Title

History of AIDS in HIV-Infected Patients Is Associated With Higher In-Hospital Mortality Following Admission for Acute Myocardial Infarction and Stroke

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HISTORY OF ACQUIRED IMMUNODEFICIENCY SYNDROME BUT NOT ASYMPTOMATIC HUMAN IMMUNODEFICIENCY VIRUS INFECTION IS ASSOCIATED WITH HIGHER IN-HOSPITAL MORTALITY FOLLOWING ADMISSION FOR ACUTE MYOCARDIAL INFARCTION AND STROKE

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ABSTRACT

Importance: Persons infected with the human immunodeficiency virus (HIV) are at increased risk for major cardiovascular events compared to the general population. However, the prognosis of HIV-infected patients after these events is unknown.

Objective: To determine whether in-hospital outcomes following acute myocardial infarction (AMI) and stroke differ between HIV-infected and uninfected persons, and whether these outcomes are associated with severity of HIV-induced immunosuppression.

Design: Serial cross-sectional analysis using hospital discharge data from the Nationwide Inpatient Sample (NIS).

Setting and Participants: Data from 18,370,325 hospitalizations from the NIS with a principal discharge diagnoses of AMI or stroke from January 1, 2002 to December 31, 2012.

Main Outcome Measures: The primary study outcome was in-hospital mortality. The secondary outcome measures included length of stay and discharge to non-hospital inpatient facility.

Results: HIV-infected persons were significantly younger than uninfected persons hospitalized for AMI (51.8 years vs 68.5 years; $p < 0.001$) and stroke (51.0 years vs 70.1 years; $p < 0.001$). Compared to uninfected persons, persons with a history of AIDS had significantly longer hospital stays for both AMI (adjusted difference 3.9 days, 95% CI 2.1, 5.1) and stroke (adjusted difference 1.6 days, 95% CI 0.7, 2.5) and were significantly more likely to die in-hospital (AMI: OR 2.93, 95% CI 1.66, 5.19; stroke: OR 2.52, 95% CI 1.91, 3.31). Persons with a history of AIDS were also more like to be discharged to non-hospital inpatient facilities after AMI (OR 3.18, 95% CI 1.73, 5.82) and stroke (OR 1.43, 95% CI 1.11, 1.85). However, there was no significant difference in rates of in-hospital mortality, discharge to non-hospital inpatient facility, or length of stay between persons with asymptomatic HIV infection and uninfected persons.

Conclusions and Relevance: Compared to uninfected persons, rates of in-hospital mortality and length of stay following hospitalization for AMI or stroke were significantly higher for persons with a history of AIDS, but not for patients with asymptomatic HIV infection.

INTRODUCTION

Cardiovascular disease (CVD) has emerged as one of the leading causes of death in HIV-infected persons in the United States[2-4]. Data from several large cohort studies indicate that persons with HIV are at higher risk for acute myocardial infarction (AMI) than uninfected persons, even after adjusting for traditional CVD risk factors[2-4]. This increased risk of CVD may be linked to the severity of HIV-associated immunosuppression. For example, a recent study found no significant difference in the incidence rates of AMI among uninfected patients and patients with less advanced HIV infection[3]. By contrast, little is known about the relationship between severity of HIV infection and clinical outcomes in patients with AMI or stroke. The current study examined the in-hospital outcomes of AMI and stroke in persons with HIV, stratified by a clinical history of the acquired immunodeficiency syndrome (AIDS), compared to uninfected persons. To accomplish this, we utilized the Nationwide Inpatient Sample (NIS), a registry of billing data for over 87 million all-payer hospitalizations in the United States.

METHODS

Data Source and Case Ascertainment

Hospital discharge data were obtained from the 2002-2012 NIS, a component of the Healthcare Cost and Utilization Project produced by the Agency for Healthcare Research and Quality. The NIS is an all-payer dataset including records for approximately 20% of non-Federal inpatient discharges in the United States [5]. Survey weights are provided with NIS to enable estimation of national trends in inpatient hospitalizations. Data provided on the NIS include demographics (age, gender, and race); primary payer, diagnosis and procedure codes, length of stay, discharge disposition, and inpatient charges. Admissions associated with HIV infection were identified based on the presence of International Classifications of Disease, Ninth Edition, Clinical Modification (ICD-9-CM) diagnosis code 042 (Human Immunodeficiency Virus) and V08 (Asymptomatic HIV), where the code could be listed on any position in the claim[6]. The “042” code is reserved for patients who have ever had a documented HIV related illness or met clinical criteria for AIDS, and is thus a surrogate indicator of current or prior severe HIV related immunosuppression. In the current study, persons with a history of AIDS were identified by an

ICD-9-CM code of 042, while persons with asymptomatic HIV illness were identified by the ICD-9-CM billing code of V08. All patients with a reported ICD-9-CM diagnosis code of 410.00-410.92 for AMI and 430.00 to 434.91 for stroke in either the first or second diagnosis code listed on the claim, were identified for inclusion in the analysis.

Statistical Analysis

Unadjusted comparisons between patient characteristics and outcomes were calculated using weighted linear and logistic regression. Adjusted associations between HIV status and outcomes were evaluated using weighted logistic, negative binomial, and gamma log-link regressions as appropriate. The dataset was constructed using SAS System, version 9.4 (SAS Institute, Cary, NC), with analyses performed using Stata/MP, version 14.0 (Statacorp, College Station, Texas). Reported odds ratios were adjusted for age, sex and race/ethnicity. In order to more easily evaluate the findings, the adjusted results are also presented as incremental effects. A two-sided alpha level of 0.05 was considered statistically significant. Authorization for this study and a waiver of informed consent were obtained from the University of North Carolina Institutional Review Board.

RESULTS

AMI Hospitalization Outcomes by HIV Status

Between 2002 and 2012, there were 8,233,608 AMI hospitalizations and 10,136,717 stroke hospitalizations in the United States, based on weighted estimates of inpatient admissions included in the NIS database (**Table 1**). Of these hospitalizations, 48,993 had a billing diagnosis code for HIV (21,117 AMI hospitalizations and 27,816 stroke hospitalizations). HIV-infected persons hospitalized for AMI were significantly younger than uninfected persons (51.8 years versus 68.6 years; p = < 0.001). There was also a higher proportion of Blacks (39.1% v. 9.5%, p < 0.001) and lower proportion of females (19.2% v. 41.3%, p < 0.001) in the HIV-infected group. Although hospitalizations for AMI decreased by 12% during the study period among uninfected persons, they increased by 21% among persons with a history of AIDS and by 83% among infected persons without a history of AIDS (p = <0.001 for trend; **Figure 1**).

AMI hospitalizations were substantially longer among patients with a history of clinical AIDS. After adjusting for risk factors, the duration of AMI inpatient admissions in persons with a history of AIDS was 3.9 days longer than for patients without HIV infection (95% CI: 2.1days, 5.1days, p < 0.001, **Table 2**). By contrast, the duration of hospitalizations for AMI for persons without a history of AIDS was significantly shorter (adjusted difference -0.9 days, 95% CI -0.7, -1.0), p < 0.0001) than that of uninfected persons (**Table 2**). Patients with a history of AIDS were also significantly more likely to be discharged to non-hospital inpatient facilities (skilled nursing facility, inpatient rehab facility, long term acute care hospital or intermediate care facility) after hospitalization than uninfected persons (OR 3.18, 95% CI 1.73, 5.82). Interestingly, there was no significant difference in the likelihood of discharge to a non-hospital inpatient facility post AMI between persons with asymptomatic HIV infection and uninfected persons. (OR 0.92, 95% CI 0.73, 1.15). Overall, persons with a history of AIDS hospitalized for AMI were significantly more likely to die during admission than uninfected persons (OR 2.93, 95% CI 1.66,5.19, p < 0.001). However, there was no significant difference in the odds of in-hospital death for AMI hospital admissions between persons with asymptomatic HIV infection and uninfected persons (OR 0.78, 95% CI 0.62,1.00)

Stroke Hospitalization Outcomes by HIV Status

HIV-infected persons hospitalized for stroke were significantly younger than uninfected persons admitted for the same diagnosis. (HIV-infected 51.0 years vs. uninfected 70.1 years; p < 0.001; Table 1). Similar to AMI hospitalizations, there was also a higher proportion of Blacks (56.8% v. 14.6%, p < 0.001) and lower proportion of females (19.2% v. 31.3%, p < 0.001) in the HIV-infected group. Although the overall number of stroke hospitalizations increased in the entire population over the study period (2002-2012), the number of stroke hospitalizations increased more rapidly among HIV-infected persons over the study period. (**Figure 1**). When hospitalized for stroke, persons with a history of AIDS remained in the hospital longer than uninfected persons. After adjusting for demographics (age, sex, race/ethnicity), stroke

hospitalizations among persons with a history of AIDS were 28% longer than those of uninfected persons (adjusted difference 1.6 days, 95% CI 0.7, 2.5 days, p <0.001; Table 3). However, stroke hospitalizations among persons with asymptomatic HIV were actually slightly shorter than those of uninfected persons (adjusted difference -0.5 days 95% CI -0.1, -0.8 days).

Stroke hospitalizations in infected persons with a history of with AIDS were also more likely to result in discharge to a non-hospital inpatient facility than those of uninfected persons (OR 1.43, 95% CI 1.11, 1.85; Figure 3). Infected persons without a history of AIDS were only slightly more likely to be discharged to non-hospital inpatient care than uninfected persons (OR 1.11, 95% CI 1.00, 1.23). After adjusting for risk factors, persons with a history of AIDS had a significantly higher risk for in-hospital mortality after a stroke than uninfected persons (OR 2.52, 95% CI 1.91, 3.31, p < 0.001) Similar to our observations for AMI, there was no significant difference in the likelihood of in-hospital mortality after stroke between infected persons without a history of symptomatic disease and uninfected persons. (OR 1.13, 95% CI 0.97, 1.31).

DISCUSSION

This study documents an association between a history of HIV-induced immunosuppression and outcomes of major CVD events. Persons with a history of AIDS who were hospitalized for either AMI or stroke had a significantly higher risk of in-hospital mortality, discharge to non-hospital inpatient facilities and longer length of stay than uninfected persons. By contrast, the outcomes of patients with asymptomatic HIV were similar to those of uninfected persons. This observation is important because CVD is now one of the leading causes of death among persons with chronic HIV infection, and because antiretroviral therapy (ART) can dramatically improve HIV-induced immunosuppression [7]. These findings are also timely given the recent reports from the recently published Strategic Timing of Antiretroviral Therapy (START) trial suggesting that even mild levels of HIV-induced immunosuppression (CD4 count of 350 cells/mm^3) adversely effects risk for non-AIDS outcomes.[8]

Our study increases the understanding of non-AIDS clinical consequences of chronic HIV infection. We found that HIV-infected patients who developed AMI or stroke were more than twice as likely to die as uninfected patients with the same CVD event, and that most of this mortality risk was borne by patients with a history of AIDS. Clarifying the disproportionate distribution of CVD-associated risk among HIV-infected patients is important because of the growing overlap between the two epidemics. Given that over half of HIV-infected persons living in the United States will be aged 50 years or older by 2017 [9], the number of HIV-infected patients with CVD will continue to climb. Thus, there is an urgent need to improve our understanding of CVD in this population.

Exposure to HIV-induced immunosuppression has been linked to an increased risk of many non-AIDS conditions[11-14]. CD4 nadirs of ≤ 350 cells/mm^3 are associated with surrogates of atherosclerosis[15,16], including increased carotid intimal-medial thickness (cIMT) and decreased arterial compliance (indicated by flow-mediated dilatation). Low CD4 nadirs have also been associated with increased levels of the inflammatory marker IL-6[17], sustained hypertension and left ventricular hypertrophy.[18,19] These findings of adverse vascular physiology associated with severe HIV-induced immunosuppression appear to corroborate published clinical experience. For example, two large studies of the Northern California Kaiser Permanente cohort showed that HIV-infected persons with a CD4 count of ≤ 200 cells/mm^3 had a 74% higher incidence of AMI and a 60% higher incidence of stroke than uninfected persons. Interestingly, there was no significant difference between the incidence rate of AMI and stroke in HIV-infected cohort members with CD4 nadir ≥ 500 cells/mm^3 and uninfected persons[3,20]. The current study provides a key finding by linking the prognosis of HIV infected patients with AMI or stroke to their patient's level of HIV-immunosuppression.

In 2012, the US Department of Health and Human Services (DHHS) recommended treatment of all HIV-infected persons regardless of CD4 count [21]. With full implementation of these guidelines, one can anticipate that more HIV-infected persons will be initiated on ART

prior to the onset of advanced HIV-related immunosuppression, and the deleterious implications on cardiovascular health associated with it. Our analysis presents evidence supporting the suggestion that the implementation of these guidelines alone will greatly improve AMI and stroke-related mortality among HIV-infected persons in the years ahead. At the very least, our study adds to the growing body of evidence that CVD in persons with asymptomatic HIV (preserved immune function) may be more similar to CVD in uninfected persons than previously recognized.

Our study has limitations. The use of billing codes renders our data subject to the accuracy of local billing practices of individual health systems. However, the size of our registry (over 18 million hospitalizations) likely addresses the influence of severe outliers. Due to the use of billing data, we are also unable to differentiate between hospitalizations that occurred in persons with active AIDS and asymptomatic persons with a history of AIDS. We also did not have access to CD4 count, HIV-1 viral load or treatment status (or history or antiretroviral exposure) at the time of hospitalization. Although data on longitudinal CD4 counts were not available for purposes of this analysis, given the association between AIDS and low CD4 counts, we believe that the billing code for AIDS is a surrogate for low CD4 nadir, and we can postulate that persons with a billing code for AIDS had lower CD4 nadir than persons with a billing code for AIDS overall. Finally, we did not have access to indicators of patient acuity on presentation and thus a potential confounder related to inpatient prognosis was not addressed by our analysis.

In summary, our study demonstrates that persons with a history of AIDS hospitalized for AMI or stroke have longer inpatient length of stay, are more likely to be discharged to non-hospital inpatient care and are significantly more likely to die while hospitalized than uninfected persons. By contrast, there is no significant difference in AMI and stroke hospital outcomes between persons with asymptomatic HIV and uninfected persons. Future studies are needed to confirm these findings and to better understand their biological basis. In the meantime, our data

add further support for the importance of early ART in improving non-AIDS outcomes in persons living with HIV.

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Data. The Nationwide Inpatient Sample is a product of the Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality, in collaboration with partner organizations listed at http://www.hcup-us.ahrq.gov/db/hcupdatapartners.jsp.

DISCLOSURES

Dr. Fowler reports participation as Chair of Scientific Advisory Board for Merck V710, Consultancy from Pfizer, Novartis, Galderma, Novadigm, Durata, Debiopharm, Genentech, Achaogen, Affinium, Medicines Co., Cerexa, Tetraphase, Trius, MedImmune, Bayer, Theravance, Cubist, Basilea, Affinergy; Institutional Grants/grants pending from NIH, MedImmune, Forest/Cerexa, Pfizer, Merck, Advanced Liquid Logics, Theravance, Novartis, and Cubist, personal fees from Royalties (UpTo-Date), personal fees from Payment for development of educational presentations (Green Cross, Cubist, Cerexa, Durata, Theravance), outside the submitted work. In addition, Dr. Fowler has a patent pending involving diagnostics.

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	AMI Hospitalizations (N=1,736,422; Weighted N = 8,233,608)			CVA Hospitalizations (n = 2,139,851; weighted n = 10,136,177)		
	HIV code on claim			HIV code on claim		
	No	Yes		No	Yes	
	(N=1,736,422) (Weighted N = 8,233,608)	Without history of symptoms (N=2,443) (Weighted N = 11,591)	With history of symptoms (N=2,371) (Weighted N = 11,240)	(N=2,139,851) (Weighted N = 10,106,142)	Without history of symptoms (N= 2,807) (Weighted N = 13,412)	With history of symptoms (N = 3,567) (Weighted N = 16,893)
Age (years), mean(SD)	68.5 (14.4)	51.7 (9.4)	51.9 (9.5)	70.1 (14.9)	52.3 (10.7)	49.5 (11.0)
Age >= 50 years, n (%)	7,323,194 (89.2)	6,855 (59.1)	6,535 (58.1)	9,183,215 (90.9)	8,272 (61.7)	8,411 (49.8)
Female, n (%)	3,418,078 (41.6)	2,258 (19.5)	2,114 (18.8)	5,270,547 (52.2)	4,264 (31.8)	5,208 (30.8)
Race, n (%)						
White	5,010,877 (77.6)	4,423 (44.9)	4,439 (44.7)	5,835,978 (72.3)	3,165 (26.7)	4,215 (28.2)
Black	611,874 (9.5)	3,906 (39.6)	3,839 (38.7)	1,177,259 (14.6)	6,879 (58.0)	8,382 (56.0)
Hispanic	462,718 (7.2)	960 (9.7)	1,084 (10.9)	600,602 (7.4)	1,274 (10.7)	1,787 (11.9)
Asian/PI	135,875 (2.1)	32 (0.3)	63 (0.6)	208,805 (2.6)	53 (0.4)	102 (0.7)
Native American	33,808 (0.5)	29 (0.3)	48 (0.5)	37,949 (0.5)	30 (0.3)	83 (0.6)
Other	198,754 (3.1)	562504 (5.1)	451 (4.5)	212,737 (2.6)	461 (3.9)	399 (2.7)
Primary payor, n (%)						
Medicare	4,915,146 (60.0)	4,027 (34.8)	5,124 (45.7)	6,713,155 (66.5)	4,752 (35.6)	6,025 (35.7)
Medicaid	442,605 (5.4)	2,556 (22.1)	2,750 (24.5)	666,102 (6.6)	4,243 (31.8)	6,017 (35.7)
Private	2,173,902 (26.5)	3,469 (30.0)	2,295 (20.5)	2,083,863 (20.7)	2,634 (19.7)	3,068 (18.2)

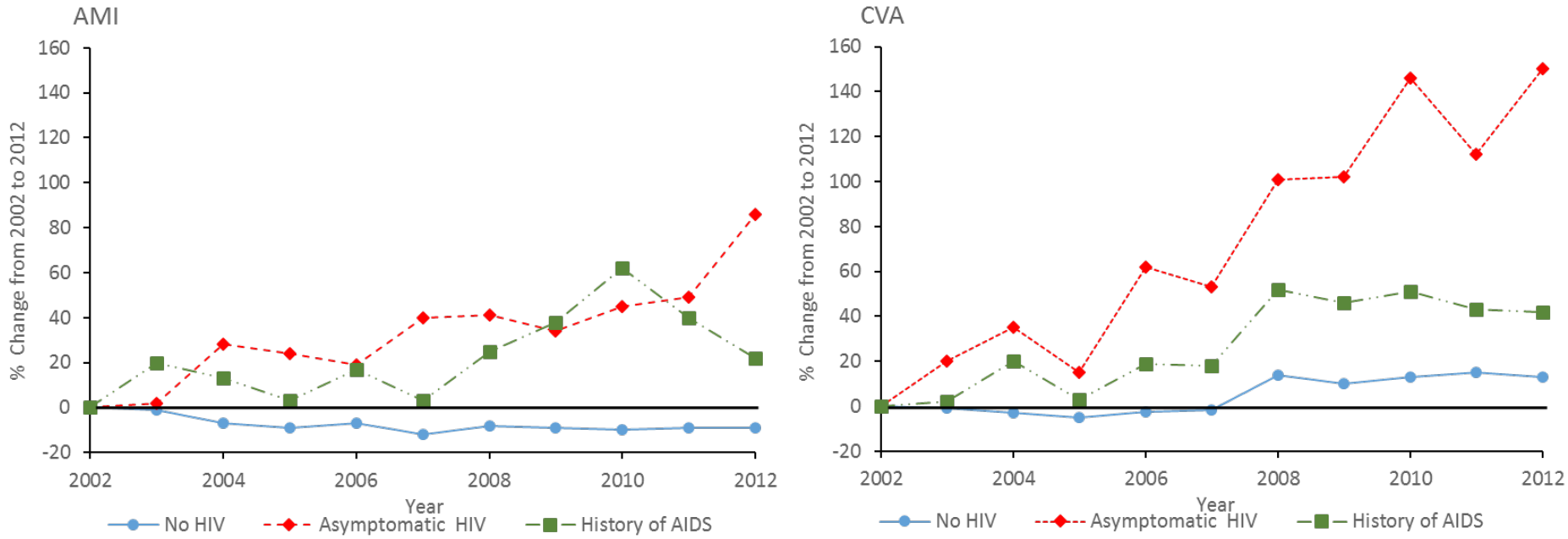
Table 1. Demographics and Clinical Characteristics of Persons with Primary Hospital Diagnoses of Myocardial Infarction and Cerebrovascular Accident, Nationwide Inpatient Sample 2002-2011.

Self-pay	418,839 (5.1)	934 (8.1)	669 (6.0)	375,938 (3.7)	1,046 (7.8)	1,142 (6.8)
No charge	38,495 (0.5)	156 (1.4)	39 (0.3)	36,808 (0.4)	199 (1.5)	134 (0.8)
Other	207,683 (2.5)	427 (3.7)	340 (3.0)	213,479 (2.1)	484 (3.6)	474 (2.8)
Facility bedsize, n (%)						
Small	830,921 (10.2)	804 (7.0)	703 (6.3)	1,070,546 (10.6)	928 (7.0)	1,183 (7.0)
Medium	1,968,215 (24.1)	2,831 (24.6)	2,527 (22.6)	2,364,164 (23.5)	3,126 (23.4)	3,711 (22.1)
Large	5,376,422 (65.8)	7,865 (68.4)	7,947 (71.1)	6,624,814 (65.9)	9,292 (69.6)	11,888 (70.8)
Hospital geographic region, n (%)						
Northeast	1,673,022 (20.4)	3,400 (29.3)	3,233 (28.8)	1,835,246 (18.2)	4,047 (30.2)	4,343 (25.7)
Midwest	1,901,460 (23.2)	1,479 (12.8)	1,309 (11.7)	2,391,689 (23.7)	1,738 (13.0)	1,751 (10.4)
South	3,269,773 (39.8)	5,888 (50.8)	4,904 (43.6)	4,063,608 (40.2)	6,997 (52.2)	8,073 (47.8)
West	1,366,523 (16.6)	824 (7.1)	1,793 (16.0)	1,815,869 (18.0)	631 (4.7)	2,725 (16.1)
Urban hospital facility, n (%)	7,201,216 (88.1)	11,073 (96.3)	10,768 (96.4)	8,825,329 (87.7)	12,940 (97.0)	16,246 (96.8)
Hospital with teaching affiliation, n (%)	3,675,357 (45.0)	7,415 (64.5)	7,306 (65.4)	4,609,401 (45.8)	9,013 (67.5)	11,446 (68.2)
Comorbid conditions, n (%)						
Congestive heart failure	2,601,977(31.7)	1,918 (16.5)	2,712(24.1)	1,159,431 (11.5)	907 (6.8)	1,080 (6.4)
Peripheral vascular disease	783,708 (9.5)	621 (5.4)	577 (5.1)	920,185 (9.1)	690 (5.1)	637 (3.8)
Hypertension	5,244,570	6,674 (57.6)	6,170 (54.9)	7,340,040	8,718 (65.0)	8,499 (50.3)

	(63.9)			(72.6)		
COPD	1,685,308(20.5)	1,792 (15.5)	1,932 (17.2)	1,488,899 (14.7)	1,873 (14.0)	2,195 (13.0)
Diabetes	2,598,395 (31.7)	2,531 (21.8)	2,496 (22.2)	2,957,299 (29.2)	3298 (24.5)	2,853 (16.9)
Obesity	713,065 (8.7)	458 (3.9)	397 (3.5)	552,971 (5.5)	428 (3.2)	263 (1.6)
Chronic blood loss anemia	108,530 (1.3)	72 (0.6)	53 (0.5)	53,414 (0.5)	38 (0.3)	79 (0.5)
Deficiency Anemias	1.058,877 (12.9)	1,376 (11.9)	1,743 (15.5)	1,003,347 (9.9)	1,591 (11.9)	3,048 (18.0)
Alcohol abuse	205,938 (2.5)	613 (5.3)	613 (5.5)	321,315 (3.2)	941 (7.0)	1,277 (7.6)
Substance Abuse	137,766 (1.7)	2,008 (17.3)	2,177 (19.4)	162,865 (1.6)	2,310 (17.2)	3,165 (18.7)
Current Smoker	1,534,799 (18.6)	4,755 (41.0)	3,239 (28.8)	1,222,506 (12.1)	3,259 (24.3)	3,406 (20.2)
Former Smoker	707,272 (8.3)	782 (6.7)	735 (6.5)	765,153 (7.6)	635 (4.7)	632 (3.7)
Hyperlipidemia	885,542 (10.8)	1,394 (12.0)	905 (8.0)	1,016,958 (10.1)	853 (6.4)	592 (3.5)

Abbreviations: AMI, acute myocardial infarction; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; HIV, human immunodeficiency virus; PI, Pacific Islander; SD, standard deviation

Figure 1. Trends in Hospitalizations for Acute Myocardial Infarction and Cerebrovascular Accident by HIV Claim Code, 2002 to 2012



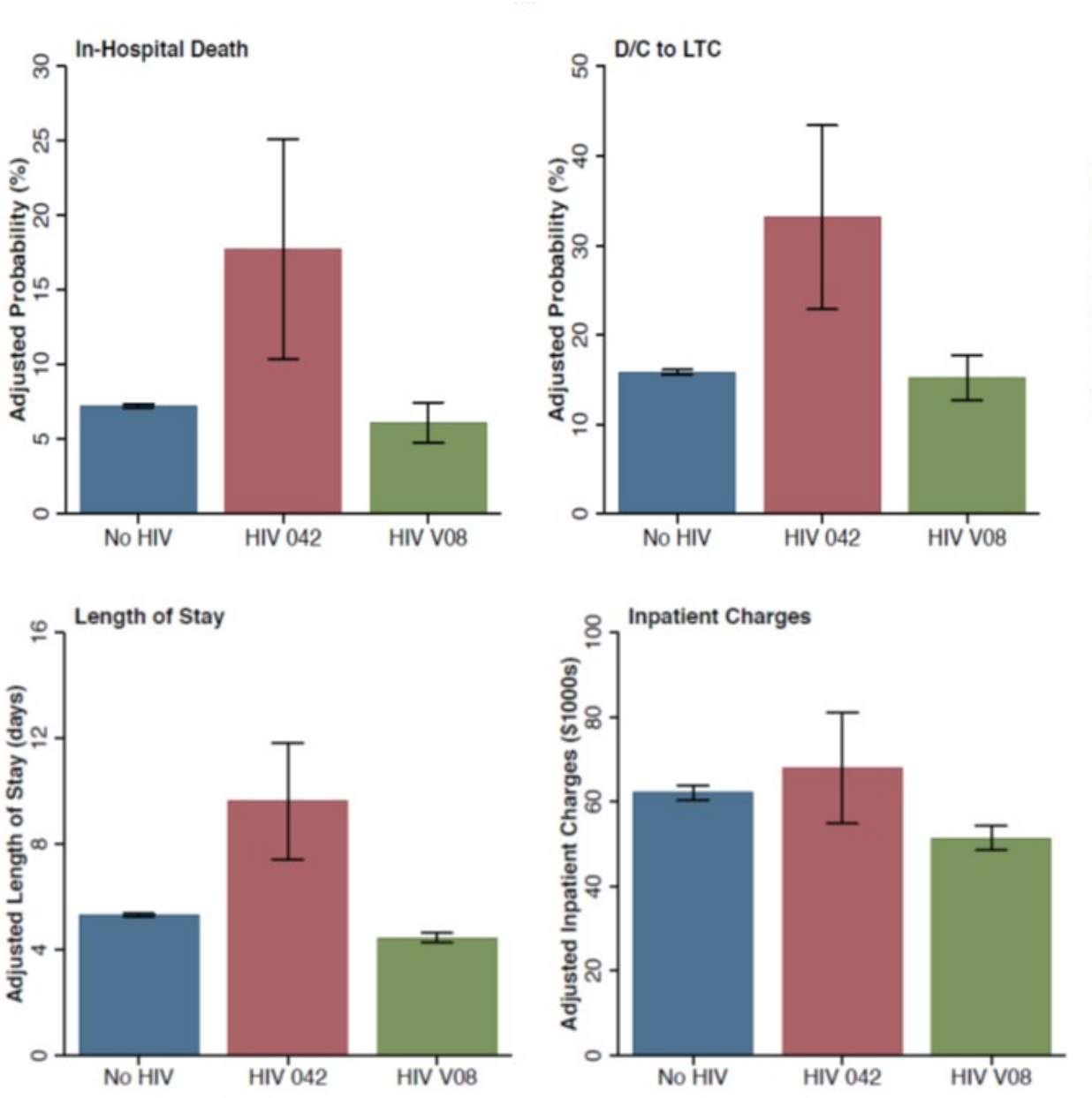
Abbreviations: AMI, acute myocardial infarction; CI, confidence interval; CVA, cerebrovascular accident; HIV, human immunodeficiency virus

Table 2. Factors associated with Major Hospitalization Outcome Metrics in Patients Hospitalized for Acute Myocardial Infarction (AMI) and Cerebrovascular Accident (CVA)

Variable	Death	Non Hospital Institutional Care	Length of Stay	Total Charge	Total Cost
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
AMI Hospitalizations					
HIV status (v. no HIV)					
HIV infection w/ history of AIDS	**2.93 (1.66,5.19)**	**3.18 (1.73, 5.82)**	**1.74 (1.39, 2.16)**	1.05 (0.87, 1.26)	1.12 (0.90, 1.41)
Asymptomatic HIV	0.78 (0.62, 1.00)	0.92 (0.73, 1.15)	**0.84 (0.80, 0.88)**	**0.84 (0.80, 0.88)**	**0.83 (0.80, 0.87)**
CVA Hospitalizations					
HIV status (v. no HIV)					
HIV infection w/ history of AIDS	**2.52 (1.91, 3.31)**	**1.43 (1.11, 1.85)**	**1.28 (1.13, 1.44)**	1.15 (0.99, 1.34)	1.08 (0.94, 1.24)
Asymptomatic HIV	1.13 (0.97, 1.31)	1.11 (1.00, 1.23)	**0.92 (0.87, 0.98)**	**0.88 (0.83, 0.93)**	**0.88 (0.83, 0.94)**

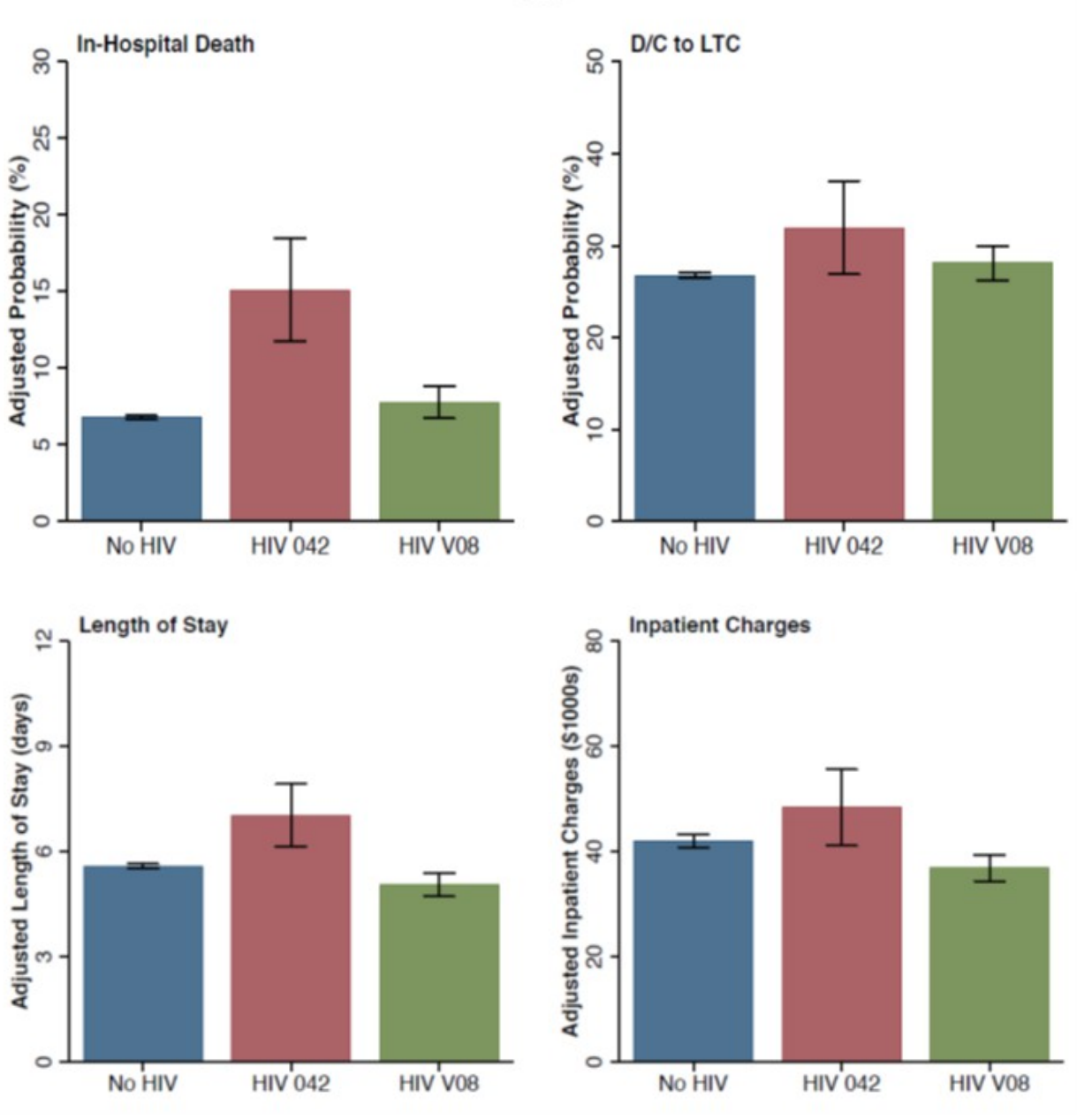
Abbreviations: AIDS, acquired immunodeficiency syndrome; AMI, acute myocardial infarction; CI, confidence interval; CVA, cerebrovascular accident; HIV, human immunodeficiency virus; OR, odds ratio

Figure 2. Adjusted Values for Major Outcome Metrics for Acute Myocardial Infarction Hospitalizations by HIV Diagnosis Code



Abbreviations: d/c, discharge; HIV, human immunodeficiency virus, LTC; long-term care

Figure 3. Adjusted Values for Major Outcome Metrics for Stroke Hospitalizations by HIV Diagnosis Code



Abbreviations: d/c, discharge; HIV, human immunodeficiency virus, LTC; long-term care

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Variable	Death	Non Hospital Institutional Care	Length of Stay	Total Charge	Total Cost
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Age	1.03 (1.03, 1.03)	1.06 (1.05, 1.06)	1.00 (1.00, 1.00)	0.99 (0.99, 0.99)	0.99 (0.99, 0.99)
Female Sex	1.05 (1.04, 1.07)	1.35 (1.33, 1.37)	1.01 (1.01, 1.02)	0.99 (0.99, 0.99)	0.99 (0.99, 0.99)
Payor (v. Medicare)					
Medicaid	1.23 (1.19, 1.28)	0.95 (0.92, 0.99)	1.13 (1.11, 1.15)	1.00 (0.98, 1.02)	0.99 (0.97, 1.01)
Private	0.80 (0.78, 0.82)	0.66 (0.65, 0.68)	0.91 (0.90, 0.92)	0.96 (0.95, 0.98)	0.96 (0.95, 0.97)
Self-pay	1.26 (1.21, 1.32)	0.41 (0.38, 0.45)	0.95 (0.93, 0.96)	0.94 (0.92, 0.97)	0.91 (0.90, 0.93)
No charge	0.90 (0.79, 1.03)	0.41 (0.32, 0.53)	0.98 (0.94, 1.02)	1.03 (0.97, 1.10)	0.97 (0.89, 1.04)
Other	1.14 (1.07, 1.22)	0.77 (0.70, 0.84)	0.97 (0.96, 0.99)	0.96 (0.93, 1.00)	0.96 (0.94, 1.00)
Hospital Bed Size (v. Small)					
Medium	1.01 (0.97, 1.04)	0.98 (0.92, 1.03)	1.13 (1.10, 1.16)	1.22 (1.12, 1.33)	1.14 (1.08, 1.21)
Large	1.02 (0.99, 1.06)	0.99 (0.94, 1.04)	1.32 (1.28, 1.35)	1.60 (1.48, 1.73)	1.39 (1.32, 1.47)
Hospital Region (v. Northeast)					
Midwest	0.92 (0.88, 0.96)	0.96 (0.91, 1.01)	0.88 (0.86, 0.91)	0.86 (0.79, 0.94)	0.97 (0.91, 1.03)
South	0.99 (0.96, 1.04)	0.80 (0.76, 0.83)	0.96 (0.93, 0.98)	0.94 (0.86, 1.03)	0.91 (0.90, 0.93)
West	1.02 (0.99, 1.06)	0.65 (0.61, 0.69)	0.86 (0.83, 0.89)	1.35 (1.23, 1.49)	1.17 (1.09, 1.25)
Urban (v. Rural)	0.96 (0.92, 0.99)	1.16 (1.10, 1.22)	1.29 (1.25, 1.33)	2.07 (1.93, 2.23)	1.44 (1.35, 1.54)
Teaching Hospital (v. Community Based)	1.00 (0.97, 1.03)	1.00 (0.95, 1.04)	1.17 (1.15, 1.19)	1.22 (1.16, 1.29)	1.27 (1.23, 1.32)
Comorbid Conditions					
CHF	1.34 (1.32,1.37)	1.54 (1.52, 1.57)	1.39 (1.38, 1.40)	1.20 (1.19, 1.21)	1.20 (1.19, 1.21)
COPD	1.06 (1.04, 1.08)	1.21 (1.20, 1.23)	1.16 (1.15, 1.16)	1.06 (1.05, 1.07)	1.06 (1.06, 1.07)
Diabetes	0.91 (0.90, 0.93)	1.03 (1.02, 1.04)	0.98 (0.97, 0.98)	0.97 (0.96, 0.97)	0.96 (0.96, 0.97)
Alcohol Abuse	1.09 (1.04, 1.15)	1.65 (1.59, 1.72)	1.16 (1.15, 1.18)	1.03 (1.02, 1.05)	1.04 (1.03, 1.06)
Substance Abuse	0.93 (0.87, 1.00)	1.41 (1.32, 1.51)	0.97 (0.95, 0.98)	0.84 (0.82, 0.86)	0.83 (0.82, 0.85)
Tobacco Use	0.47 (0.46, 0.49)	0.56 (0.55, 0.58)	0.79 (0.78, 0.80)	0.90 (0.89, 0.91)	0.89 (0.88, 0.90)
HIV status (v. no HIV)					
HIV infection w/ history of symptomatic disease	**2.93 (1.66,5.19)**	**3.18 (1.73, 5.82)**	**1.74 (1.39, 2.16)**	1.05 (0.87, 1.26)	1.12 (0.90, 1.41)
HIV infection with no history of symptomatic disease	0.78 (0.62, 1.00)	0.92 (0.73, 1.15)	**0.84 (0.80, 0.88)**	**0.84 (0.80, 0.88)**	**0.83 (0.80, 0.87)**

343**Supplemental Table 1a.** Factors associated with major hospitalization outcome metrics in
344patients hospitalized for acute myocardial infarction.

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346Abbreviations: CI, confidence interval; CHF, congestive heart failure, COPD, chronic obstructive pulmonary disease;
347HIV, human immunodeficiency virus; OR, odds ratio

Variable	Death	Non-Hospital Institutional Care	Length of Stay	Total Charge	Total Cost
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Age	1.02 (1.02, 1.02)	1.03 (1.03, 1.03)	1.00 (1.00, 1.00)	0.99 (0.99, 0.99)	0.99 (0.99, 0.99)
Female Sex	1.11 (1.09, 1.12)	1.12 (1.11, 1.13)	1.00 (1.00, 1.01)	0.98 (0.98, 0.99)	0.99 (0.98, 0.99)
Payor (v. Medicare)					
Medicaid	1.46 (1.40, 1.51)	1.05 (1.03, 1.08)	1.38 (1.34, 1.42)	1.13 (1.11, 1.16)	1.14 (1.12, 1.16)
Private	1.29 (1.24, 1.33)	0.81 (0.80, 0.83)	1.01 (1.00, 1.02)	1.02 (1.01, 1.04)	1.02 (1.01, 1.03)
Self-pay	2.31 (2.18, 2.44)	0.58(0.55, 0.60)	1.15 (1.11, 1.18)	1.01 (0.98, 1.05)	1.01 (0.98, 1.03)
No charge	1.39 (1.16, 1.60)	0.55 (0.50, 0.61)	1.22 (1.12, 1.33)	1.11 (1.02, 1.21)	1.06 (0.95, 1.18)
Other	2.37 (2.11, 2.67)	0.66 (0.63, 0.70)	1.10 (1.07, 1.13)	1.00 (0.96, 1.03)	1.00 (0.97, 1.03)
Hospital Bed Size (v. Small)					
Medium	1.10 (1.05, 1.16)	0.98 (0.94, 1.01)	1.04 (1.00, 1.07)	1.20 (1.13, 1.28)	1.06 (1.02, 1.10)
Large	1.21 (1.15, 1.26)	0.97 (0.94, 1.00)	1.14 (1.10, 1.17)	1.47 (1.39, 1.56)	1.19 (1.15, 1.23)
Hospital Region (v. Northeast)					
Midwest	0.81 (0.76, 0.85)	0.92 (0.88, 0.97)	0.86 (0.83, 0.89)	0.73 (0.67,0.79)	0.80 (0.76, 0.85)
South	0.93 (0.88, 0.99)	0.83 (0.80, 0.87)	0.91 (0.89, 0.94)	0.82 (0.76, 0.89)	0.78 (0.74, 0.83)
West	1.02 (0.96, 1.09)	0.80 (0.77, 0.84)	0.90 (0.87, 0.93)	1.25 (1.13, 1.37)	1.04 (0.98, 1.11)
Urban (v. Rural)	0.92 (0.88, 0.95)	0.97 (0.94, 1.01)	1.05 (1.02, 1.08)	1.77 (1.69, 1.85)	1.22 (1.18, 1.25)
Teaching Hospital (v. Community Based)	1.25 (1.20, 1.30)	1.02 (0.98, 1.05)	1.14 (1.11, 1.16)	1.27 (1.21, 1.33)	1.30 (1.26, 1.35)
Comorbid Conditions					
CHF	1.64 (1.61, 1.67)	1.27 (1.25, 1.28)	1.22 (1.21, 1.23)	1.21 (1.20, 1.22)	1.21 (1.20, 1.22)
COPD	1.03 (1.01, 1.05)	0.99 (0.98, 1.00)	1.03 (1.02, 1.03)	1.08 (1.07, 1.09)	1.07 (1.06, 1.08)
Diabetes	0.85 (0.83, 0.86)	1.15 (1.14, 1.16)	0.99 (0.99, 1.00)	0.97 (0.96, 0.97)	0.96 (0.95, 0.96)
Alcohol Abuse	1.13 (1.10, 1.17)	1.59 (1.56, 1.63)	1.18 (1.17, 1.19)	1.07 (1.05, 1.08)	1.08 (1.06, 1.09)
Substance Abuse	1.50 (1.42, 1.57)	1.28 (1.24, 1.33)	1.06 (1.04, 1.08)	1.00 (0.98, 1.02)	1.00 (0.98, 1.02)
Tobacco Use	0.56 (0.54, 0.58)	0.80 (0.79,0.81)	0.76 (0.76, 0.77)	0.89 (0.88, 0.90)	0.87 (0.86, 0.88)
HIV status (v. no HIV)					
HIV infection w/ history of symptomatic disease	**2.52 (1.91, 3.31)**	**1.43 (1.11, 1.85)**	**1.28 (1.13, 1.44)**	1.15 (0.99, 1.34)	1.08 (0.94, 1.24)
HIV infection with no history of symptomatic disease	1.13 (0.97, 1.31)	1.11 (1.01, 1.23)	**0.92 (0.87, 0.98)**	**0.88 (0.83, 0.93)**	**0.88 (0.83, 0.94)**

348**Supplemental Table 1b.** Factors associated with major hospitalization outcome metrics in
349patients hospitalized for stroke

Abbreviations: CI, confidence interval; CHF, congestive heart failure, COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; OR, odds ratio

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