Clinical Infectious Diseases Advance Access published August 4, 2014

Beyond Core Indicators of Retention in HIV Care: Missed Clinic Visits are Independently Associated with All-cause Mortality

Michael J. Mugavero[1], Andrew O. Westfall[1], Stephen R. Cole[2], Elvin H. Geng[3], Heidi M. Crane[4], Mari M. Kitahata[4], W. Christopher Mathews[5], Sonia Napravnik[3], Joseph J. Eron[3], Richard D. Moore[6], Jeanne C. Keruly[6], Kenneth H. Mayer[7,8], Thomas P. Giordano[9,10], James L. Raper[1], on behalf of CFAR Network of Integrated Clinical Systems (CNICS)

[1]University of Alabama at Birmingham

[2]University of North Carolina, Chapel Hill

[3]University of California, San Francisco

[4]University of Washington

[5]University of California, San Diego

[6]Johns Hopkins University

[7]Fenway Community Health Center

[8]Harvard University

[9]Michael E. DeBakey VA Medical Center

[10]Baylor College of Medicine

Corresponding author: Michael J. Mugavero, MD, MHSc, 1720 7th Avenue South, BBRB 206H, Birmingham, AL 35294-2170, E-mail: mmugavero@uab.edu

Key points: Missed HIV care visits have independent prognostic value for clinical events beyond core indicators of retention in care. As this information is readily available and immediately actionable, missed HIV care visits should be incorporated into clinical, programmatic and policy initiatives.

Abstract

Background: The continuum of care is at the forefront of the domestic HIV agenda, with the Institute of Medicine (IOM) and Department of Health and Human Services (DHHS) recently releasing clinical core indicators. Retention in care core indicators are calculated based upon attended HIV care clinic visits. Beyond these retention core indicators, we evaluated the additional prognostic value missed clinic visits for all-cause mortality.

Methods: We conducted a multi-site cohort study of 3,672 antiretroviral-naïve patients initiating ART from 2000-2010. Retention in care was measured by the IOM and DHHS core indicators (2 attended visits at defined intervals per 12 month period), and also as a count of missed primary HIV care visits (no show) during a 24-month measurement period following ART initiation. All-cause mortality was ascertained by query of the Social Security Death Index and/or National Death Index, with adjusted survival analyses starting at 24-month post-ART initiation.

Results: Among participants, 64% and 59% met the IOM and DHHS retention core indicators at 24-months. Subsequently, 332 patients died during 16,102 person-years follow-up. Failure to achieve the IOM and DHHS indicators through 24 months post-ART initiation increased mortality (HR=2.23;95% CI:1.79,2.80 and HR=2.36;95%CI:1.89,2.96, respectively). Among patients classified as retained by the IOM or DHHS clinical core indicators, >2 missed visits further increased mortality risk (HR=3.61;95%CI: 2.35,5.55 and HR=3.62;95%CI: 2.30,5.68, respectively).

Conclusions: Beyond HIV retention core indicators, missed clinic visits were independently associated with all-cause mortality. Caution is warranted in relying solely upon retention in care core indicators for policy, clinical and programmatic purposes.

Introduction

In recent years, considerable attention has focused on the importance of engagement in HIV medical care in contributing to individual and public health outcomes. The HIV care continuum ("treatment cascade") has become the sentinel image depicting the domestic HIV epidemic across a sequence of steps including acquisition of HIV infection, HIV diagnosis, linkage to medical care, retention in medical care, antiretroviral therapy (ART) receipt, and plasma viral suppression (<200 copies/mL) [1-4]. Of the estimated 1.2 million Americans living with HIV infection, only 25% have achieved plasma viral suppression, with dramatic drop-offs in linkage and retention in medical care representing the most prominent barriers to achieving this vital surrogate marker of effective treatment. Research has clearly shown that achieving and sustaining plasma viral suppression is associated with a decreased frequency of clinical events, including mortality, and with dramatic reductions in HIV transmission [5-7]. However, over half of persons diagnosed with HIV infection in the US are not engaged in ongoing medical care [8], making retention in care the greatest barrier to fully achieving the individual and population health benefits afforded by viral suppression [9, 10]. Accordingly, the US National HIV/AIDS Strategy and HIV Care Continuum Initiative, recently released by Executive Order, place considerable focus on HIV care engagement as a critical component to achieving the overarching goals of reducing new HIV infections, improving health outcomes for people living with HIV, and reducing HIV-related health disparities [11, 12]. In response to these initiatives, the Institute of Medicine (IOM) and Department of Health and Human Services (DHHS) have put forth clinical core indicators, including measures for retention in HIV care, which now serve as national benchmarks, with reporting on these indicators required by agencies receiving federal funding for the provision of HIV services [13, 14].

While hundreds of trials have comparatively evaluated ART regimens over the past 2 decades, a paucity of rigorous scientific research has been conducted on the early steps of the HIV care continuum [15]. In particular, studies on engagement in care including initial linkage, subsequent retention, and re-

engagement in medical care among those who drop out are limited, but rapidly emerging in the literature. As a nascent field, a number of approaches have been developed to quantify and measure retention in care, with no clear gold standard established [16, 17]. In broad terms, retention measures include both those based solely on attended clinic visits and others that account for missed (no show) clinic visits. Recent research indicates these two approaches to quantification (attended vs. missed) may tap into different aspects of HIV care retention [16]. To date, most studies have utilized single retention measures in isolation, and have not evaluated the added value of using multiple measures concomitantly or sequentially. We evaluated the association of missed clinic visits for all-cause mortality when used in conjunction with the IOM and DHHS clinical indicators of retention in care, which are both calculated based solely upon attended visits. We hypothesized that beyond retention in care classification according to these core indicators (retained vs. not retained), that missed clinic visits would have independent and substantial associations with all-cause mortality.

Methods

Design Overview

We conducted an analysis of systematically captured data from a multi-site HIV clinical cohort collaboration, the Centers for AIDS Research (CFAR) Network of Integrated Clinical Systems (CNICS).

Setting and Participants

CNICS is a nationally distributed HIV clinical cohort that has been described in detail previously [18]. Briefly, the CNICS cohort includes over 28,000 HIV-infected adults (contributing >125,000 person-years follow-up, on average 4.5 years per patient) who have received HIV care at one of eight CFAR sites, dating back to 1995. Every three months, sites transmit comprehensive and well defined data elements captured from point-of-care electronic health record systems using standardized terminology and

format. Systematic and rigorous processes for data verification and quality assurance are in place to generate a centralized high quality clinical database. The participating cohorts and this study were approved by local institutional review boards.

For this study, we included antiretroviral-naïve HIV-infected patients starting ART at one of 5 participating CNICS sites contributing comprehensive clinic visit data. All patients starting ART between January 2000 and July 2010 who were alive 24-months following ART initiation were included. Because retention in care was calculated for the 24-months following ART start, in accordance with the 24-month measurement period for the DHHS retention core indicator [14], patients who died prior to this date (n=105) were excluded as they did not have a complete observation measurement period. No other exclusion criteria were employed, and as retention was the primary independent variable under study, participants lost to care within 24-months after ART start were not excluded or censored, but rather, this information was implicitly captured by the retention measures under study.

Exposures and Outcomes

Retention in HIV medical care during a 24-month measurement period following ART initiation was the principal exposure of interest. Retention was calculated using 3 measures including the IOM core indicator (based upon the Health and Resources Services Administration HIV/AIDS Bureau measure), the DHHS core indicator, and a count of missed primary HIV care clinic visits that were not cancelled in advance by patient or provider (no show visits). All retention measures were calculated based upon scheduled appointments with the primary HIV care provider only, with subspecialty and urgent care visits excluded. The IOM retention indicator is defined as 2 attended visits separated by ≥90 days during a 12-month measurement period [13]. For study purposes, achieving this indicator for each of 2 consecutive 12-month periods following the ART start date was used to define IOM retention at 24-months. The DHHS core indicator is defined as at least 1 attended visit in each 6 month period during a

24-month measurement period, with ≥60 days between visits in adjacent 6 month periods [14]. Missed visits over the 24-months following ART start were categorized as zero, 1-2 and >2 missed visits. For each patient, a 24-month observation measurement period was determined individually based upon the ART start date. Attended visits on the ART initiation date were not counted in the calculation of the IOM and DHHS core indicators, which included scheduled visits subsequent to this date.

All-cause mortality, the principal outcome of interest, was ascertained via query of the Social Security Death Index and/or National Death Index. Because we used these national databases, assessment of vital status as an outcome was not contingent upon participants remaining in care and under observation in the clinical cohorts contributing to CNICS.

Statistical Analysis

Descriptive statistics including means, medians, frequencies and proportions were calculated and visual plots assessed to evaluate the distribution of all study variables. Separate Cox proportional hazards models assessed the relationships between the three measures of retention at 24-months following ART start (excluding patients who died within 24-months) and all-cause mortality with the origin for the timescale being 24-months after ART initiation. Next, separate Cox proportional hazards models assessed the independent association of missed clinic visits with all-cause mortality among patients grouped by retention classification (retained vs. not retained) at 24-months according to the IOM and DHHS core indicators. Adjusted models control for age at ART start, race, gender, baseline plasma HIV RNA and CD4 count (date nearest ART start date within -180 to +14 days window), and are stratified by site. We did not adjust for time-updated CD4 count and plasma HIV RNA, as these biomarkers are on the causal pathway between our primary exposure, retention in care, and outcome, all-cause mortality. For all models, participants were censored on the date of death or administratively in July 2012. All analyses were conducted with SAS, version 9.3.

Results

Among 3,672 study participants, the mean age was 38 years and the majority were white (53%) and male (80%), with patients starting ART with a baseline mean CD4 count and plasma HIV RNA of 220 cells/mm^3 and 4.9 log_{10} c/mL, respectively (Table 1). Participants were followed for a median of 6.0 years (IQR 3.8-8.7 years) from ART initiation. At 24-months following ART initiation, 64% and 59% of patients met the IOM and DHHS retention core indicators, respectively, with an average of 2.1 missed (no show) visits accrued. Subsequently, 332 patients (9.0%) died during 16,102 person-years follow-up (20.6 deaths per 1,000 person-years). Mortality rates were lower among patients classified as retained by the IOM indicator, DHHS indicator and with zero missed visits (16.0, 15.3, and 11.3 deaths per 1,000 person years, respectively) com pared to those classified as not retained or experiencing missed clinic visits. In separate multivariable Cox proportional hazards models, failure to achieve the IOM indicator (HR=2.23; 95%CI=1.79-2.80; 29.5 deaths per 1,000 person years), the DHHS indicator (2.36;1.89-2.96; 29.0), and missed clinic visits at 24-months (1-2 no shows: 1.98; 1.45-2.72; 20.4, >2 no shows: 3.20; 2.33-4.41; 30.9) were all associated with increased subsequent mortality (Table 2). Across all three models, older age, black/African American race, and lower baseline CD4 count were consistently associated with increased mortality. Notably, the distribution of all three retention measures were fairly consistent in analyses stratified by year of ART initiation, with no clear temporal trends observed. Similarly, the relationship between each retention measure and all-cause mortality remained relatively stable over time during the study period (data not shown).

Among patients classified as retained at 24 months by the IOM (n=2,358) and DHHS (n=2,166) retention core indicators, missed visits were common with roughly two-thirds of persons having at least 1 no show visit, and one quarter of patients missing more than 2 visits over this interval (Table 3). Separate multivariable Cox proportional hazards models restricted to patients classified as retained by

the IOM and DHHS retention core indicators demonstrated increased mortality risk among patients accruing more missed clinic visits over the 24-months following ART initiation (IOM: 1-2 no shows 1.78; 1.17-2.70; 15.3, >2 no shows: 3.61; 2.35-5.55; 24.9 and DHHS: 1-2 no shows 1.71; 1.10-2.65; 14.4, >2 no shows: 3.62; 2.30-5.68; 23.8, Tables 3, 4, Figure 1).

Missed visits were more common among patients classified as not retained at 24 months by the IOM (n=1,314) and DHHS (n=1,506) retention core indicators compared to those classified as retained, although roughly a quarter of "not retained" patients had zero no show visits (Table 3). Separate multivariable Cox proportional hazards models restricted to patients classified as not retained by the core indicators demonstrated increased mortality risk among patients accruing more missed clinic visits over the 24-months following ART initiation (IOM: 1-2 no shows 1.63; 0.98-2.72; 28.5, >2 no shows: 2.11; 1.26-3.51; 40.7 and DHHS: 1-2 no shows 1.76; 1.08-2.85; 28.2, >2 no shows: 2.32; 1.43-3.77; 39.8, Tables 3, 5, Figure 1). Moreover, while increased mortality rates were observed overall among patients classified as not retained by core indicators, and clear dose-response relationships were observed with increasing missed visits within retention categories, interesting relationships were observed when comparing mortality rates across retention categories (Table 3). For example, patients classified as retained by either core indicator who accrued 1-2 missed visits during the 24-months following ART initiation had mortality rates comparable to those classified as not retained and who had zero missed visits (Table 3).

Discussion

These data are among the first to provide empirical validation of the IOM and DHHS core indicators of retention in care with definitive clinical outcomes. When measured over the 24-months following ART initiation, failure to achieve these retention core indicators was strongly associated with subsequent all-cause mortality. However, study findings indicate that assessment of missed clinic visits (no show), in

conjunction with these core indicators, provides additional, independent prognostic value. Among patients grouped by retention in care classification (retained vs. not retained) by the IOM and DHHS retention core indicators, missed visits were exceedingly common and were associated with a substantially elevated mortality risk. Accordingly, caution is warranted in relying solely upon retention core indicators for HIV policy, clinical and programmatic purposes. While these measures have clear value, considerable additional prognostic information is provided, for both patients classified as retained and not retained, by further evaluating missed clinic visits, a readily available and immediately actionable clinical marker.

The HIV care continuum and retention in care are at the forefront of the domestic HIV policy, public health and clinical agenda, with enhanced emphasis garnered by the recently released HIV Care Continuum Initiative, which magnifies the focus of the US National HIV/AIDS Strategy on this pivotal area [11, 12]. In response to these initiatives from the federal government, the IOM and DHHS have released clinical core indicators [13, 14], including measures for retention in care, which are being widely implemented with required reporting on these measures for agencies receiving federal funding for the provision of HIV services. Implementation and adoption of these core indicators are important to assess progress towards local and national goals, and to standardize assessment and comparison across settings, but there is a potential shortcoming in using these indicators alone to define HIV care retention. Our findings suggest that the additional inclusion of missed clinic visits in HIV policy, clinical and public health planning is prudent to optimize classification, risk stratification, and resource allocation to those in greatest need. Agencies with access to missed clinic visits should be encouraged to take advantage of these additional data, as our findings demonstrate their value.

In recent years a number of approaches to measuring retention in care have emerged, each with strengths and limitations, and with no clear gold standard established [16]. Broadly speaking, retention measures include those based solely on attended clinic visits (e.g., the IOM and DHHS core indicators)

and others that account for missed (no show) clinic visits. Prior research has shown that both types of measures predict mortality among patients newly entering HIV care or initiating ART [19-21]. A novel contribution of this study is the concomitant use of a measure from each broad category, rather than using them in isolation as has typically been the approach to date. This observation supports recent research suggesting that measures based upon attended and missed visits may be tapping into different aspects of retention [16], and that there is complementary value in using measures in combination.

Recent guidelines have recommended systematic monitoring of linkage and retention in HIV care for all persons living with HIV infection [15]. It has been noted that a number of data systems are available to monitor HIV care engagement including public health surveillance, administrative claims and clinic-based utilization databases. As for retention measures, each monitoring system has distinct advantages and limitations, and integration of systems has been shown to enhance correct classification of HIV care engagement [15]. In recent years there has been a dramatic shift in paradigm, with the use of CD4 counts and plasma HIV RNA laboratory tests reported to public health surveillance being used as a proxy for care visits to monitor HIV care engagement and to inform interventions for persons identified as out of care [22]. Notably, laboratory surveillance data can be used to calculate retention measures only, since they are a proxy for attended visits, and missed clinic visits are not reported to public health agencies including CDC. Importantly, surveillance allows for improved classification of retention status of persons who have transferred from one clinic to another, which may not be captured at the clinic level. However, information about missed (no show) clinic visits are uniquely available through administrative, billing or clinical data systems at the clinic level. Accordingly, our findings are germane to HIV clinic directors, providers and staff. The added value of missed clinic visits for identifying patients at increased mortality risk can help guide allocation of limited resources to those who may derive the greatest benefits. For example, cost and time-intensive peer mentor, patient navigation, and intensive case management programs are among the few evidenced-based approaches to enhancing

HIV care engagement [15, 23]. Such programs could be targeted to those with missed clinic visits – even among patients considered retained according to the IOM and DHHS core indicators, as resources allow. Moreover, integration of surveillance and clinic based data systems to comprehensively capture retention in a given geographical area affords the opportunity to improve classification of HIV care engagement. Such integrated approaches could capitalize upon the strengths and overcome the limitations of each data system and allow for retention in care programs that leverage the unique information provided by measures based upon and attended and missed clinic visits, captured by public health departments and clinics, respectively.

Our study has limitations. Findings may not generalize to other settings, although we note the geographic diversity of study sites within the US. As an observational study, we can identify associations but cannot attribute causality. We measure retention over a relatively short observation period of 24 months. While longer term retention over decades of treatment is the current paradigm of HIV management, discrete measurement over shorter time periods as evaluated here are highly actionable in terms of risk stratification for programmatic purposes. Additional studies are on-going within CNICS to evaluate the impact of retention over longer measurement periods on health outcomes. There is potential for misclassification of study variables, but this is believed to be minimal based upon the CNICS data quality systems and use of national vital status databases.

In conclusion, our study contributes novel findings germane to the HIV care continuum, with implications for the policy, clinical, and population health communities. The additional assessment of missed clinic visits in conjunction with the IOM and DHHS HIV retention in care core indicators meaningfully enhanced prognostic value for all-cause mortality among patients initiating ART. Accordingly, caution is warranted in relying solely upon core indicators to define retention in care and to inform local, state and national programmatic planning. Missed clinic visits are an important indicator

with independent value that can be used along with core indicators to guide allocation of limited resources in an effort to optimize individual and population health outcomes.

Acknowledgments

We extend our sincere appreciation to the patients, providers, and clinic staff at participating sites, and to the CNICS investigators, research and informatics staff at each site. We also thank the CNICS Administrative, Data Management and Epidemiology / Biostatistics Cores. This study was supported by grants R24AI067039, P30AI027767, R01AI100654 and R01AI103661 from the National Institutes of Health.

The authors have no conflicts of interest related to the content of this manuscript.

Table 1. Characteristics of 3,672 antiretroviral naïve HIV-1-infected patients initiating combination antiretroviral therapy at 5 CFAR Network of Clinical Systems (CNICS) sites, 2000-10.

Characteristic	N (%) or Mean ± Standard Deviation
Age	38.2 ± 10.1
Race	
White	1950 (53%)
Black/African American	1377 (38%)
Other/Unknown	345 (9%)
Gender	
Male	2952 (80%)
Female	720 (20%)
CNICS site	
Case Western Reserve University	405 (11%)
University of Alabama at Birmingham	798 (22%)
University of California at San Diego	876 (24%)
University of North Carolina at Chapel Hill	723 (20%)
University of Washington	870 (24%)
Baseline^ CD4 count	220 ± 183
<50 cells/mm^3	815 (22%)
50-199 cells/mm^3	948 (26%)
200-349 cells/mm^3	1092 (30%)
350-500 cells/mm^3	487 (13%)
>500 cells/mm^3	244 (7%)
Missing/Unknown	86 (2%)
Baseline^ viral load (log_{10} c/mL)	4.9 ± 0.7
<10,000 c/mL	453 (12%)
10,000-100,000c/mL	1521 (41%)
>100,000 c/mL	1577 (43%)
Missing/Unknown	121 (3%)
IOM Retention Core Indicator* at 24 months	
Retained	2358 (64%)
Not retained	1314 (36%)
DHHS Retention Core Indicator† at 24 months	
Retained	2166 (59%)
Not retained	1506 (41%)
Cumulative missed (no show) Visits at 24 months	2.1 ± 2.6
0 no show visits	1175 (32%)
1-2 no show visits	1414 (39%)
>2 no show visits	1083 (29%)

IOM, Institute of Medicine; DHHS, Department of Health and Human Services
^Baseline defined as value nearest antiretroviral therapy start date within a window of -180 to +14 days.

*IOM Retention Core Indicator based upon the HRSA HAB measure defined as 2 attended visits per 12 month period with >90 days between visits. Patients achieving this measure in each of the 12-month periods following ART initiation were classified as retained.
[†]DHHS Retention Core Indicator defined as at least 1 attended visit in each 6 month period during a 24-month measurement period, with ≥60 days between visits in adjacent 6 month periods.

Table 2. Separate multivariable Cox proportional hazards models evaluating the associations of retention in care over the 24-months following ART initiation according to 3 retention indicators with subsequent mortality among 3,672 HIV-1-infected patients initiating combination antiretroviral therapy at 5 CFAR Network of Clinical Systems (CNICS) sites, 2000-10.

Characteristic	IOM Model HR (95% CI)	DHHS Model HR (95% CI)	Missed Visits Model HR (95% CI)
IOM Retention Core Indicator* at 24 months		-----	-----
Retained	Referent		
Not retained	2.23 (1.79-2.80)		
DHHS Retention Core Indicator† at 24 months	-----		-----
Retained		Referent	
Not retained		2.36 (1.89-2.96)	
Cumulative missed (no show) Visits at 24 months	-----	-----	
0 no show visits			Referent
1-2 no show visits			1.98 (1.45-2.72)
>2 no show visits			3.20 (2.33-4.41)
Age (per 10 years)	1.51 (1.36-1.68)	1.53 (1.37-1.70)	1.53 (1.37-1.70)
Race			
White	Referent	Referent	Referent
Black/African American	1.72 (1.34-2.20)	1.70 (1.32-2.18)	1.48 (1.15-1.91)
Other/Unknown	0.71 (0.42-1.21)	0.72 (0.42-1.22)	0.68 (0.40-1.15)
Gender			
Male	Referent	Referent	Referent
Female	0.93 (0.71-1.22)	0.94 (0.72-1.23)	0.90 (0.69-1.17)
Baseline^ CD4 count			
<50 cells/mm^3	2.61 (1.35-5.04)	2.59 (1.34-5.01)	2.37 (1.23-4.58)
50-199 cells/mm^3	1.93 (1.00-3.73)	1.88 (0.97-3.63)	1.80 (0.93-3.49)
200-349 cells/mm^3	1.18 (0.60-2.31)	1.16 (0.59-2.26)	1.17 (0.60-2.28)
350-500 cells/mm^3	1.00 (0.47-2.13)	0.97 (0.46-2.06)	1.00 (0.47-2.12)
>500 cells/mm^3	Referent	Referent	Referent
Missing/Unknown	1.06 (0.39-2.90)	1.02 (0.37-2.80)	1.43 (0.53-3.86)
Baseline^ viral load			
<10,000 c/mL	Referent	Referent	Referent
10,000-100,000c/mL	1.30 (0.83-2.02)	1.34 (0.86-2.08)	1.27 (0.81-1.98)
>100,000 c/mL	1.32 (0.85-2.07)	1.37 (0.88-2.15)	1.28 (0.82-2.01)
Missing/Unknown	1.77 (0.88-3.56)	1.85 (0.92-3.73)	1.81 (0.91-3.59)

IOM, Institute of Medicine; DHHS, Department of Health and Human Services

Multivariable models stratified by study site

^Baseline defined as value nearest antiretroviral therapy start date within a window of -180 to +14 days.

*IOM Retention Core Indicator based upon the HRSA HAB measure defined as 2 attended visits per 12 month period with >90 days between visits. Patients achieving this measure in each of the 12-month periods following ART initiation were classified as retained.

†DHHS Retention Core Indicator defined as at least 1 attended visit in each 6 month period during a 24-month measurement period, with ≥60 days between visits in adjacent 6 month periods.

Table 3. Frequency of missed (no show) clinic visits and mortality rates (deaths per 1,000 person-years follow-up) among patients classified as retained and not retained at 24-months following ART initiation according to IOM and DHHS core indicators at 5 CFAR Network of Clinical Systems (CNICS) sites, 2000-10.

Characteristic	Retained at 24-months by IOM core indicator* (n=2358)	Not Retained at 24-months by IOM core indicator* (n=1314)	Retained at 24-months by DHHS core indicator† (n=2166)	Not Retained at 24-months by DHHS core indicator† (n=1506)
Missed (no show) Visits at 24 months				
0 no show visits	861 (37%); 9.9	314 (24%); 15.4	827 (38%); 9.8	348 (23%); 15.0
1-2 no show visits	848 (36%); 15.3	566 (43%); 28.5	766 (35%); 14.4	648 (43%); 28.2
>2 no show visits	649 (28%); 24.9	434 (33%); 40.7	573 (26%); 23.8	510 (34%); 39.8

Data presented as n (%); deaths per 1,000 person-years follow-up
IOM, Institute of Medicine; DHHS, Department of Health and Human Services
*IOM Retention Core Indicator based upon the HRSA HAB measure defined as 2 attended visits per 12 month period with >90 days between visits. Patients achieving this measure in each of the 12-month periods following ART initiation were classified as retained.
†DHHS Retention Core Indicator defined as at least 1 attended visit in each 6 month period during a 24-month measurement period, with ≥60 days between visits in adjacent 6 month periods.

Table 4. Separate Cox proportional hazards models evaluating the association of missed (no show) clinic visits with long-term mortality among patients classified as retained at 24-months following ART initiation according to IOM and DHHS core indicators at 5 CFAR Network of Clinical Systems (CNICS) sites, 2000-10.

Characteristic	Retained at 24-months by IOM core indicator* (n=2358) HR (95% CI)	Retained at 24-months by DHHS core indicator† (n=2166) HR (95% CI)
Missed (no show) Visits at 24 months		
0 no show visits	Referent	Referent
1-2 no show visits	1.78 (1.17-2.70)	1.71 (1.10-2.65)
>2 no show visits	3.61 (2.35-5.55)	3.62 (2.30-5.68)
Age (per 10 years)	1.66 (1.42-1.94)	1.63 (1.38-1.92)
Race		
White	Referent	Referent
Black/African American	1.14 (0.80-1.61)	1.15 (0.80-1.66)
Other/Unknown	0.65 (0.31-1.36)	0.65 (0.29-1.43)
Gender		
Male	Referent	Referent
Female	0.69 (0.46-1.03)	0.75 (0.50-1.14)
Baseline^ CD4 count		
<50 cells/mm^3	1.80 (0.76-4.24)	1.49 (0.63-3.53)
50-199 cells/mm^3	1.38 (0.58-3.24)	1.23 (0.52-2.91)
200-349 cells/mm^3	0.93 (0.38-2.23)	0.78 (0.32-1.91)
350-500 cells/mm^3	0.92 (0.34-2.47)	0.92 (0.34-2.48)
>500 cells/mm^3	Referent	Referent
Missing/Unknown	3.31 (0.95-11.57)	2.44 (0.59-10.13)
Baseline^ viral load		
<10,000 c/mL	Referent	Referent
10,000-100,000c/mL	1.00 (0.58-1.75)	0.96 (0.53-1.73)
>100,000 c/mL	0.78 (0.44-1.37)	0.71 (0.39-1.29)
Missing/Unknown	1.62 (0.69-3.77)	1.42 (0.57-3.52)

IOM, Institute of Medicine; DHHS, Department of Health and Human Services
Multivariable models stratified by study site
^Baseline defined as value nearest antiretroviral therapy start date within a window of -180 to +14 days.
*IOM Retention Core Indicator based upon the HRSA HAB measure defined as 2 attended visits per 12 month period with >90 days between visits. Patients achieving this measure in each of the 12-month periods following ART initiation were classified as retained.
†DHHS Retention Core Indicator defined as at least 1 attended visit in each 6 month period during a 24-month measurement period, with ≥60 days between visits in adjacent 6 month periods.

Table 5. Separate Cox proportional hazards models evaluating the association of missed (no show) clinic visits with long-term mortality among patients classified as not retained at 24-months following ART initiation according to IOM and DHHS core indicators at 5 CFAR Network of Clinical Systems (CNICS) sites, 2000-10.

Characteristic	Not retained at 24-months by IOM core indicator* (n=1314) HR (95% CI)	Not retained at 24-months by DHHS core indicator† (n=1506) HR (95% CI)
Missed (no show) Visits at 24 months		
0 no show visits	Referent	Referent
1-2 no show visits	1.63 (0.98-2.72)	1.76 (1.08-2.85)
>2 no show visits	2.11 (1.26-3.51)	2.32 (1.43-3.77)
Age (per 10 years)	1.56 (1.34-1.83)	1.60 (1.38-1.86)
Race		
White	Referent	Referent
Black/African American	1.89 (1.29-2.76)	1.80 (1.27-2.57)
Other/Unknown	0.72 (0.33-1.57)	0.73 (0.35-1.52)
Gender		
Male	Referent	Referent
Female	1.16 (0.80-1.69)	1.10 (0.77-1.58)
Baseline^ CD4 count		
<50 cells/mm^3	3.58 (1.27-10.08)	3.86 (1.38-10.79)
50-199 cells/mm^3	2.65 (0.94-7.46)	2.63 (0.94-7.37)
200-349 cells/mm^3	1.53 (0.53-4.36)	1.62 (0.57-4.59)
350-500 cells/mm^3	1.13 (0.35-3.68)	1.02 (0.31-3.33)
>500 cells/mm^3	Referent	Referent
Missing/Unknown	0.89 (0.19-4.24)	1.29 (0.30-5.45)
Baseline^ viral load		
<10,000 c/mL	Referent	Referent
10,000-100,000c/mL	1.84 (0.87-3.91)	1.76 (0.89-3.47)
>100,000 c/mL	2.26 (1.06-4.82)	2.24 (1.13-4.41)
Missing/Unknown	2.32 (0.76-7.06)	2.29 (0.81-6.44)

IOM, Institute of Medicine; DHHS, Department of Health and Human Services
Multivariable models stratified by study site
^Baseline defined as value nearest antiretroviral therapy start date within a window of -180 to +14 days.
*IOM Retention Core Indicator based upon the HRSA HAB measure defined as 2 attended visits per 12 month period with >90 days between visits. Patients achieving this measure in each of the 12-month periods following ART initiation were classified as retained.
†DHHS Retention Core Indicator defined as at least 1 attended visit in each 6 month period during a 24-month measurement period, with ≥60 days between visits in adjacent 6 month periods.

Figure legend:

Figure 1. Kaplan-Meier survival curves for all-cause mortality among patients classified as retained and not retained at 24-months following ART initiation according to the IOM (panels a and b, respectively) and DHHS (panels c and d, respectively) core indicators stratified by missed (no show) clinic visits.

Figure 1a) Retained at 24 months according to IOM Core Indicator (n=2358)

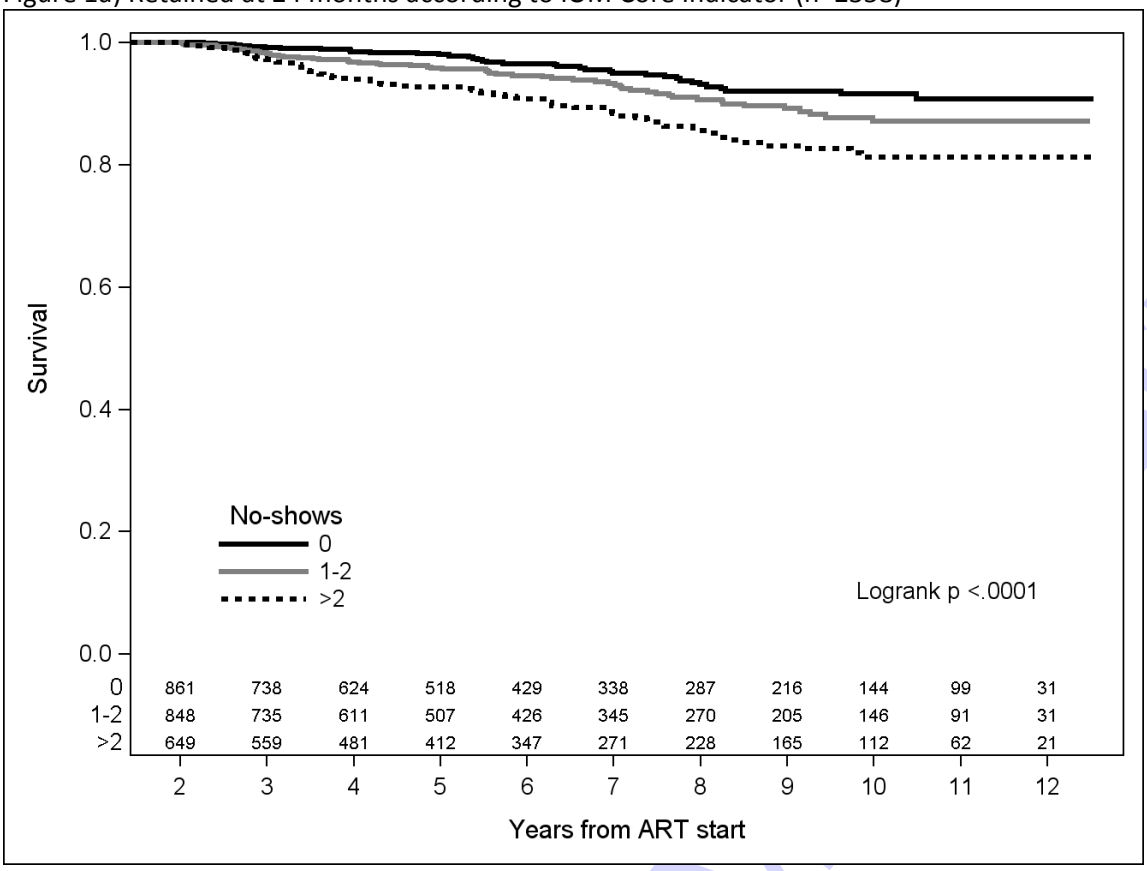


Figure 1b) Not retained at 24 months according to IOM Core Indicator (n=1314)

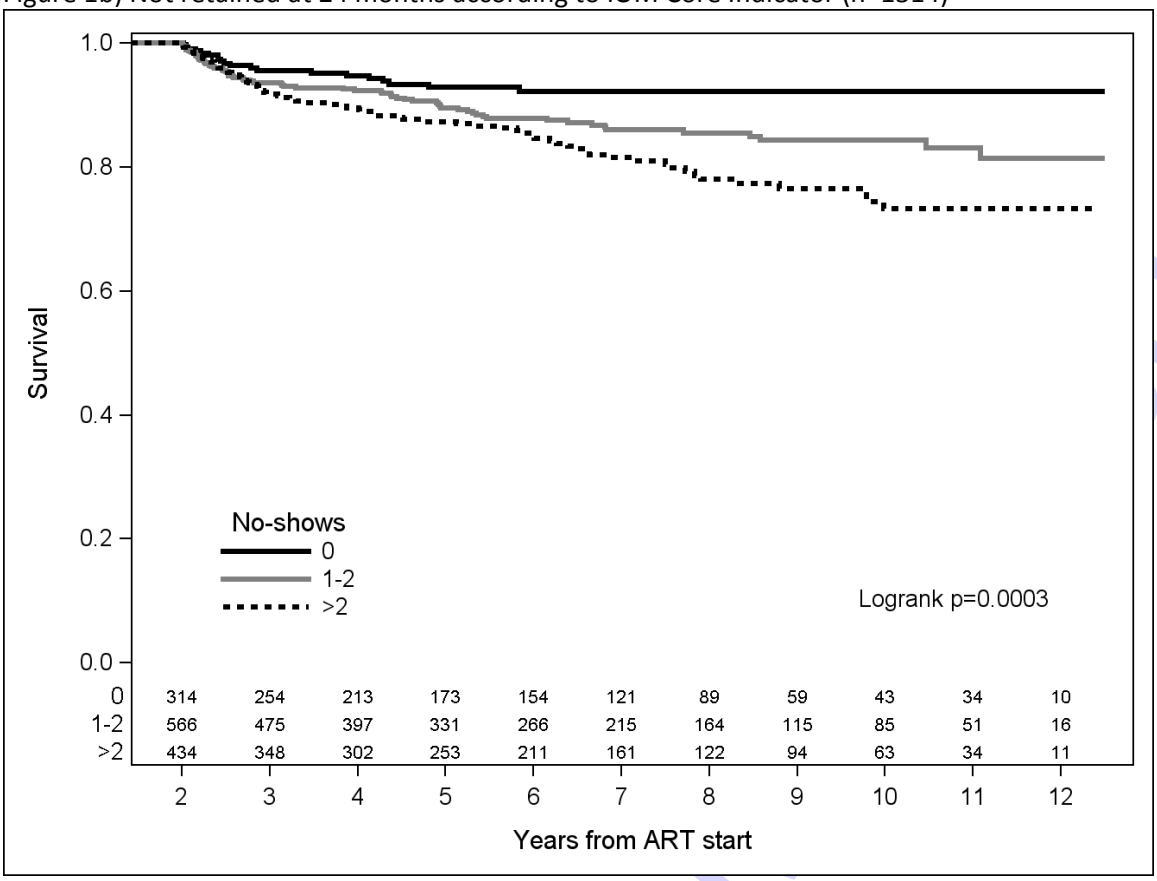


Figure 1c) Retained at 24 months according to DHHS Core Indicator (n=2166)

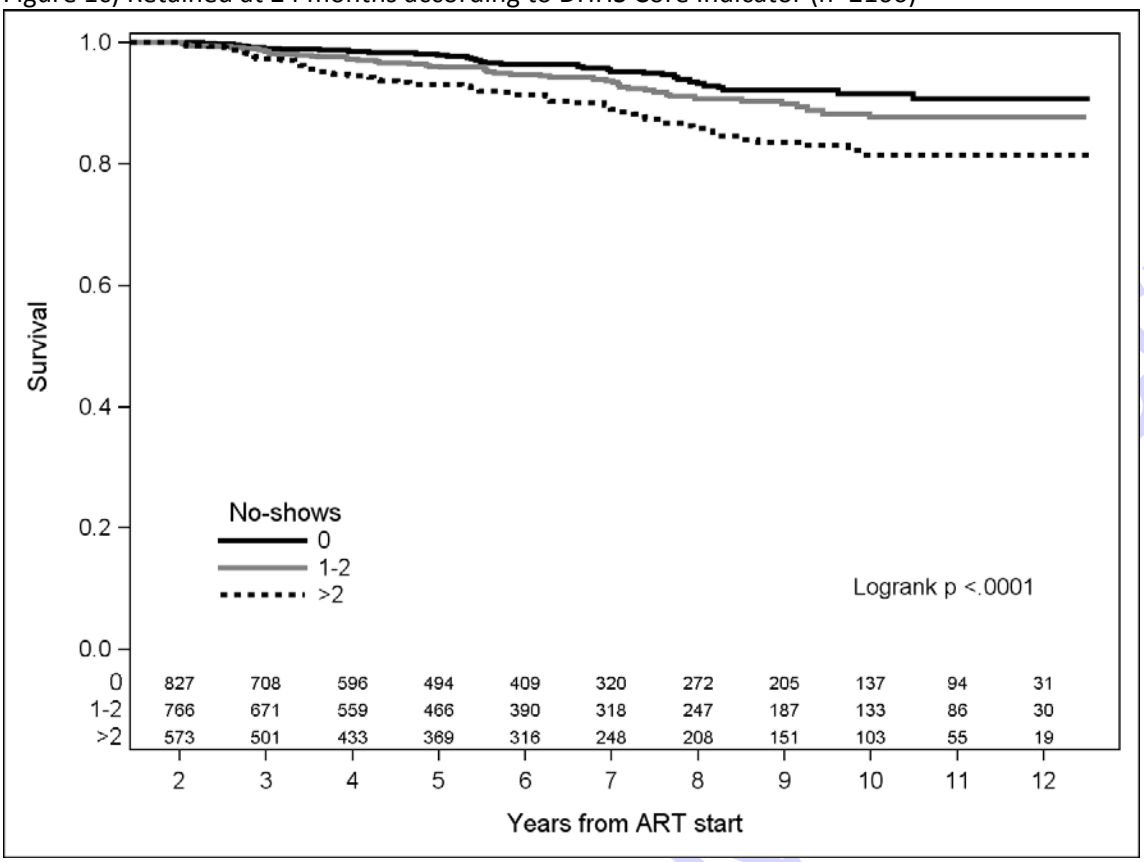
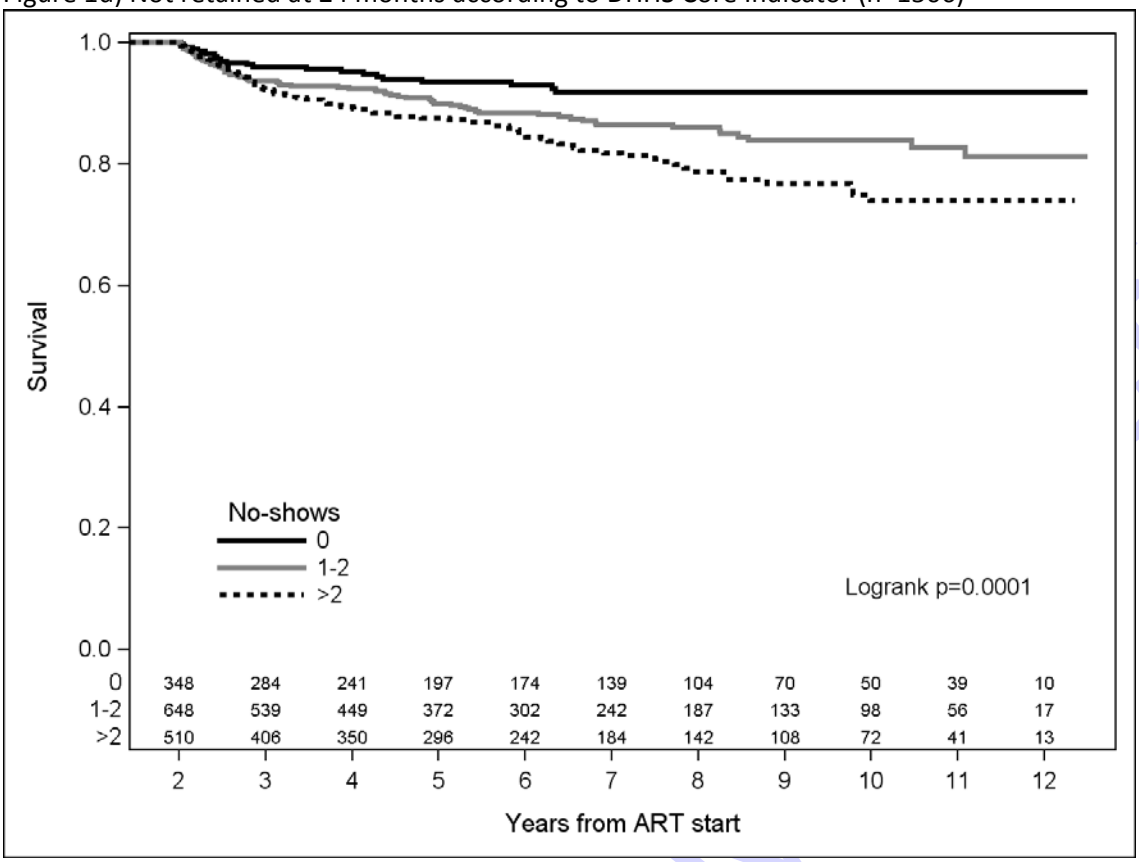


Figure 1d) Not retained at 24 months according to DHHS Core Indicator (n=1506)



Citations

1. Gardner EM, McLees MP, Steiner JF, Del Rio C, Burman WJ. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis* 2011,**52**:793-800.
2. Centers for Disease Control and Prevention (CDC). Vital Signs: HIV prevention through care and treatment — United States. MMWR Morb Mortal Wkly Rep 2011 Dec 2; 60:1618.
3. Centers for Disease Control and Prevention. HIV in the United States: The Stages of Care. Available at: http://www.cdc.gov/nchhstp/newsroom/docs/2012/Stages-of-CareFactSheet-508.pdf. Last accessed 3 February 2013.
4. Greenberg AE, Hader SL, Masur H, Young AT, Skillicorn J, Dieffenbach CW. Fighting HIV/AIDS in Washington, D.C. *Health Aff (Millwood)* 2009,**28**:1677-1687.
5. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N*, et al.* Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011,**365**:493-505.
6. Thompson MA, Aberg JA, Hoy JF, Telenti A, Benson C, Cahn P*, et al.* Antiretroviral treatment of adult HIV infection: 2012 recommendations of the International Antiviral Society-USA panel. *JAMA* 2012,**308**:387-402.
7. Das M, Chu PL, Santos GM, Scheer S, Vittinghoff E, McFarland W*, et al.* Decreases in community viral load are accompanied by reductions in new HIV infections in San Francisco. *PLoS One* 2010,**5**:e11068.
8. Hall HI, Gray KM, Tang T, Li J, Shouse L, Mermin J. Retention in care of adults and adolescents living with HIV in 13 U.S. areas. *J Acquir Immune Defic Syndr* 2012,**60**:77-82.
9. Mugavero MJ, Amico KR, Horn T, Thompson MA. The state of engagement in HIV care in the United States: from cascade to continuum to control. *Clin Infect Dis* 2013,**57**:1164-1171.
10. Horstmann E, Brown J, Islam F, Buck J, Agins BD. Retaining HIV-infected patients in care: Where are we? Where do we go from here? *Clin Infect Dis* 2010,**50**:752-761.
11. White House Office of National AIDS Policy. National HIV/AIDS Strategy for the United States. Washington, DC: The White House; July 13, 2010. Available at: http://www.whitehouse.gov/sites/default/files/uploads/NHAS.pdf2.
12. The White House. Executive Order -- HIV Care Continuum Initiative. Available at: http://www.whitehouse.gov/the-press-office/2013/07/15/executive-order-hiv-care-continuum-initiative. Last accessed: 1 November 2013.
13. Institute of Medicine. Monitoring HIV Care in the United States: Indicators and Data Systems. Available at: http://www.iom.edu/Reports/2012/Monitoring-HIV-Care-in-the-United-States.aspx, Last accessed: 3 February 2013.
14. United States Department of Health and Human Services HIV Core Indicators. Available at: http://blog.aids.gov/2012/08/secretary-sebelius-approves-indicators-for-monitoring-hhs-funded-hiv-services.html. Last accessed: 3 February 2013.
15. Thompson MA, Mugavero MJ, Amico KR, Cargill VA, Chang LW, Gross R*, et al.* Guidelines for Improving Entry Into and Retention in Care and Antiretroviral Adherence for Persons With HIV: Evidence-Based Recommendations From an International Association of Physicians in AIDS Care Panel. *Ann Intern Med* 2012.
16. Mugavero MJ, Westfall AO, Zinski A, Davila J, Drainoni ML, Gardner LI*, et al.* Measuring retention in HIV care: the elusive gold standard. *J Acquir Immune Defic Syndr* 2012,**61**:574-580.
17. Yehia BR, Fleishman JA, Metlay JP, Korthuis PT, Agwu AL, Berry SA*, et al.* Comparing different measures of retention in outpatient HIV care. *AIDS* 2012,**26**:1131-1139.
18. Kitahata MM, Rodriguez B, Haubrich R, Boswell S, Mathews WC, Lederman MM*, et al.* Cohort profile: the Centers for AIDS Research Network of Integrated Clinical Systems. *Int J Epidemiol* 2008,**37**:948-955.
19. Giordano TP, Gifford AL, Clinton White A, Suarez-Almazor ME, Rabeneck L, Hartman C*, et al.* Retention in Care: A Challenge to Survival with HIV Infection. *Clin Infect Dis* 2007,**44**:1493-1499.
20. Horberg MA, Hurley LB, Silverberg MJ, Klein DB, Quesenberry CP, Mugavero MJ. Missed office visits and risk of mortality among HIV-infected subjects in a large healthcare system in the United States. *AIDS Patient Care STDS* 2013,**27**:442-449.
21. Mugavero MJ, Lin HY, Willig JH, Westfall AO, Ulett KB, Routman JS*, et al.* Missed visits and mortality among patients establishing initial outpatient HIV treatment. *Clin Infect Dis* 2009,**48**:248-256.

22. Sweeney P, Gardner LI, Buchacz K, Garland PM, Mugavero MJ, Bosshart JT*, et al.* Shifting the paradigm: using HIV surveillance data as a foundation for improving HIV care and preventing HIV infection. *Milbank Q* 2013,**91**:558-603.
23. Higa DH, Marks G, Crepaz N, Liau A, Lyles CM. Interventions to improve retention in HIV primary care: a systematic review of U.S. studies. *Curr HIV/AIDS Rep* 2012,**9**:313-325.