Published in final edited form as:
JAMA. 2012 July 25; 308(4): 339–342. doi:10.1001/jama.2012.5927.

Sustained Viral Suppression in HIV-Infected Patients Receiving Antiretroviral Therapy

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To the Editor

Antiretroviral therapy (ART) can be used to reduce human immunodeficiency virus (HIV) transmission.[1] For this treatment-as-prevention strategy to be effective, patients must adhere to ART and suppress plasma HIV RNA (viral load). Among patients receiving ART, 77% have been estimated to achieve viral suppression based on last recorded viral load, which may not accurately represent a patient's complete viral load history.[2] We examined the change in and determinants of sustained viral suppression over time in HIV-infected adults receiving ART.

Methods

We retrospectively evaluated consecutive HIV-infected adults who initiated care at 12 high-volume HIV clinics that are part of the HIV Research Network (HIVRN) and provided complete data between 2001 and 2010. Clinics are located in the Northeastern (n = 6), Midwestern (n=1), Southern (n=2), and Western (n=3) sections of the United States and had a median panel size of 1598 patients in 2010. All patients were offered enrollment in the

Author Contributions: Dr Yehia had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Yehia, Gebo.
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Statistical analysis: Yehia, Fleishman.
Obtained funding: Moore, Gebo.
Administrative, technical, or material support: Moore, Gebo.
Study supervision: Metlay, Moore, Gebo.

Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Moore reported receiving or having grants pending with the National Institutes of Health, Pfizer, and Bristol-Meyers Squibb. Dr Gebo reported having served as a consultant, served on a scientific advisory board, and having received research funding from Tibotec. No other disclosures were reported.

Disclaimer: The views expressed in this article are those of the authors. No official endorsement by the Department of Health and Human Services, the National Institutes of Health, or the Agency for Healthcare Research and Quality is intended or should be inferred.

Additional Contributions: A list of the investigators from the HIV Research Network participating sites and data coordinating center are available at https://cds.johnshopkins.edu/hivrn/index.cfm?do=sens.content&page=contacts.html.

HIVRN, excluding 1-time consultations and incarcerated individuals; and 99% of patients participated. All clinics had institutional review board (IRB) approval; IRBs at some clinics required written informed consent, others waived the requirement because only existing deidentified data were collected. Data from patients' medical records were abstracted, quality assured, and assembled into a uniform database.

For patients receiving ART, we calculated the percentage who maintained viral loads of 400 copies/mL or lower throughout the entirety of each calendar year. Assays capable of detecting virus below 400 copies/mL were not in universal use at all clinics throughout the study period. Viral loads prior to and within the first 6 months after initial prescription of ART were not analyzed. We tested the association between patient sociodemographic characteristics and year receiving care using the χ^2 test of independence. Multivariate logistic regression was conducted to determine if the proportion of patients with sustained viral suppression changed over time, adjusting for sociodemographic characteristics. Because patients contributed data in multiple years, we used generalized estimating equations, clustered on patient, exchangeable working correlation, and robust standard errors to deal with the correlation across years for individual patients. Two-sided testing was used, with a *P* value of less than .05 considered significant. Statistical analyses were performed using Stata version 11.1 (StataCorp).

Results

A total of 32 483 patients received care at the 12 clinics between 2001 and 2010 (Table 1). The percentage of patients receiving ART with sustained viral suppression increased from 45% (95% CI, 43%–47%) in 2001 to 72% (71%–73%) in 2010.

In a linear time trend, the proportion of patients with sustained viral suppression significantly increased (unadjusted odds ratio, 1.14 [95% CI, 1.13–1.14] per year; adjusted odds ratio, 1.14 [95% CI, 1.14–1.15]). Sustained viral suppression was lower for blacks and injection drug users during all 10 years. Older individuals and those with private insurance were more likely to have sustained viral suppression compared with younger patients and those with Medicaid, Medicare, or who were uninsured (Table 2).

Comment

The proportion of patients receiving ART with sustained viral suppression increased over the past decade. New drugs and combination fixed-dose tablets have enhanced the efficacy, safety, and tolerability of regimens. Better access to care and adherence to treatment may also have contributed to improved virologic suppression. Despite these improvements, in 2008–2010, only 64% to 72% of patients receiving ART had suppressed viral loads throughout the year. Our results differ from prior studies, which documented viral suppression in 77% to 87% of patients during this same period and used median or last recorded value to measure viral load.[2–4]

Lower sustained viral suppression among younger patients, blacks, injection drug users, and those without private insurance may represent poor adherence to treatment, drug resistance, or drug intolerance or toxicity.[5,6]

This study is limited by its retrospective nature and inability to measure adherence to treatment. While our findings may not be generalizable to all HIV-infected patients receiving ART, they are relevant for HIV treatment-as-prevention programs because suboptimal viral suppression may lead to worse clinical outcomes and increased costs.

Acknowledgments

Funding/Support: This study was supported by grant 290-01-0012 from the Agency for Healthcare Research and Quality. Dr Metlay was supported by grant K24 AI073957 from the National Institutes of Health. Dr Moore was supported by grants K24 DA 00432, R01DA11602, and R01 AA 16893 from the National Institutes of Health.

Role of the Sponsors: The funding agencies had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

References

1. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011; 365(6):493–505. [PubMed: 21767103]
2. Centers for Disease Control and Prevention (CDC). Vital signs: HIV prevention through care and treatment—United States. MMWR Morb Mortal Wkly Rep. 2011; 60:1618–1623. [PubMed: 22129997]
3. Moore RD, Bartlett JG. Dramatic decline in the HIV-1 RNA level over calendar time in a large urban HIV practice. Clin Infect Dis. 2011; 53(6):600–604. [PubMed: 21844006]
4. Gill VS, Lima VD, Zhang W, et al. Improved virological outcomes in British Columbia concomitant with decreasing incidence of HIV type 1 drug resistance detection. Clin Infect Dis. 2010; 50(1):98–105. [PubMed: 19951169]
5. Department of Health and Human Services; Panel on Antiretroviral Guidelines for Adults and Adolescents. [Accessed March 30, 2012.] Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. http://www.aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-treatment-guidelines/0/
6. Thompson MA, Mugavero MJ, Amico KR, et al. Guidelines for improving entry into and retention in care and antiretroviral adherence for persons with HIV. Ann Intern Med. 2012; 156(11):817–833. [PubMed: 22393036]

Table 1

Demographics of Study Sample by Calendar Year

	No. (%) of Patients by Calendar Year									
	2001 (n = 5445)	**2002 (n = 6433)**	**2003 (n = 8287)**	**2004 (n = 9537)**	**2005 (n = 10 137)**	**2006 (n = 11 030)**	**2007 (n = 12 194)**	**2008 (n = 13 719)**	**2009 (n = 14 684)**	**2010 (n = 15 944)**
Age group, y										
18–29	729 (13.4)	869 (13.5)	1012 (12.7)	1212 (12.7)	1171 (11.6)	1269 (11.5)	1343 (11.0)	1536 (11.2)	1754 (11.9)	1977 (12.4)[b]
30–39	2214 (40.7)	2436 (37.9)	2950 (35.6)	3164 (33.2)	3035 (29.9)	3009 (27.3)	3081 (25.3)	3263 (23.8)	3316 (22.6)	3434 (21.5)
40–49	1782 (32.7)	2200 (34.2)	3032 (36.6)	3523 (36.9)	3930 (38.8)	4322 (39.2)	4857 (39.8)	5382 (39.2)	5624 (38.3)	5871 (36.8)
≥50	720 (13.2)	928 (14.4)	1292 (15.6)	1638 (17.2)	2001 (19.7)	2430 (22.0)	2913 (23.9)	3537 (25.8)	3990 (27.2)	4662 (29.2)
Sex										
Male	3776 (69.3)	4602 (71.6)	5879 (71.0)	6721 (70.5)	7167 (70.7)	7731 (70.1)	8562 (70.2)	9568 (69.7)	10 337 (70.4)	11 339 (71.1)
Female	1669 (30.7)	1830 (28.4)	2407 (29.0)	2816 (29.5)	2970 (29.3)	3299 (29.9)	3632 (29.8)	4151 (30.3)	4347 (29.6)	4605 (28.9)
Race/ethnicity										
White	1379 (25.3)	1757 (27.3)	2294 (27.7)	2599 (27.3)	2672 (26.4)	2748 (24.9)	3005 (24.6)	3250 (23.7)	3449 (23.5)	3705 (23.2)[b]
Black	2658 (48.8)	3163 (49.2)	4039 (48.7)	4637 (48.6)	4944 (48.8)	5535 (50.2)	6099 (50.0)	6977 (50.9)	7464 (50.8)	8164 (51.1)
Hispanic	1295 (23.8)	1358 (21.1)	1786 (21.6)	2106 (22.1)	2258 (22.3)	2406 (21.8)	2726 (22.4)	3106 (22.6)	3336 (22.7)	3548 (22.3)
HIV risk factor										
MSM	1804 (33.1)	2397 (37.3)	3132 (37.8)	3570 (37.4)	3866 (38.1)	4207 (38.1)	4666 (38.3)	5145 (37.5)	5742 (39.1)	6377 (40.0)[b]
HET	2072 (38.1)	2308 (35.8)	3140 (37.9)	3756 (39.4)	4056 (40.0)	4583 (41.6)	5033 (41.3)	5700 (41.6)	6110 (41.6)	6518 (40.9)
IDU	1290 (23.7)	1349 (21.0)	1617 (19.5)	1737 (18.2)	1750 (17.3)	1832 (16.6)	1993 (16.4)	2208 (16.1)	2158 (14.7)	2175 (13.6)
Insurance										
Private	642 (11.8)	825 (12.8)	757 (9.1)	905 (9.5)	1317 (13.0)	1440 (13.1)	1835 (15.1)	2028 (14.8)	2105 (14.3)	2695 (17.3)[b]
Medicaid	2353 (43.2)	2390 (37.2)	2824 (34.1)	2956 (31.0)	3849 (38.0)	3957 (35.9)	4330 (35.5)	5225 (38.1)	5396 (36.8)	5075 (32.5)

	No. (%) of Patients by Calendar Year									
	2001 (n = 5445)	**2002 (n = 6433)**	**2003 (n = 8287)**	**2004 (n = 9537)**	**2005 (n = 10 137)**	**2006 (n = 11 030)**	**2007 (n = 12 194)**	**2008 (n = 13 719)**	**2009 (n = 14 684)**	**2010 (n = 15 944)**
Medicare	425 (7.8)	545 (8.5)	762 (9.2)	903 (9.5)	1118 (11.0)	1667 (15.1)	1812 (14.9)	2097 (15.3)	2287 (15.6)	2690 (17.3)
Uninsured	1823 (33.5)	2181 (33.9)	2816 (34.0)	3073 (32.2)	3276 (32.3)	3577 (32.4)	3674 (30.1)	3836 (28.0)	4204 (28.6)	4711 (30.2)
CD4 T-cell count, /μL										
≤200	1653 (30.4)	1711 (26.6)	2062 (24.9)	2271 (23.8)	2357 (23.3)	2382 (21.6)	2515 (20.6)	2767 (20.2)	2728 (18.6)	2674 (16.8)
>200	3792 (69.6)	4722 (73.4)	6224 (75.1)	7266 (76.2)	7780 (76.8)	8648 (78.4)	9679 (79.4)	10 952 (79.8)	11 956 (81.4)	13 270 (83.2)
Receiving ART										
Recommended[c]	1596 (77.6)	1752 (79.2)	2166 (77.2)	2280 (77.5)	2475 (80.9)	2498 (81.7)	4956 (80.9)	5905 (85.5)	6320 (89.9)	6313 (91.3)[b]
All	3597 (66.1)	4340 (67.5)	5490 (66.3)	6254 (66.0)	6887 (69.2)	7769 (72.0)	8773 (74.9)	10 609 (79.3)	11 980 (83.7)	13 372 (86.3)[b]
HIV RNA ≤400 copies/mL[d]	1008 (44.7)	1432 (44.9)	1895 (45.8)	2543 (51.5)	3146 (55.2)	3831 (58.6)	4358 (60.5)	5591 (63.8)	6852 (68.6)	8061 (72.2)[b]

Abbreviations: ART, antiretroviral therapy; HET, heterosexual transmission; HIV, human immunodeficiency virus; IDU, injection drug use; MSM, men who have sex with men.

[a] Median follow-up time of care for the cohort was 2 years (mean, 3.3 years). The number of patients receiving care was defined as attending 1 or more clinic visit and having 1 or more CD4 test recorded during the year.

[b] For test of association between row variable and year (2001–2010), the *P* value was less than .05.

[c] Among patients recommended to receive ART: CD4 T-cell count of 200/μL or less for 2001–2006; CD4 T-cell count of 350/μL or less for 2007–2010.

[d] Among all patients receiving ART; median number of HIV RNA tests per patient per year was 2 for 2001 and 3 for 2002–2010.

Table 2

Factors Associated With Sustained Viral Suppression

Characteristic	No. of Patients (n = 79 071)[a]	Model 1 AOR (95% CI)[b]	Model 2 AOR (95% CI)[c]
Year			
2001	3597	1 [Reference]	1 [Reference]
2002	4340	0.95 (0.85–1.05)	0.98 (0.89–1.08)
2003	5490	0.96 (0.87–1.06)	1.01 (0.92–1.11)
2004	6254	1.18 (1.07–1.30)	1.24 (1.13–1.36)
2005	6887	1.41 (1.28–1.56)	1.46 (1.33–1.60)
2006	7769	1.58 (1.43–1.76)	1.65 (1.51–1.80)
2007	8773	1.67 (1.52–1.84)	1.76 (1.60–1.92)
2008	10 609	1.94 (1.77–2.14)	2.04 (1.87–2.23)
2009	11 980	2.45 (2.23–2.69)	2.55 (2.33–2.79)
2010	13 372	2.83 (2.57–3.11)	3.01 (2.76–3.29)
Age group, y			
18–29	7411	1 [Reference]	1 [Reference]
30–39	21 276	1.19 (1.10–1.28)	1.12 (1.04–1.20)
40–49	31 316	1.35 (1.25–1.46)	1.26 (1.16–1.36)
≥50	19 068	1.97 (1.81–2.15)	1.85 (1.70–2.01)
Sex			
Male	57 235	1 [Reference]	1 [Reference]
Female	21 836	0.94 (0.88–0.99)	1.04 (0.98–1.11)
Race/ethnicity			
White	20 408	1 [Reference]	1 [Reference]
Black	38 497	0.74 (0.69–0.79)	0.69 (0.65–0.74)
Hispanic	18 136	1.00 (0.90–1.09)	0.97 (0.90–1.04)
Unknown	2030	1.18 (1.00–1.39)	1.12 (0.95–1.32)
HIV risk factor			
MSM	30 941	1 [Reference]	1 [Reference]
HET	31 618	0.94 (0.88–1.00)	0.88 (0.83–0.94)
IDU	13 183	0.67 (0.62–0.72)	0.63 (0.58–0.67)

Characteristic	No. of Patients (n = 79 071)[a]	Model 1 AOR (95% CI)[b]	Model 2 AOR (95% CI)[c]
Unknown	3329	0.93 (0.82–1.06)	0.85 (0.75–0.96)
Insurance			
Private	10 698	1 [Reference]	1 [Reference]
Medicaid	28 355	0.70 (0.65–0.75)	0.67 (0.64–0.72)
Medicare	11 955	0.72 (0.67–0.77)	0.71 (0.66–0.76)
Uninsured	23 493	0.90 (0.84–0.97)	0.90 (0.84–0.96)
Unknown	4561	0.90 (0.81–1.00)	0.89 (0.80–0.98)
No. of months eligible for viral load measurement			
<12	4587	1 [Reference]	1 [Reference]
12	74 484	0.44 (0.41–0.47)	0.55 (0.52–0.59)
CD4 T-cell count, /μL			
≤200	18 740	1 [Reference]	
>200	60 071	4.01 (3.83–4.21)	

Abbreviations: AOR, adjusted odds ratio; HET, heterosexual transmission; HIV, human immunodeficiency virus; IDU, injection drug use; MSM, men who have sex with men.

[a] The number of patients represents totals across years; many patients contributed multiple observations.

[b] Adjusted for demographic and clinical factors (age, sex, race/ethnicity, HIV risk factor, insurance type, number of months eligible for viral load measurement, CD4 T-cell count), and site of care. Demographic and clinical factors were selected a priori based on a review of the literature; site of care was included to account for possible heterogeneity among clinics.

[c] Including CD4 in the model may lead to overcorrection; therefore, a second model was fit that included all variables in model 1 except CD4 T-cell count.