintenance of Viral Suppression†			Improvement in Viral Suppression Status‡		
Subgroups	% (n/N)	Univariate PR and 95% CI	Multivariable§ PR and 95% CI	% (n/N)	Univariate PR and 95% CI	Multivariable§ PR and 95% CI
E	90.9 (797/876)	1.22 (1.17 to 1.28)¶	1.18 (1.13 to 1.24)¶	72.0 (121/168)	1.27 (1.11 to 1.44)¶	1.21 (1.06 to 1.38)¶
F	85.8 (2183/2545)	1.15 (1.10 to 1.20)¶	1.13 (1.08 to 1.18)¶	73.6 (563/765)	1.30 (1.17 to 1.43)¶	1.19 (1.07 to 1.32)¶

*Cohort patients had at least 2 viral load tests during 12 months of observation.

†The analysis of maintenance of viral suppression included only patients whose cohort entry viral load was suppressed. Maintenance = all subsequent viral loads suppressed (vs. not all subsequent results suppressed). n = 8139 for the adjusted model.

‡The analysis of improvement in viral load status comprised patients with discordant viral suppression status at the first and last measurement occasions. Improvers were patients whose first viral load was unsuppressed and the last was suppressed during observation, and patients with worsening status were those whose first viral load was suppressed and the last was unsuppressed. n = 2049 for the adjusted model.

§The multivariable model included all variables listed in the table.

‖The 69 transgender patients were not included as a separate subgroup because of small numbers, and they were not included in the denominators of the other stratification variables in this table.

¶$P < 0.01$.

#$P < 0.05$.

**The HIV acquisition (exposure) variable included 170 cases of missing data.

††No-show without prior cancellation during 12-month observation period.

percentage suppressed from entry to latest test may have stemmed from newly diagnosed patients entering the cohort, starting ART during observation, and thus contributing to an increase in the number of cohort patients with viral suppression on the latest test.

Based on the multiple-values method, we found that 65.9% of cohort members had a suppressed viral load on all of their tests during the 12 months of observation and, thus, were stably suppressed. Comparing this percentage against the conservative average of the 2 single-value findings above (74.0% + 83.0%/2 = 78.5%) indicates that there was a 16.1% relative reduction in the estimate of stable viral suppression when compared with the prevalence of viral suppression based on a single test. Each of these 2 operational definitions (prevalence at a single point in time and stability across time) has epidemiologic and clinical value. The different estimates generated by these 2 approaches are informative for understanding the magnitude of overestimation that may occur when using a single viral load test to infer the percentage of patients with stable viral suppression.

There were several encouraging findings. First, as mentioned above, nearly two-thirds of the cohort patients were stably virally suppressed across a 12-month interval. Second, 90.7% of the cohort patients had at least 1 viral load result that was suppressed; only 9.3% had no suppressed results during observation. Third, maintenance of viral suppression was quite high; once suppression was reached, 87.5% had suppressed viral loads on all subsequent tests in the next 12 months. Fourth, very few patients exhibited a worsening viral suppression status from first to last measurement occasions. In fact, over twice as many patients showed improving status (13.3% went from unsuppressed to suppressed) as worsening status (5.6% went from suppressed to unsuppressed).

The interpretation of these outcomes is informed by the analyses that stratified patients on clinical factors. One consistent picture that emerged was that patients who had missed HIV primary care visits (no-shows without prior cancellation) during the 12 months of observation were less likely to exhibit stable viral suppression, maintenance of suppression, or improvement in viral load status. This finding adds to a long line of studies demonstrating the importance of engagement in care in achieving positive viral suppression outcomes.[10–12] Other clinical variables were differentially associated with the outcomes, yet in understandable ways. For example, compared with patients with long-standing HIV diagnosis, newly diagnosed patients were less likely to exhibit stable viral suppression but more likely to exhibit improvement in viral suppression status from first to last measurement occasions. Most newly diagnosed patients entering care (and potentially entering our cohort) have relatively high viremia, thus not stably suppressed during 12 months of observation. But with clinical intervention and onset of ART, they may exhibit improvement in viral load status and achieve stable suppression in the future if they adhere to their treatment regimen. We were not able to confirm this explanation because we did not have patient-level data on ART onset, continued use, or adherence in the cohort data set.

The patients' CD4 cell-count category and the number of viral load tests performed also had differential associations with the outcomes. First, patients who were stably suppressed, and those who maintained suppression, were more likely than their counterparts to have had a CD4 count greater than 500 cells per microliter at the time they entered the cohort and fewer viral load tests during the observation period. Having fewer viral load tests is probably a consequence of having stable suppressed viral load and high CD4 cell count, thus less need for frequent viral monitoring. An ancillary analysis (data not shown) confirmed that patients with higher CD4 cell counts had fewer viral load tests conducted. Second, a different pattern was observed among patients who showed improvement in viral load status. Recall, the analysis of improvement was conducted among patients who had discordant viral load status on first and last measurement occasions during the 12 months of observation. Improvement (unsuppressed to suppressed) relative to

worsening status (suppressed to unsuppressed) was more likely among patients who had a CD4 count of <200 cells per microliter when they entered the cohort and among patients who had many viral load tests during the observation period. Here, the patients' lower CD4 cell count coupled with an unsuppressed viral load may have prompted more frequent viral monitoring and clinical intervention (eg, attempts to improve adherence to ART, change in therapeutic regimen), which increased the likelihood that patients improved their viral load status.

Several demographic differences were found in the viral suppression outcomes. Targeting resources and efforts to the following subgroups may decrease approximately one-third of HIV clinic patients who may not have stable suppressed viral load. Stable viral suppression and maintenance of suppression once achieved were less likely among female patients than among male patients and also less likely among younger patients (18–39 years vs. older) and patients of black race (vs. white) consistent with other studies.[13,14] There was a mixed picture for patients in the MSM or MSM + IDU acquisition risk groups. The MSM + IDU group was less likely to have stable suppression but more likely to exhibit maintenance of suppression compared with the heterosexual risk group. The MSM risk group was also more likely than the heterosexual risk group to exhibit maintenance. Finally, 1 clinic (the referent in the analysis) had a somewhat lower percentage of patients who reached the 3 viral suppression outcomes. This may have been due to system factors at this clinic, such as barriers stemming from preapproval requirements for access to medications, case management services that were administratively disconnected from medical care services, and no Medicaid expansion under the Affordable Care Act. In addition, unmeasured patient factors, such as employment, housing, mental health, and substance-use problems, may have contributed to clinic differences.

Our analysis is not without limitations. Not having patient-level ART data available in the cohort database, we could not document its role in our outcomes. However, as context for interpreting our findings on a clinic-wide level, approximately 90% of the patients at the participating clinics had been prescribed ART, comparable with national estimates.[2] Our analytic cohort consisted of patients who had 2 or more viral load tests during the 12 months of observation; thus, our findings on the stability of suppressed viral load, maintenance of suppression, and improvement in viral load status reflect patients who are, at least, minimally engaged in care. This inclusion criterion for selecting cohort members allowed for a longitudinal analysis of viral load patterns. Our study follow-up was limited to 12 months; the percentage of patients with stable suppression may potentially diminish with longer observation. Observation ended in December of 2013 because 3 of the clinics initiated an intervention in January of 2014 to help patients reduce their viral loads. The 6 clinics that participated in this analysis may not be representative of the national picture, thus our findings should be interpreted cautiously.

In conclusion, we found that using single viral load measurements overestimated the percent of HIV patients with stable suppressed viral load by 16% (relative difference). This finding has implications for strategic monitoring of public health programs aimed at increasing the number of HIV patients with viral suppression across time. Clinically, many of the patients in the cohort exhibited a very encouraging viral load profile, but still one-third of the patients did not have stable suppression during 12 months of observation. Targeting clinical interventions to subgroups less likely to achieve or maintain stable suppression may increase the percentage of patients with optimal viral suppression status.

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