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Michael J. Mugavero
University of Alabama

Et al.

Missed Visits and Mortality among Patients Establishing Initial Outpatient HIV Treatment

Michael J. Mugavero,[1] Hui-Yi Lin,[2] James H. Willig,[1] Andrew O. Westfall ,[4] Kimberly B. Ulett,[1] Justin S. Routman,[1] Sarah Abroms,[1] James L. Raper,[1] Michael S. Saag,[1] and Jeroan J. Allison[3]

Divisions of [1]Infectious Diseases, [2]Medical Statistics Section, and [3]General Internal Medicine, Department of Medicine, and [4]Department of Biostatistics, University of Alabama at Birmingham

Background. Dramatic increases in the number of patients requiring linkage to treatment for human immunodeficiency virus (HIV) infection are anticipated in response to updated Centers for Disease Control and Prevention HIV testing recommendations that advocate routine, opt-out HIV testing.

Methods. A retrospective analysis nested within a prospective HIV clinical cohort study evaluated patients who established initial outpatient treatment for HIV infection at the University of Alabama at Birmingham 1917 HIV/AIDS Clinic from 1 January 2000 through 31 December 2005. Survival methods were used to evaluate the impact of missed visits during the first year of care on subsequent mortality in the context of other baseline sociodemographic, psychosocial, and clinical factors. Mortality was ascertained by query of the Social Security Death Index as of 1 August 2007.

Results. Among 543 study participants initiating outpatient care for HIV infection, 60% missed a visit within the first year. The mortality rate was 2.3 deaths per 100 person-years for patients who missed visits, compared with 1.0 deaths per 100 person-years for those who attended all scheduled appointments during the first year after establishing outpatient treatment ($P = .02$). In Cox proportional hazards analysis, higher hazards of death were independently associated with missed visits (hazard ratio, 2.90; 95% confidence interval, 1.28–6.56), older age (hazard ratio, 1.58 per 10 years of age; 95% confidence interval, 1.12–2.22), and baseline $CD4^+$ cell count <200 cells/mm^3 (hazard ratio, 2.70; 95% confidence interval, 1.00–7.30).

Conclusions. Patients who missed visits within the first year after initiating outpatient treatment for HIV infection had more than twice the rate of long-term mortality, compared with those patients who attended all scheduled appointments. We posit that early missed visits are not causally responsible for the higher observed mortality but, rather, identify those patients who are more likely to exhibit health behaviors that portend increased subsequent mortality.

In September 2006, the US Centers for Disease Control and Prevention (CDC) released updated HIV testing recommendations that advocated routine, opt-out HIV testing for adults in all health care settings [1]. The rationale for this paradigm shift from risk-based, opt-in testing to routine, opt-out testing included the high proportion of HIV-infected individuals who are unaware of their status, the common occurrence of late diagnosis with advanced disease progression, and the consistently high number of incident cases of HIV infection that are reported annually despite extensive prevention efforts. An estimated 25% of individuals living with HIV infection in the United States are unaware of their HIV infection status [2]. Furthermore, late presentation is frequently observed, with more than one-half of patients with newly diagnosed infection entering care with initial $CD4^+$ cell counts <200 cells/mm^3 [3–7]. The updated recommendations aim to reduce the number of infected persons who are unaware of their infection status and to facilitate earlier diagnosis of HIV infection [1], which may ultimately benefit the health of individuals, as well as the public health, through reduced transmission and a reduction in the number of secondary infections.

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Reprints or correspondence: Dr. Michael J. Mugavero, CCB 142, 908 20th St. South, Birmingham, AL 35294-2050 (mmugavero@uab.edu).

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Dramatic increases in the number of individuals in need of HIV treatment are anticipated in response to the implementation of the updated CDC HIV testing recommendations [8, 9]. The recommendations emphasize the importance of linkage to clinical and preventive services for patients with newly diagnosed infection [1]. Studies show that 20%–40% of patients with recently diagnosed HIV infection do not attend an outpatient clinic visit within 6 months after receipt of their diagnosis [10, 11]. Among those who successfully initiate outpatient care, missed visits and loss to follow-up during the year after attending a first HIV clinic visit are common and are associated with delays in the receipt of antiretroviral medications [7, 12, 13]. However, to our knowledge, no published study has evaluated the relationship between missed visits in the first year of HIV care and long-term survival. We hypothesized that patients who missed visits in the year after establishing outpatient HIV treatment would have higher subsequent mortality in the context of other baseline sociodemographic, psychosocial, and clinical factors that are associated with survival.

PATIENTS AND METHODS

Cohort description. The University of Alabama at Birmingham (UAB) 1917 HIV/AIDS Clinic Cohort Observational Database Project (UAB 1917 Clinic Cohort) is described in detail elsewhere [14–16]. Here, we conduct a retrospective cohort study nested in the UAB 1917 Clinic Cohort to evaluate the impact of missed visits on long-term survival among patients establishing initial outpatient HIV treatment.

Eligibility criteria. Patients who attended an initial primary HIV care visit at the UAB 1917 Clinic from 1 January 2000 through 31 December 2005 and had received no prior outpatient HIV treatment at another facility were included in this analysis. Medical records of patients attending a first visit at the UAB 1917 Clinic during the study period were reviewed independently by 2 abstractors (J.S.R. and S.A.) to determine whether a patient had previously received HIV treatment elsewhere and was therefore ineligible for study participation. Discrepancies in reporting (<2% of records) were arbitrated by 2 physician HIV care providers at the UAB 1917 Clinic (M.J.M. and J.H.W.). These criteria were employed because of our interest in studying a homogeneous sample of patients who were establishing initial outpatient HIV treatment, while excluding patients who had previously received care at other facilities (who represent a different sample group). We were interested in evaluating the impact of missed visits within the first year after establishing care (exposure) on long-term survival (outcome); therefore, patients who died within 1 year after their initial visit were excluded from analyses, because they did not have appointment attendance data for the entire exposure period.

Measures. Appointment attendance during the first year after establishing outpatient care was the primary independent variable of interest. Missed visit status was determined for all study participants by evaluating appointment attendance records for 365 days after an initial attended primary HIV care visit. Urgent care and subspecialty visits (e.g., dermatology) at the clinic were excluded. Appointment status at the UAB 1917 Clinic is managed with a Web-based software program that is updated daily. Consistent with previous studies [17–20], only missed visits for which a patient did not call the clinic to cancel or reschedule (i.e., "no show" visits) were included in the missed visit measure. Appointments that were cancelled by the clinic, those that a patient called to cancel in advance, or those that were cancelled because the patient was hospitalized are not included in the missed visit measure. Missed visit status was recorded as a dichotomous measure, with patients characterized as having no missed visits or $\geqslant$1 missed visit during the first year of outpatient HIV treatment.

Other covariates were selected a priori and included sociodemographic (age, sex, race, HIV risk group, and insurance status), psychosocial (affective mental health, substance abuse, and alcohol abuse disorders), and clinical measures (baseline $CD4^+$ cell count, plasma HIV RNA level, and receipt of antiretroviral therapy during the first year of care). All measures were determined by query of the UAB 1917 Clinic Cohort Database, which includes psychosocial measures that are captured from diagnosis lists in patients' medical records. All cause mortality, which was the primary outcome measure, was ascertained by an electronic query of the Social Security Death Index performed on 1 August 2007.

Statistical analysis. Descriptive statistics were performed for all study variables to evaluate distributions and to ensure that assumptions of statistical tests to be used were met. Unadjusted analyses using $\chi 2$ tests and logistic regression and multivariable logistic regression analysis controlling for the aforementioned covariates were used to evaluate factors associated with missing a primary HIV care clinic visit during the first year after establishing initial outpatient care. The discriminative capacity and fit of the multivariable model were assessed by the C-statistic and Hosmer-Lemeshow goodness-of-fit test, respectively.

A Kaplan-Meier plot was used to evaluate long-term survival among patients according to missed visit status during the first year of outpatient HIV care. Unadjusted and adjusted Cox proportional hazards models were used to evaluate factors associated with long-term survival. Because of the relatively modest number of deaths relative to the number of covariates in the primary Cox model, a sensitivity analysis was conducted that used propensity score methods [21]. In brief, a propensity score for "missed visit" was determined for all study participants with use of the multivariable logistic regression model

to evaluate missed visit status in the year of HIV treatment. This approach serves to combine covariates into a single propensity score and thereby reduces the number of variables and addresses potential concerns of model over-fitting. Next, a Cox proportional hazards model was used to evaluate the relationship between missed visit status and long-term survival while adjusting for propensity score and for antiretroviral medication receipt during the first year of treatment. All analyses were conducted using SAS, version 9.0 (SAS). *P* values <.05 were considered to be statistically significant.

RESULTS

During the study period, 567 (49%) of 1165 patients who attended a first primary HIV care visit at the UAB 1917 Clinic had not previously received HIV care elsewhere and were establishing initial outpatient HIV treatment. Twenty-four patients (4%) died within 1 year after their initial visit, leaving 543 patients who were included in statistical analyses. The sociodemographic, psychosocial, and clinical characteristics of the study sample (543 patients) were largely similar to those of the overall population (1165 patients) (data not shown). Among the 543 study participants, 325 patients (60%) had a missed visit within the first year of care (mean no. of missed visits ± SD, 1.8 ± 1.1), whereas 218 patients (40%) attended all scheduled appointments. Thirty-two (10%) of the patients with missed visits and 10 (5%) of the patients with perfect appointment attendance died during longitudinal follow-up (figure 1). Among the 325 patients with missed visits within the first year of care, a similar mean number of missed visits (±SD) were observed among the 32 patients who died (1.9 ± 1.6 missed visits) and the 293 patients who survived (1.8 ± 1.1 missed visits) during follow-up.

The baseline characteristics of the 543 study participants include a mean age (±SD) of 37.7 ± 9.4years; 25% of the patients were female, and 54% were black (table 1). The HIV risk group was men who have sex with men in 52% of the patients, heterosexual transmission in 40%, and injection drug use in 8%. At initial presentation for care, one-half of the study patients lacked private health insurance (15% had public insurance, and 35% were uninsured). Affective mental health, substance abuse, and alcohol abuse disorders were documented in 48%, 26%, and 20% of patients, respectively. The mean (±SD) baseline HIV RNA load was 4.4 ± 1.1 $\log_{10}$ copies/mL; 38% of patients had a baseline $CD4^+$ cell count <200 cells/mm^3, and 67% were prescribed antiretroviral therapy within the first year of care. Compared with the 543 patients who were included in the analysis, the 24 patients who died within the first year were more likely to have baseline $CD4^+$ cell counts <200 cells/mm^3 ($P < .01$), lack private health insurance ($P < .01$), and belong to an HIV risk group other than men who have sex with men ($P < .01$; data not shown).

Factors associated with missed visits within the first year of care. In unadjusted analyses, missed visits within the first year of HIV care were more common among younger patients, female patients, black patients, HIV risk groups other than men who have sex with men, patients lacking private health insurance, and patients with substance abuse disorders (table 2). In multivariable logistic regression analysis, missed visits were associated with younger age (OR, 0.81 per 10 years of age, 95% CI, 0.66–0.99 per 10 years of age), black race (OR, 2.74; 95% CI, 1.77–4.23), and having public health insurance (OR, 2.09; 95% CI, 1.10- 3.96); they were inversely associated with a baseline $CD4^+$ cell count of 200–350 cells/mm^3 (vs. ⩾350 cells/mm^3; OR, 0.59; 95% CI, 0.37–0.92) (table 2). Propensity scores for missed visits were determined for each study participant

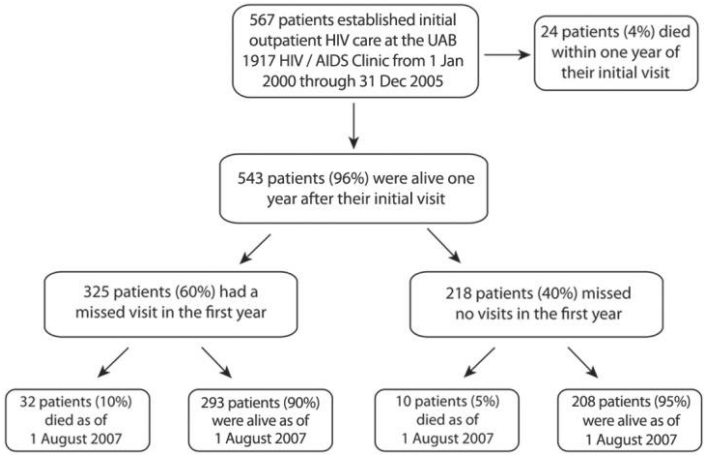

Figure 1. Short-term (1 year) and long-term vital status of 567 HIV-infected patients establishing initial outpatient HIV care at the University of Alabama at Birmingham (UAB) 1917 HIV/AIDS Clinic from 1 January 2000 through 31 December 2005.

Table 1. Baseline characteristics of 543 patients who were alive 1 year after establishing initial outpatient HIV care at the University of Alabama at Birmingham 1917 HIV/AIDS Clinic from 1 January 2000 through 31 December 2005.

Variable	Patients (n = 543)
Age, mean years ± SD (range)	37.7 ± 9.4 (19–70)
Sex	
Male	410 (75.5)
Female	133 (24.5)
Race	
White	250 (46.0)
Black	293 (54.0)
HIV infection risk factor	
Men who have sex with men	277/537 (51.6)
Heterosexual sex	215/537 (40.0)
Injection drug use	45/537 (8.4)
Health insurance	
Private	273 (50.3)
Public	79 (14.6)
None	191 (35.2)
Affective mental health disorder	
No	280 (51.6)
Yes	263 (48.4)
Substance abuse	
No	401 (73.8)
Yes	142 (26.1)
Alcohol abuse	
No	437 (80.5)
Yes	106 (19.5)
Baseline $CD4^+$ cell count	
<200 cells/mm^3	205/537 (38.2)
200–350 cells/mm^3	95/537 (17.7)
⩾350 cells/mm^3	237/537 (44.1)
Baseline viral load, $\log_{10}$ copies/mL	4.4 ± 1.1
Missed visit in first year[a]	
No	218 (40.1)
Yes	325 (59.8)
Antiretroviral therapy initiated within the first year of treatment	
No	177 (32.6)
Yes	366 (67.4)

NOTE. Data are no. (%) of patients, unless otherwise indicated. Of 567 patients who established initial outpatient HIV care during this period, 543 (96%) were alive 1 year after the first clinic visit.

[a] Only those missed visits for which patients did not notify the clinic in advance that they would not attend their appointment were included in this measure ("no show" visits). Appointments cancelled by a patient in advance, those scheduled while a patient was hospitalized, and those cancelled by the clinic were not included in the missed visit measure.

using this multivariable model and were subsequently employed in the long-term survival sensitivity analysis.

Factors associated with long-term survival. Kaplan Meier survival analysis revealed lower survival rates for patients who missed a visit within the year after establishing initial outpatient HIV treatment ($P = .02$) (figure 2). Observed mortality was 2.3 deaths per 100 patient-years of follow-up for patients who missed a visit, compared with 1.0 deaths per 100 patient-years of follow-up for those who attended all clinic visits during the first year of HIV care. In univariate survival analyses, older patients, patients with public health insurance, and patients who missed a visit within the first year of care had higher hazards of death (table 3). Multivariable Cox proportional hazards analysis revealed higher hazards of death among older patients (hazard ratio [HR], 1.58 per 10 years of age; 95% CI, 1.12–2.22 per 10 years of age), patients with baseline $CD4^+$ cell

Table 2. Factors associated with missing an outpatient HIV clinic appointment within the first year of care among 543 patients who were alive 1 year after establishing initial outpatient HIV care at the University of Alabama at Birmingham 1917 HIV/AIDS Clinic, 2000–2005.

Variable	Missed visit within the first year of care: No (n = 218)	Missed visit within the first year of care: Yes (n = 325)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]
Age, mean years ± SD	38.9 ± 9.6	36.9 ± 9.2	**0.79 (0.66–0.95)**[b]	**0.81 (0.66–0.99)**[b]
Sex				
Male	180 (82.6)	230 (70.8)	1.0	1.0
Female	38 (17.4)	95 (29.2)	**1.96 (1.28–2.99)**	1.11 (0.62–1.98)
Race				
White	134 (61.5)	116 (35.7)	1.0	1.0
Black	84 (38.5)	209 (64.3)	**2.87 (2.02–4.10)**	**2.74 (1.77–4.23)**
HIV infection risk factor				
Men who have sex with men	133/217 (61.3)	144/320 (45.0)	1.0	1.0
Heterosexual sex	72/217 (33.2)	143/320 (44.7)	**1.83 (1.27–2.65)**	1.23 (0.73–2.06)
Injection drug use	12/217 (5.5)	33/320 (10.3)	**2.54 (1.26–5.12)**	1.82 (0.78–4.25)
Health insurance				
Private	129 (59.2)	144 (44.3)	1.0	1.0
Public	18 (8.2)	61 (18.8)	**3.04 (1.71–5.41)**	**2.09 (1.10–3.96)**
None	71 (32.6)	120 (36.9)	**1.51 (1.04–2.21)**	1.23 (0.81–1.86)
Affective mental health disorder				
No	105 (48.2)	175 (53.9)	1.0	1.0
Yes	113 (51.8)	150 (46.1)	0.80 (0.57–1.12)	0.91 (0.61–1.35)
Substance abuse				
No	174 (79.8)	227 (69.9)	1.0	1.0
Yes	44 (20.2)	98 (30.1)	**1.71 (1.14–2.56)**	1.60 (0.93–2.74)
Alcohol abuse				
No	174 (79.8)	263 (80.9)	1.0	1.0
Yes	44 (20.2)	62 (19.1)	0.93 (0.61–1.43)	0.82 (0.50–1.34)
Baseline viral load, $\log_{10}$ copies/mL	4.4 ± 1.1	4.3 ± 1.1	0.95 (0.81–1.11)	1.01 (0.84–1.20)
Baseline CD4$^+$ cell count				
⩾350 cells/mm^3	73/215 (34.0)	132/322 (41.0)	1.0	1.0
200–350 cells/mm^3	36/215 (16.7)	59/322 (18.3)	0.68 (0.47–1.00)	**0.59 (0.37–0.92)**
<200 cells/mm^3	106/215 (49.3)	131/322 (40.7)	0.91 (0.25–1.50)	0.76 (0.44–1.31)

NOTE. Data are no. (%) of patients, unless otherwise indicated. Values in bold are statistically significant ($P < .05$). Only those missed visits for which patients did not notify the clinic in advance that they would not attend their appointment were included in this measure ("no show" visits). Appointments cancelled by a patient in advance, those scheduled while a patient was hospitalized, and those cancelled by the clinic were not included in the missed visit measure.

[a] Multivariable logistic regression model characteristics with a Hosmer-Lemeshow goodness-of-fit P value of .19 and a C-statistic of 0.71

[b] Per 10 years of age.

counts <200 cells/mm^3 (HR, 2.70; 95% CI, 1.00–7.30), and patients who missed a visit within the first year of treatment (HR, 2.90; 95% CI, 1.28–6.56). Similar hazards of death were observed in patients with 1 missed visit and ⩾2 missed visits, relative to patients who had no missed visits during the first year of outpatient treatment (data not shown). No other sociodemographic or psychosocial factors were significantly associated with long-term mortality, and receipt of antiretroviral therapy within the first year of care was not associated with reduced hazards of death in subsequent years (table 3). Sensitivity analysis using propensity score methods yielded findings similar to those obtained by the primary analysis, with missed visits during the first year of care increasing the hazards of long-term mortality (HR, 2.52; 95% CI, 1.15–5.52) while controlling for propensity for a missed visit and receipt of antiretroviral therapy (table 3).

DISCUSSION

Missed primary HIV care visits in the year after establishing initial outpatient treatment were associated with subsequent mortality, even when controlling for baseline CD4$^+$ cell count

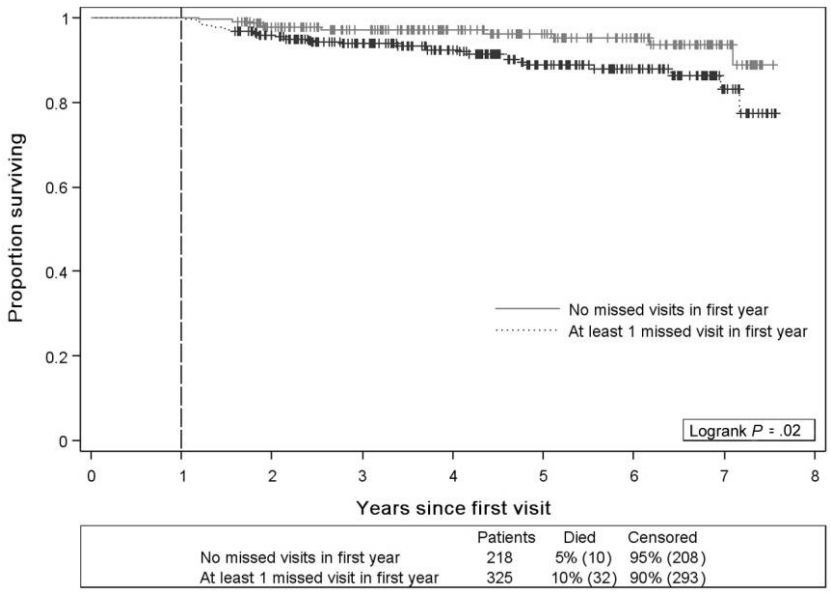

Figure 2. Kaplan-Meier survival plot for patients establishing initial outpatient HIV care at the University of Alabama at Birmingham (UAB) 1917 HIV/AIDS Clinic from 1 January 2000 through 31 December 2005, categorized by missed visit status during the first year of care.

and receipt of antiretroviral therapy within the first year. Mortality rates were >2 times higher for patients with missed visits, compared with mortality rates for patients who attended all scheduled appointments during the first year of care (2.3 vs. 1.0 deaths per 100 patient-years of follow-up; $P = .02$). Although a modest absolute difference in mortality rate was observed, these findings may have profound public health implications. Because tens of thousands of patients with newly diagnosed infection require linkage to HIV care in the United States annually [22], extrapolation of our findings to the level of the general population results in considerable mortality, particularly in light of the high proportion of patients who miss visits shortly after establishing outpatient HIV treatment [7, 12].

We posit that missed visits during the first year of care are not causally responsible for reduced long-term survival but, rather, may identify a subset of patients whose health behaviors portend increased mortality. We speculate that worse subsequent retention in care and lower antiretroviral medication adherence among those with missed visits ultimately places them at increased risk of death. Accordingly, missed visits in patients establishing initial outpatient treatment may serve as a marker in identifying individuals at risk for poor future health outcomes.

The current study advances earlier research by focusing on patients who are establishing an initial linkage to outpatient HIV treatment, which is a vulnerable population that has not been well evaluated previously and is expected to increase dramatically in coming years [8, 9]. Studies assessing survival among patients with HIV infection typically focus on individuals who are initiating antiretroviral therapy or who are participating in ongoing cohort studies [23–32]. Many new patients miss appointments and/or are lost to follow-up shortly after attending an initial clinic visit, and they often fail to initiate antiretroviral therapy as a result [7, 12, 13]. Furthermore, antiretroviral medications may not be indicated in patients who are establishing care based on baseline $CD4^+$ cell counts and plasma HIV RNA levels [33]. Among our sample, one-third of patients did not receive antiretroviral therapy within the first year of outpatient HIV treatment, which is a group that would not have been evaluated if the current study employed inclusion criteria that were based on initiation of antiretroviral therapy. Therefore, the evaluation of missed visits and other factors associated with survival among patients who initiate outpatient HIV care complements earlier research and provides novel insight into an understudied group. Our finding that 60% of patients missed at least 1 visit within the first year of care underscores the importance of the higher observed mortality in this group. These results can be applied in clinical practice to identify a priority population and to inform the development of focused interventions designed to improve long-term survival in new patients initiating outpatient HIV treatment.

Similar to the association observed in this study between missed visits and mortality in patients who are establishing HIV care, a relationship was recently reported between retention in care and survival among patients starting antiretroviral therapy [23, 30]. In a study of HIV-infected male patients who received treatment through the US Department of Veterans Affairs system, Giordano et al. [23] also found a significant relationship between retention in care and antiretroviral medication ad-

Table 3. Factors associated with long-term survival among 543 patients who were alive 1 year after establishing initial outpatient HIV care at the University of Alabama at Birmingham 1917 HIV/AIDS Clinic, 2000–2005.

Analysis, variable	Univariate hazard ratio (95% CI)	Multivariable hazard ratio (95% CI)[a]
Primary analysis		
Age (per 10 years)	**1.61 (1.21–2.17)**	**1.58 (1.12–2.22)**
Female sex	1.11 (0.56–2.20)	1.20(0.49–2.96)
Black race	1.05 (0.57–1.93)	0.73 (0.33–1.64)
HIV infection risk factor		
Men who have sex with men	1.0	1.0
Heterosexual sex	1.23 (0.62–2.43)	0.91 (0.38–2.20)
Injection drug use	2.06 (0.81–5.23)	1.05 (0.33–3.31)
Health insurance		
Private	1.0	1.0
Public	**2.11 (1.03–4.32)**	1.30 (0.54–3.14)
None	0.79 (0.37–1.68)	0.74 (0.32–1.71)
Affective mental health disorder	0.80 (0.44–1.47)	0.80 (0.39–1.62)
Substance abuse	1.80 (0.96–3.35)	2.08 (0.86–5.07)
Alcohol abuse	1.12 (0.53–2.35)	0.75 (0.31–1.84)
Baseline $CD4^+$ cell count		
$\geq$350 cells/mm^3	1.0	1.0
200–350 cells/mm^3	1.32 (0.48–3.65)	1.49 (0.47–4.67)
<200 cells/mm^3	2.00 (0.95–4.20)	**2.70 (1.00–7.30)**
Baseline viral load (log_{10})	1.11 (0.84–1.48)	1.02 (0.75–1.39)
Missed visit in first year	**2.34 (1.15–4.77)**	**2.90 (1.28–6.56)**
Antiretroviral therapy initiated within first year of treatment	1.00 (0.51–1.93)	0.64 (0.25–1.62)
Propensity score sensitivity analysis		
Missed visit within the first year of treatment	**2.34 (1.15–4.77)**	**2.52 (1.15–5.52)**
Antiretroviral therapy initiated within the first year of treatment	1.00 (0.51–1.93)	1.18 (0.58–2.41)
Propensity score for missed visit (per 10%)	1.05 (0.87–1.26)	0.98 (0.80–1.19)

NOTE. Data in bold are statistically significant ($P < .05$).

[a] In the primary analysis, the Cox proportional hazards model (i.e., multivariable hazard ratio) includes the variables listed in the table (age, sex, race, HIV infection risk factor, health insurance, affective mental health disorder, substance abuse, alcohol abuse, baseline $CD4^+$ cell count, baseline viral load, missed visit status during the first year of treatment, and antiretroviral therapy receipt within the first year of treatment). In the sensitivity analysis, the Cox proportional hazards model includes missed visit status during the first year of treatment, propensity score for missed visit during the first year of treatment (derived from the multivariable logistic regression model in table 2, which included age, sex, race, HIV infection risk factor, health insurance, affective mental health disorder, substance abuse, alcohol abuse, baseline $CD4^+$ cell count, and baseline viral load), and antiretroviral therapy receipt within the first year of treatment.

herence, supporting our hypothesis that missed visits may identify patients who are at risk for worse outcomes during subsequent care.

In addition to those individuals with missed outpatient appointments, older patients and those with more-advanced HIV infection when establishing outpatient treatment had higher mortality rates in our study. These findings are important, because older patients account for an increasing proportion of patients with newly diagnosed infection who are establishing HIV care [22]. In addition, recent studies have found that >50% of patients with newly diagnosed HIV infection who present for initial care have baseline $CD4^+$ cell counts that are <200 cells/mm^3 [3–6], which is a characteristic that was associated with higher rates of observed mortality in our study. Part of the rationale behind the updated CDC HIV testing recommendations is the desire to facilitate earlier diagnosis of HIV infection and linkage to HIV care before progression to advanced disease [1]. Our study suggests that there may be long-term benefits to patient survival if these recommendations are successfully implemented and result in improved timeliness of HIV infection diagnosis. Accordingly, our findings provide empirical evidence to support the CDC HIV testing recommendations and may serve as a call to action for health care providers.

Of note, receipt of antiretroviral therapy during the first year of care was not associated with subsequent mortality. After antiretroviral treatment initiation, continuous receipt of medication is necessary to achieve optimal clinical outcomes. Importantly, initial receipt of antiretroviral medication does not necessarily translate to subsequent long-term treatment; pa-

tients are often lost to follow-up after establishing HIV care [7, 12, 13]. It is possible that patients with missed visits within the first year of HIV care had worse subsequent retention and resultant poor longitudinal receipt of and adherence to antiretroviral medications, which contributed to the higher observed long-term mortality in this group.

Our study also contributes additional knowledge regarding engagement in care among HIV-infected individuals, which is an area of growing interest [34]. In this study, there were strong associations between missed visits and younger age, black race, and public health insurance. Previously, we found that these sociodemographic groups were less likely to attend an initial clinic visit and establish care at our treatment center after calling to schedule an appointment [15]. Similarly, others have reported that missed visits were more common in these groups, which bear a growing and disproportionate burden of the US HIV infection epidemic [17, 18, 22, 35].

Formative research is needed to better understand the barriers and facilitators of clinic attendance and use of services, such that informed interventions may be developed to improve the initial linkage and subsequent retention of infected individuals in outpatient HIV care. Case management and patient navigation models hold promise and may link patients with community resources and provide social support, as well as foster problem-solving skills and build self-efficacy through strength-based approaches that enable patients to remain better engaged in care [11, 36]. The impact of these interventions on long-term survival remains to be seen. Successful interventions may have important implications not only for individual patients but also for public health and secondary HIV infection prevention efforts. Patients who are engaged in treatment may benefit from prevention messages and reduce their risk transmission behaviors [37]. In addition, the reduction of plasma HIV RNA levels in response to antiretroviral therapy may reduce sexual transmission among patients engaging in risk behaviors [38, 39]. Receipt of prevention messages and antiretroviral therapy is contingent on linkage to and retention in outpatient HIV treatment services after diagnosis, which highlights the vital role played by engagement in care [34].

The findings of our study should be interpreted with respect to the limitations of the current analyses. As with all observational studies, we are able to identify associations but cannot attribute causality, and there is the potential for unmeasured confounding. Our study was conducted at a single center in the southeastern United States, and therefore, our findings may not be generalizable to other regions of the country or to different patient populations. However, our patient population is largely reflective of the sociodemographic composition of the national HIV epidemic [22]. Mental health, substance abuse, and alcohol abuse disorders were recorded from diagnosis lists in the medical record and were not determined using validated instruments. These comorbid conditions may be underrecognized in clinical practice. Mortality was ascertained by query of the Social Security Death Index, which may experience reporting delays from time of death to entry in the database. However, we have no reason to believe that delayed reporting should differentially impact individuals on the basis of appointment attendance within the first year of care. Accordingly, we do not feel that this introduced a systematic bias that impacted our findings or their interpretation.

In conclusion, patients with missed visits in the year after establishing initial outpatient HIV care had more than twice the rate of subsequent mortality, compared with patients who did not miss visits, even when controlling for baseline $CD4^+$ cell count and antiretroviral receipt within the first year. These findings are particularly relevant in light of revised CDC HIV testing recommendations and the anticipated large increase in patients with newly diagnosed infection who will require linkage to HIV care in the coming years [1, 8, 9]. Future research is needed to identify barriers and facilitators to initial connection and early retention in HIV care, such that informed interventions can be developed to ensure that individuals derive maximal benefits from the tremendous recent advances in the treatment of HIV infection.

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