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The Impact of Age on Retention in Care and Viral Suppression

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Abstract

Background—Retention in care is important for all HIV-infected persons and is strongly associated with initiation of antiretroviral therapy and viral suppression. However, it is unclear how retention in care and age interact to effect viral suppression. We evaluated whether the association between retention and viral suppression differed by age at entry into care.

Methods—Cross-sectional analysis (2006-2010) involving 17,044 HIV-infected adults in 14 clinical cohorts across the U.S. and Canada. Patients contributed one year of data during their first full calendar year of clinical observation. Poisson regression examined associations between retention measures [U.S. National HIV/AIDS Strategy (NHAS), U.S. Department of Health and Human Services (DHHS), 6-month gap, and 3-month visit constancy] and viral suppression (HIV RNA 200 copies/mL) by age group: 18-29, 30-39, 40–49, 50–59, and 60 years old.

Results—Overall, 89% of patients were retained in care using the NHAS measure, 74% with the DHHS indicator, 85% did not have a 6-month gap, and 62% had visits in 3-4 quarters of the year; 54% achieved viral suppression. For each retention measure, the association with viral suppression was significant for only the younger age groups (18-29 and 30-39 years): 18-29 [adjusted prevalence ratio (APR)=1.33, 95% confidence interval (CI)=1.03-1.70]; 30-39 (APR=1.23, CI=1.01-1.49); 40-49 (APR=1.06, CI=0.90-1.22); 50-59 (APR=0.92, CI=0.75-1.13); 60 years (APR=0.99, CI=0.63-1.56) using the NHAS measure as a representative example.

Conclusions—These results have important implications for improving viral control among younger adults, emphasizing the crucial role retention in care plays in supporting viral suppression in this population.

Keywords

Retention in Care; Viral Suppression; Age; Engagement; HIV

Introduction

HIV-infected persons must complete several steps along a care continuum – HIV testing and diagnosis, linkage to and retention in primary HIV care, and receipt and adherence to antiretroviral therapy (ART) – to optimize individual and public health outcomes.^{1,2}

Retention in care is a key step in this process, associated with initiation of ART, decreased mortality, and reduced HIV transmission to others.³⁻¹²

Multiple **surveillance and cohort** studies indicate that both patients' age and retention in care status may impact HIV viral suppression.¹³⁻²² Among 35,433 HIV-infected adults followed at 18 primary and specialty care clinics in the United States (U.S.) between 2006 and 2011, older individuals and those retained in care were more likely to achieve viral suppression than younger persons and those poorly engaged in care, respectively.¹⁵ Similarly, of 338,959 persons living with HIV in 19 U.S. jurisdictions in 2010, older age and retention in care were both significantly associated with viral suppression.¹⁹

However, it is unclear how retention in care and age interact to effect viral suppression. Retention in care may enhance medication adherence in younger adults, who are reported to have lower rates of ART compliance compared to older populations.²³⁻²⁶ Alternatively, consistent engagement in care may support ART adherence in older individuals by minimizing drug-drug interactions and treating comorbid conditions.^{27,28} Gaining a better understanding of the relationships between retention in care, age, and viral suppression may assist in designing interventions to improve HIV care and outcomes. We used data from a multisite cohort collaboration to evaluate whether the association between retention in care and viral suppression varied by age at entry into care.

Methods

Study Design and Population

We conducted a cross-sectional analysis from 2006-2010 using data from the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD), a multisite collaboration of cohort studies of HIV-infected adults (age 18 years) receiving care in the U.S. and Canada. NA-ACCORD is one of the multinational cohort studies sponsored by the International Epidemiological Databases to Evaluate AIDS consortium of the National Institutes of Health. Details on the NA-ACCORD collaboration have been published previously.²⁹ Briefly, contributing cohorts have standardized cohort-specific methods of data collection. At scheduled intervals, **investigators at** these cohorts submit data regarding participants' demographic characteristics, ART prescription information, dates and results of laboratory tests including HIV-1 RNA and CD4 count, clinical diagnoses, and vital status. These data are transferred securely to the NA-ACCORD central Data Management Core, where they undergo quality control for completeness and accuracy before they are combined into harmonized data files. The activities of the NA-ACCORD have been reviewed and approved by the local institutional review boards for each site and at Johns Hopkins School of Medicine.

Data from 14 NA-ACCORD clinical cohorts, with participants residing in all 50 U.S. states, the District of Columbia, Puerto Rico, and 10 Canadian provinces and territories, were included in analyses. HIV-infected adults (age 18 years) **newly enrolled in** care at these NA-ACCORD sites (**i.e. first visit to these sites**) between January 1, 2006 and December 31, 2010 were eligible for inclusion.³⁰ To assure exclusion of those who may have received care previously (e.g. transferring care from a clinic outside the NA-ACCORD to an NA-

ACCORD site), we excluded patients with first recorded HIV-1 RNA 200 copies/mL and individuals with ART use prior to NA-ACCORD enrollment. Interval cohort studies that participate in NA-ACCORD were excluded from this analysis because of our focus on the nature of HIV care in the U.S. and Canada.³¹

Retention Measures

Since multiple measures of retention in care are currently in use, with no clear gold standard,^{13,32} we applied four commonly used measures of retention for each patient in their first full calendar year of observation (subsequent to their year of entry **at an NA-ACCORD site**) to describe their pattern of attendance at primary HIV care visits. For some patients this also represented their first full calendar year after initial HIV diagnosis. The use of the first full calendar year reflects the common practice of measuring retention in care on a calendar year basis.³²

First, the U.S. National HIV/AIDS Strategy (NHAS) retention in care measure dichotomously defines retention as having 2 or more HIV visits separated by 90 days during a calendar year.³³ Second, the U.S. Department of Health and Human Services (DHHS) retention in HIV care indicator defines retention as having 1 HIV visits in each half of the calendar year (Jan-Jun and Jul-Dec), at least 60 days apart.³⁴ Third, the 6- month gap in care measure reflects whether a patient had 6 months between sequential outpatient visits, with no gap signifying retention in care. Fourth, 3-month visit constancy, an ordinal measure, is the number of 3-month intervals in a calendar year in which a patient completes at least 1 HIV visit (range, 1-4). **For all four measures evaluated in this study**, HIV visits refer only to completed primary HIV care appointments at NA-ACCORD clinics and do not include nursing, pharmacy, laboratory, social services, or other types of visits.

Each retention measure has its particular advantages and limitations.^{13,32,35} Constancy measures, such as the NHAS measure, DHHS indicator, 3-month visit constancy measure, and the 6-month gap in care measure, do not require scheduled and missed visit data to be calculated; data elements which are not always readily available. The NHAS measure and DHHS indicator are unique in that several federal programs utilize them to monitor HIV outcomes. However, they may overestimate retention for patients needing more frequent visits. Conversely, the 3-month visit constancy measure is at risk of underestimating retention for patients needing less frequent monitoring. The 6-month gap in care measure is able to capture long breaks between visits, but may be difficult to calculate when there is no recently attended visit. Multiple studies have compared different measures of retention in care, demonstrating moderate to strong correlation between measures and modest discrimination for viral suppression.^{13,15,32,36}

Outcome Variable

HIV viral suppression was the outcome of interest, defined by the U.S. Health Resources and Services Administration (HRSA) HIV/AIDS Bureau HIV viral load suppression performance measure.³⁷ Persons were categorized as suppressed (HIV-1 RNA 200 copies/mL) and not suppressed (HIV-1 RNA > 200 copies/mL) using the last HIV-1 RNA value reported in the calendar year. Those with missing HIV-1 RNA values (10% of the

sample) were excluded from regression analyses; sensitivity analyses were conducted classifying these individuals as "not suppressed."³⁸

Sociodemographic and Clinical Variables

Patients' age as of January 1 of the calendar year was divided into five groups: 18-29, 30-39, 40–49, 50–59, and 60 years old. Race/ethnicity was categorized as non-Hispanic White, non-Hispanic Black, Hispanic, and other/unknown. HIV transmission risk factor was grouped into men who had sex with men (MSM), heterosexual transmission (HET), injection drug use (IDU), and other/unknown. Patients who had IDU in combination with another risk factor (e.g. MSM, HET) were classified as IDU. Patients were considered to be on ART if they concomitantly were prescribed 3 antiretroviral drugs from at least 2 classes or triple nucleoside/nucleotide reverse transcriptase inhibitor regimen containing abacavir or tenofovir for at least 6 months during the calendar year. First CD4 count recorded in the calendar year was grouped as < 350, 350-499, or 500 cells/mm³.

Statistical Analyses

Standard descriptive analyses of demographic and clinical characteristics of the sample were conducted. Chi-squared tests for differences in proportion were used to detect unadjusted differences in viral suppression status by age group, within retention strata. Multivariable Poisson regression models with robust variance were used to estimate adjusted prevalence ratios (APR) and 95% confidence intervals of the association between each measure of retention and viral suppression, adjusting for age group, gender, race/ethnicity, HIV transmission risk factor, use of ART, first CD4 count, calendar year, and cohort. **Covariates were selected** *a priori* based on a literature review of factors influencing retention in care and viral suppression.¹³⁻¹⁸ Insurance status was not uniformly collected by NA-ACCORD cohorts and thus was not included in analyses. Separate models were estimated for each retention measure. To evaluate whether the association between retention in care and viral suppression differs by age group, we included an interaction term between age group and each measure of retention; an adjusted Wald test was used to determine if there was statistical evidence of interaction. Statistical analyses were performed using Stata 12.1 (Stata Corporation, College Station, TX).

Results

A total of 17,044 adults who met study criteria initiated care at NA-ACCORD clinical sites between 2006 and 2010. (Table 1) The majority of the patients were <50 years old (15% of patients were 18-29 years, 25% were 30-39 years, 34% were 40-49 years), male (81%), and of minority race/ethnicity (56%). The predominant HIV risk factor was MSM (40%) followed by HET (27%) and IDU (11%). Overall, 89% of patients were retained in care according to the NHAS measure, 74% according to the DHHS indicator, 85% did not have a 6-month gap, and 62% had visits in 3-4 quarters of the year. Fifty-five percent of the sample was prescribed ART in their first full calendar year of observation. Among those with available viral load data (n=15,378 or 90% of the 17,044 who initiated care), 54% achieved viral suppression.

Figure 1 shows the unadjusted proportions of patients with viral suppression, by age group and retention measure. For each measure, three significant (p < 0.05) results **from chi-squared tests** are clear: (1) the older the individual, the greater the probability of viral suppression in both the retained and not retained in care groups; (2) patients who were retained in care had a greater probability of viral suppression than those not retained in care, but this difference decreased as age groups increased; and (3) the association between retention in care and viral suppression was greatest for younger versus older age groups.

Table 2 shows APRs for the joint effect of retention in care on viral suppression at different age groups. For each retention measure, the association with viral suppression was significant (p < 0.05) for only the younger age groups (18-29 years and 30-39 years): NHAS measure (APR=1.33 [1.03, 1.70] for 18-29; APR=1.23 [1.01, 1.49] for 30-39), DHHS indicator (APR=1.19 [1.02, 1.39] for 18-29; APR=1.23 [1.09, 1.39] for 30-39), 6-month gap in care measure (APR=1.28 [1.04,1.57] for 18-29; APR=1.16 [1.01, 1.35] for 30-39), and 3-month visit constancy (APR=1.36 [1.09, 1.69] for 3 quarters and APR=1.47 [1.18, 1.82] for 4 quarters for 18-29; APR=1.27 [1.07, 1.50] for 3 quarters and APR=1.41 [1.19, 1.66] for 4 quarters for 30-39). Pairwise comparisons of APR between the two youngest age groups were significant (p < 0.05). We did not observe any significant differences in the probability of viral suppression for older individuals who were retained versus not retained in care. Sensitivity analyses categorizing those with missing viral load data as "not suppressed" yielded similar results. (Appendix Table 1)

Appendix Tables 2 and 3 present associations between patient factors and viral suppression. In models adjusting for gender, race/ethnicity, HIV transmission risk factor, use of ART, first CD4 count, calendar year, cohort, and including a interaction term between age group and retention in care, persons with black race/ethnicity (vs. white) and HET risk or IDU risk (vs. MSM) were significantly (p < 0.05) less likely to achieve viral suppression, regardless of the retention measure assessed. Persons on ART and those who entered care in more recent years were significantly (p < 0.05) more likely to be virally suppressed.

Discussion

This study evaluate the relationship between age, retention in care, and viral suppression, and suggests that viral suppression is significantly more prevalent in younger HIV-infected adults (18-39 years old) retained in care than in similarly aged persons not retained in care. The U.S. Centers for Diseases Control and Prevention estimate that approximately 14,200 individuals aged 20-29 and 11,200 individuals aged 30-39 were newly infected with HIV in 2010, representing the highest burden of new HIV infections among all age groups.³⁹ Retaining younger HIV-infected persons in care may be particularly important to improving clinical outcomes and reducing transmission of HIV in this population.⁴⁰

While older patients were more likely to achieve viral suppression, we demonstrate that the effect of retention in care on viral suppression was greatest for patients aged 18-39 compared to those 40 years and older. This pattern persisted independent of the measure of retention utilized. Prior research indicates that younger adults have lower rates of ART adherence than older adults.^{23,24,26} Of 5,090 HIV-infected patients enrolled in a large

integrated health care system, patients 50 years or older sustained higher therapy adherence (88.9%) than 18-39 (83.7%) and 40-49 years old (85.7%), respectively.²⁶ Among 148 HIVinfected adults on ART and receiving care in Los Angeles, CA, adherence to HIV therapy was significantly higher in older (50 years old) versus younger (<50 years old) patients (87.5% versus 78.3%, respectively).²⁴ Similarly, a recent systematic review and metaanalysis noted that older age reduced the risk of ART non-adherence by 27% (relative risk 0.72, [0.64, 0.82]).²⁵ These studies suggest that differences in ART adherence between older and younger adults exist and may mediate the relationships with viral suppression. Unfortunately, ART adherence data was unavailable and thus was not included in our analyses. Regular clinic attendance may help younger adults comply with HIV treatment and achieve viral suppression by providing one-on-one ART education and counseling, tools to improve medication adherence (e.g. pillboxes, reminder devices), and access to case management and ancillary services to address competing food insecurity, housing, and transportation needs.⁴¹ These resources may be equally important to maintaining ART adherence in older adults.

HIV-related stigma, fear of disclosure, and stress significantly impact the experiences and health of people living with HIV.⁴²⁻⁴⁴ Some data suggest that younger individuals may confront these challenges at higher rates than older adults, while other report no difference between age groups.⁴⁵⁻⁴⁸ Among 147 HIV-infected adolescents and young adults aged 16-29 years living in New York, Los Angeles, and San Francisco, almost all (89%) reported perceived stigma (a stigmatized person's fear or anticipation of discrimination and rejection, and internal sense of shame) and 64% reported enacted stigma (actual experiences of stigma and discrimination) during their lifetime.⁴⁹ In an analysis exploring the relationship between age and patterns of disclosure, younger adults were significantly more likely to fear losing their job because of their HIV status than older adults.⁴⁵ Likewise, among 102 adults living with HIV in a large city, individuals 50 years old had more social isolation than those >50 years old.⁴⁷ Maintaining a continuous relationship with a provider may offer younger adults access to resources to better manage HIV-related stigma and barriers to care, which may contribute to improved ART adherence and achievement of viral suppression. However, the availability and quality of these resources may differ by provider and clinic.

Our finding that the association between retention in care and viral suppression was strongest for younger patients does not preclude the possibility that there may be subgroups of older individuals for whom retention may be equally or more important to achieving viral control and other health outcomes. For example, continuous engagement in care may be key to managing comorbid conditions (e.g. diabetes, heart failure) in older people with HIV infection.⁵⁰ Further studies examining these nuances may help in the development of more personalized measures of retention in care.

Our analysis has several limitations. First, our data do not reflect visits to multiple providers by the same patient. It is possible that patients may switch facilities or providers in the same locality, emigrate from the area, or become incarcerated, institutionalized, or hospitalized but still be receiving care. Younger adults may be more mobile than older adults, impacting engagement in care.⁵¹ Second, we measured use of ART and viral suppression, but did not specifically assess adherence to HIV treatment. Future studies are warranted to investigate

the relationship between ART adherence, age, retention in care, and viral suppression. Third, we focused on the first full calendar year in primary HIV care to allow sufficient time to observe retention measures. Thus, patients who were linked to outpatient care with less than one year of follow-up were excluded; additional research to better understand persons who are unable to establish consistent care is warranted.^{2,52}. Fourth, HIV-infected individuals are living longer,⁵³ which requires new evaluations of longer-term retention in care and viral suppression. Similarly, as HIV therapy, national treatment guidelines, and telehealth continue to advance new standards and methods for assessing retention in care will be needed. Fifth, our cross-sectional study design precludes inference of causality. Sixth, we are limited by the current retention measures in use, which only include primary HIV care appointments and do not account for nursing, pharmacy, laboratory, or other types of visits. Exclusion of these points of contact with the healthcare system may underestimate retention in care. Lastly, while NA-ACCORD constitutes a patient population that is a large proportion of and demographically similar to persons living with HIV/AIDS in the U.S.,⁵⁴ care sites vary in operations and support services provided, which may impact generalizability of our findings.

In summary, we reported that retention in care is more strongly associated with viral suppression in younger adults. These results have important implications for the test and treat approach to HIV prevention, emphasizing the crucial role retention in care plays in supporting viral suppression in younger adults.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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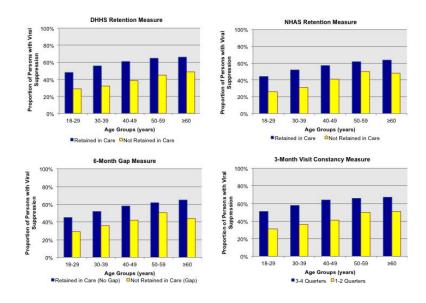


Figure1.

Unadjusted Proportion of HIV-Infected Persons with Viral Suppression by Retention Measure and Age Group

Table 1

Demographic and Clinical Characteristics of the Sample

Characteristic	Overall N=17,044 (%)		
Age (years)			
18-29	2,560 (15%)		
30-39	4,261 (25%)		
40-49	5,826 (34%)		
50-59	3,259 (19%)		
60	1,138 (7%)		
Sex			
Male	13,764 (81%)		
Female	3,289 (19%)		
Race/Ethnicity			
White	6,244 (37%)		
Black	7,101(42%)		
Hispanic	2,143 (13%)		
Unknown	1,364 (8%)		
HIV Risk Factor			
MSM	6,789 (40%)		
Heterosexual	4,591 (27%)		
IDU	1,850 (11%)		
Unknown	3,409 (22%)		
First CD4 Count in Year			
$< 350 \text{ cell/mm}^3$	7,511 (44%)		
350-499 cell/mm ³	3,669 (22%)		
500 cell/mm ³	4,321 (25%)		
Missing	1,534 (9%)		
Use of ART in Year			
No	7,590 (45%)		
Yes	9,454 (55%)		
Calendar Year			
2006	3,719 (22%)		
2007	3,510 (21%)		
2008	3,611 (21%)		
2009	3,346 (20%)		
2010	2,858 (16%)		
NHAS Retention Measure			
Not Retained	1,846 (11%)		

Characteristic	Overall N=17,044 (%)		
Retained	15,198 (89%)		
DHHS Retention Indicator			
Not Retained	4,473 (26%)		
Retained	12,571 (74%)		
6-Month Gap			
Yes (Not Retained)	2,563 (15%)		
No (Retained)	14,481 (85%)		
3-Month Visit Constancy			
1	2,901 (17%)		
2	3,586 (21%)		
3	4,806 (28%)		
4	5,751 (34%)		
Viral Suppression			
No	7,119 (42%)		
Yes	8,259 (48%)		
Missing	1,666 (10%)		

Abbreviations: ART, antiretroviral therapy; DHHS, Department of Health and Human Services; HET, heterosexual transmission; HIV, human immunodeficiency virus; IDU, injection drug use; MSM, men who have sex with men; NHAS, National HIV/AIDS Strategy.

Table 2

Association between Retention in Care Measures and Viral Suppression by Age Group

Retention Measure	Age Group					
	18-29 years APR (95% CI)	30-39 years APR (95% CI)	40-49 years APR (95% CI)	50-59 years APR (95% CI)	60 years APR (95% CI)	
NHAS Measure						
Not Retained	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]	
Retained	1.33 (1.03-1.70)	1.23 (1.01-1.49)	1.06 (0.90-1.22)	0.92 (0.75-1.13)	0.99 (0.63-1.56)	
DHHS Indicator						
Not Retained	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]	
Retained	1.19 (1.02-1.39)	1.23 (1.09-1.39)	1.08 (0.97-1.19)	0.99 (0.87-1.14)	0.97 (0.75-1.25)	
6-Month Gap in Care						
Yes (Not Retained)	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]	
No (Retained)	1.28 (1.04-1.57)	1.16 (1.01-1.35)	1.12 (0.99-1.27)	0.96 (0.81-1.14)	1.09 (0.74-1.60)	
3-Month Visit Constancy						
1	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]	
2	1.22 (0.97-1.55)	1.16 (0.97-1.40)	0.98 (0.85-1.14)	1.02 (0.83-1.25)	1.01 (0.67-1.52)	
3	1.36 (1.09-1.69)	1.27 (1.07-1.50)	1.12 (0.98-1.29)	1.00 (0.83-1.20)	0.95 (0.65-1.37)	
4	1.47 (1.18-1.82)	1.41 (1.19-1.66)	1.13 (0.99-1.29)	1.03 (0.86-1.23)	1.01 (0.71-1.45)	

Abbreviations: APR, adjusted prevalence ratio; CI, confidence interval; DHHS, Department of Health and Human Services; NHAS, National HIV/AIDS Strategy.

Models included an interaction between retention measure and age group, and adjusted for sex, race/ethnicity, HIV risk factor, first CD4 cell count in the year, use of ART for >6 months during the year, calendar year, and cohort as time-fixed covariates.

Bold signifies adjusted prevalence ratios with p-vale <0.05.