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Prevalence and predictors of hospitalizations among HIV-Infected and at-risk HIV-Uninfected Women

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Abstract

Objectives—We evaluated the Veterans Aging Cohort Study (VACS) Index score, an index composed of age, CD4 count, viral load, hemoglobin, Hepatitis C (HCV) co-infection, Fibrosis Index-4 (FIB-4), and estimated glomerular filtration rate (EGFR), and psychosocial and clinical risk factors for all-cause hospitalization among HIV-infected women on HAART and HIV-uninfected women.

Methods—Data were collected from 2008 - 2014 from 1585 HAART-experienced HIV-infected and 692 uninfected women. Cox proportional hazards regression evaluated predictors of first hospitalization over 2 years.

Results—Among HIV-infected women, VACS Index score (per 5 points) (adjusted hazard ratio [aHR] 1.08; 95% CI 1.06-1.11), Centers for Epidemiologic Studies-Depression (CES-D) scores 16 (aHR 1.61; 95% CI 1.30-1.99), smoking (aHR 1.26; 95% CI 1.02-1.55), abuse history (aHR 1.52; 95% CI 1.20-1.93), diabetes (aHR 1.63; 95% CI 1.31-2.04), and black race (aHR 1.28; 95% CI 1.03-1.59) increased risk of hospitalization. Among HIV-uninfected women, VACS Index score

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Ethical Standards: Procedures for the protection of human subjects were in accordance with the ethical standards of the institutional review board of the Cook County Health and Hospitals System and with the Helsinki Declaration of 1975, as revised in 2000

(aHR 1.08; 95% CI 1.03-1.13), CES-D 16 (aHR 1.38; 95% CI 1.02-1.86), diabetes (aHR 2.15; 95% CI 1.57-2.95), and black race (aHR 1.61; 95% CI 1.15-2.24) predicted subsequent hospitalization.

Conclusions—Psychosocial and clinical factors were associated with risk of hospitalization independently of the VACS Index score. Additional research on contextual and psychosocial influences on health outcomes among women is needed.

Keywords

HIV; hospitalizations; women

Background

Rates of hospitalization due to AIDS-related illnesses have declined substantially since the widespread availability of highly active antiretroviral therapy (HAART) ^{1,2}. However, hospitalizations among HIV infected persons remain relatively common ^{3,4}. The steep declines in hospitalizations observed soon after HAART became available have not declined as dramatically in recent years, likely due to aging of the HIV infected population, complications from co-morbidities, and side effects of HAART ⁵. Longer survival with HIV has increasingly been associated with aging-related conditions that may be accelerated among HIV infected persons, impacting morbidity and mortality even when HIV disease is controlled ⁶. HIV clinicians now treat a broad spectrum of chronic illnesses associated with aging and a comprehensive approach to care for HIV infected patients is needed ^{6,7}.

Rates of hospitalization are higher and declines in hospitalizations have been less pronounced among women, African-Americans, and those with a history of injection drug use ^{5,8,9}. Indeed, HIV-infected women disproportionately experience substance use, gender based violence, and mental health problems, which may lead to increased morbidity and mortality ¹⁰. Many of these issues also impact HIV uninfected women. Understanding factors that predict hospitalization in HIV infected and uninfected women may reduce morbidity, associated healthcare costs, and health disparities. During the earlier years of the HIV epidemic, HIV infected and uninfected women had very different clinical profiles and treatment needs. In contrast, HIV infected and uninfected women currently share many of the same aging-related comorbidities, particularly those from similar sociodemographic backgrounds. Understanding similarities and differences in patterns and predictors of hospitalization is important for effectively targeting interventions and improving care for women.

The Veterans Aging Cohort Study (VACS) Index, a score composed of age and HIV and non-HIV biomarkers, accurately predicts mortality among HIV infected men and women across varying stages of HIV disease progression and duration of HAART use. The VACS Index ^{11,12} has also been associated with a number of morbidities and markers of morbidity, including hospitalizations and readmissions, frailty indices, and cognitive function ¹³⁻¹⁵. Although the VACS Index also predicted mortality among treated HIV infected women in the Women's Interagency HIV Study (WIHS), depression and transactional sex history predicted mortality risk independently of the VACS Index score among WIHS women ¹⁶.

Assessment of the impact of psychosocial factors on morbidity among women may thus be important for understanding and improving women's overall health. The goals of the current study were to 1.) compare trends over time in rates of hospitalization among HIV infected and uninfected WIHS women; 2.) examine associations between the VACS Index and risk for all-cause hospitalization among HIV infected and uninfected women; and 3.) examine associations between psychosocial and clinical factors and hospitalizations among WIHS women.

Methods

Sample and recruitment

The WIHS is an ongoing prospective cohort study of HIV infection among women in the United States. Data for this analysis were obtained from WIHS women enrolled during 1994-1995, 2000-2001, and 2011-2012 at six sites, including Bronx and Brooklyn, NY, Chicago, IL, Los Angeles and San Francisco, CA, and the Washington, D.C. metropolitan area. Detailed descriptions of the WIHS cohort, and recruitment, enrollment, retention, and data collection methods have been reported elsewhere ¹⁷. Of note, because the WIHS sought to enroll a comparison group of HIV uninfected women at risk of acquiring HIV based on sexual and substance use behaviors, with similar sociodemographic characteristics as HIV infected women, HIV uninfected WIHS women are not representative of HIV uninfected women in the general population. Women undergo clinical examination and structured face-to-face interviews and provide laboratory specimens at semi-annual visits. Analyses of predictors of hospitalization were restricted to the period beginning in 2008, the first year that reasons for hospitalizations were available (hereby defined as the index visit). To be included in the analysis women had to have at least one follow-up visit at which hospitalization data were ascertained. HIV infected women who had not initiated HAART were excluded because our goal was to examine predictors of hospitalization among women with relatively controlled HIV. Hospitalizations due to childbirth (<2% of hospitalizations during the analytic period) were also excluded. While the primary analysis focused on this more recent period, time trends in hospitalizations are reported descriptively for the entire WIHS cohort from 1994 through 2014. The study was approved by the Institutional Review Board at each participating site. All women provided written informed consent.

Variable definitions and classification

The VACS Index score was calculated using the formula developed by Justice and colleagues^{11,12} by adding points for age, CD4 count, viral load, hemoglobin, Hepatitis C (HCV) co-infection, Fibrosis Index-4 (FIB-4) ¹⁸, and estimated glomerular filtration rate (EGFR) ¹⁹. For analysis, the VACS Index score was categorized into 4 ordered groups with approximately equal number of events in each group, and it was analyzed as a continuous variable, using 5-point increments ^{11,12,20}. VACS Index scores were calculated for HIV uninfected women by assigning the lowest possible number of points (0) for CD4 and viral load, a method consistent with prior research²⁰.

Explanatory variables included the index visit VACS Index score; current smoking (yes vs. no); recent (since the last visit) hazardous alcohol use (defined according to NIAAA

criteria ²¹ as >7 drinks per week or 4 drinks per day); a clinically relevant burden of depressive symptoms defined as scores ≥16 on the Center for Epidemiologic Studies-Depression (CES-D) scale ²²; history of any physical, sexual, or emotional abuse; ever-use of crack, cocaine, or heroin; any history of transactional sex (defined as ever having had sex for drugs, money, or shelter); race/ethnicity (categorized as White non-Hispanic, Black non-Hispanic, Hispanic, Other non-Hispanic; and dichotomized as Black non-Hispanic vs. all other categories); current hypertension, defined as systolic blood pressure ≥140, diastolic blood pressure ≥90, or self-reported use of anti-hypertensives; and current or past history of diabetes, determined by self-report or use of anti-diabetic medications, fasting glucose ≥126 or HgbA1C ≥6.5%. Year of index visit and index visit hospitalization were examined to assess secular trends in hospitalization and because index visit hospitalization was expected to predict subsequent hospitalization. Sensitivity analyses yielded similar magnitude and direction of effects when index visit hospitalization was excluded from the models; models presented adjust for index visit hospitalization.

At each visit, women reported all hospitalizations since their last semiannual study visit. Reasons for hospitalization were assessed by self-report in pre-defined categories and reasons not listed on the questionnaire were reported via open-ended response. Open-ended responses were reviewed by the authors and classified into pre-existing categories when possible. The final categories included surgeries/procedures; pneumonia; infections other than pneumonia; cardiovascular disease; gastrointestinal problems; psychiatric or mental health problems; lung problems other than pneumonia, including asthma; injuries/accidents; central nervous system disorders; gynecologic procedures; kidney problems; blood disorders; liver problems (including Hepatitis related issues); cancer; endocrine disorders, and “other” reasons that did not fit into any of the above categories. Limitation in documentation precluded the classification of infections and cancers as AIDS-defining illnesses. Women could report multiple reasons for hospitalization and reasons were not classified as “primary” or “secondary”; thus, it was not possible to identify a primary admitting diagnosis. Reasons for hospitalization are reported descriptively, but predictors of cause-specific hospitalization were not analyzed due to the difficulty in interpreting such an analysis given data and sample size limitations.

Statistical Analysis

Sociodemographic, behavioral, and clinical characteristics were compared among HIV infected and uninfected women using Pearson chi-square tests for categorical variables and Wilcoxon rank-sum tests for continuous variables. Trends over time in hospitalizations among HIV infected and uninfected women were assessed using the Jonckheere-Terpstra nonparametric trend test. Time-adjusted analyses compared hospitalization (yes/no) at each visit by HIV status using generalized estimating equations with logit link to account for correlation among repeated measures. For multivariable analysis, the outcome was the time to first hospitalization within 2 years of the index visit. Cox survival analysis models were used to account for varying person-time contributions. Person-time was calculated as the time between the date of the index visit and the first visit at which hospitalization was reported, the last observed visit, or 2 years from the index visit. VACS Index scores and all additional variables were treated as fixed exposures at the index visit. The log-rank test was

used to compare time to first hospitalization across categories of explanatory variables. Variables with p-values <0.2 in univariate analysis and those considered conceptually important based on published literature were entered in multivariable Cox proportional hazards regression models to evaluate associations with time to first hospitalization over 2-year follow-up. All variables were initially entered into the models and were then removed one by one in an iterative model selection process; those with $p < 0.05$ were retained in the final multivariable models. The proportional hazards assumption was assessed by graphical examination of log-log survival curves for each explanatory variable and by statistical testing for non-zero slope of scaled Schoenfeld residuals on functions of time²³. The Efron method was used to approximate the exact probability of tied failures. Standard errors were calculated using robust variance estimation. Sensitivity analyses were conducted to examine the impact of predictors on 5-year hospitalization rates and use of time-varying vs. fixed covariates. Findings were similar using the extended follow-up and with fixed vs. time-varying exposures, so the analysis of fixed exposures is reported since we were interested in identifying index visit characteristics to predict risk of subsequent hospitalization. Data were analyzed using SAS software version 9.3 (SAS Institute, Cary, NC) and STATA/IC version 13.1 for Windows (Stata Corp, College Station, TX).

Results

Participant characteristics

Data were collected between April 2008 and March 2014 from 1622 HIV-infected women who had initiated HAART and 700 HIV uninfected women. The final analytic sample included 1585 HIV infected and 692 uninfected women who provided data on hospitalization at the index visit and at least one subsequent visit; follow-up occurred through March 2014. Over half of HIV infected and uninfected women reported history of substance use, nearly one third had history of transactional sex, and 60% had history of physical, sexual, and/or emotional abuse (table 1). At the index visit, 35% of HIV infected and 32% of uninfected women had CESD scores ≥ 16 ; over one third had hypertension, and 20% had a history of diabetes. HIV infected women were less likely than uninfected women to report current smoking (38% vs. 51%), hazardous alcohol use (18% vs. 31%), recent substance use (7% vs. 15%), recent abuse (6% vs. 9%) and recent transactional sex (1% vs. 4%) ($p < 0.05$ for all comparisons). The median VACS Index score was 23 (IQR 16-39; range 0-106) among HIV infected women and 10 (IQR 10-22; range 0-86) among HIV uninfected women.

Frequency of hospitalization by diagnostic category

Multiple hospitalizations were reported at 11% and 5% of visits among HIV infected and uninfected women respectively (Table 2). Across all visits at which reasons for hospitalization were reported, surgeries or procedures were reported at 22% and 23% of visits for HIV infected and uninfected women respectively. After surgeries the most common reasons for hospitalization among HIV infected women were infections (non-pneumonia at 17%, and pneumonia at 16% of visits), gastrointestinal disorders (13%), cardiovascular disease (11%), and lung problems other than pneumonia (9% of visits). For HIV uninfected women, the most common reasons for hospitalization after surgeries were

cardiovascular disease (18%), gastrointestinal disorders (11%), followed by psychiatric/mental health problems, lung problems, and injuries (each reported at approximately 9% of visits) (Table 2).

Trends over time in hospitalization

Over two years of follow-up, 462 first hospitalizations occurred over 2308.6 person-years of observation among HIV infected women, resulting in an incidence rate of 20.01 (95% CI 18.27-22.92) per 100 person-years (Table 3). Among HIV uninfected women, there were 184 first hospitalizations in 1041.6 person-years, for an incidence rate of 17.66 (95% CI 15.29-20.41) per 100 person-years ($p=0.095$). In time-adjusted analysis, across all visits, HIV infected women were more likely than HIV uninfected women to be hospitalized ($p<0.001$). Among HIV infected women, hospitalizations declined over time (p for trend <0.001); the trend of declining hospitalizations over time among HIV uninfected women was not statistically significant ($p=0.276$) (Figure 1). Over time, the gap between hospitalization rates for women with and without HIV infection decreased.

Predictors of Hospitalization among HIV Infected Women

Among HIV infected women, in multivariable Cox regression, VACS Index score was associated with an 8% increased risk of hospitalization per 5-point increase (HR 1.08; 95% CI 1.06-1.11). Depressive symptoms (HR 1.61; 95% CI 1.30-1.99), current smoking (HR 1.26; 95% CI 1.02-1.55), history of abuse (HR 1.52; 95% CI 1.20-1.93), diabetes (HR 1.63; 95% CI 1.31-2.04), and Black race (HR 1.28; 95% CI 1.03-1.59) were statistically significant independent predictors of hospitalization in models including VACS Index score and index visit hospitalization (Table 4).

Predictors of Hospitalization among HIV uninfected women

Among HIV uninfected women, in multivariable Cox regression, VACS Index score was associated with an 8% increased risk of hospitalization per 5-point increase (HR 1.08; 95% CI 1.03-1.13). Depressive symptoms (HR 1.38; 95% CI 1.02-1.86), diabetes history (HR 2.15; 95% CI 1.57-2.95), and Black race (HR 1.61; 95% CI 1.15-2.24) predicted subsequent hospitalization in models including VACS Index score and index visit hospitalization (Table 4).

We also assessed the association of index visit VACS Index score and other exposures on risk of hospitalization over 5 years of follow-up; these analyses yielded similar final models and equivalent conclusions in terms of the direction, magnitude, and statistical significance of effects, except that among HIV infected women, the effect of Black race was attenuated over 5 year follow-up (5-year HR 1.08; 95% CI 0.91-1.28). The effect of race remained statistically significant for HIV uninfected women over 5 year follow-up. Analyses excluding hospitalizations due to surgeries and procedures also yielded similar final models and effect estimates.

Discussion

Consistent with several recent studies ^{3,5}, we observed declines over time in hospitalizations among HIV infected women in the WIHS, and while these declines appear to have been most pronounced shortly after HAART became widely available, they have persisted, though to a lesser extent, in recent years. However, a significant proportion of HIV infected and HIV uninfected women continue to be hospitalized at each visit (10-15%), and rates among HIV negative women have remained stable over time. While the convergence of hospitalization rates among HIV-infected and uninfected women are encouraging, rates of hospitalization are still higher among both groups of women than in the general population. Estimates of annual inpatient hospitalizations from recent population surveys range from approximately 11 – 14 stays per 100 women aged 18-64 ²⁴. While not directly comparable due to differences in populations and calculation of rates, in our study, incidences of first hospitalization were 20 and 17 per 100 person-years among HIV infected and uninfected women respectively. HIV infected and uninfected women in our sample reported high prevalence of smoking, history of substance and alcohol use, abuse, depression, and other comorbidities, all of which make women vulnerable to development and progression of comorbidities as they age. There is a need for interventions that address clinical and psychosocial factors that predispose women to comorbidities, increase risk of hospitalization, and potentially create added social and financial hardship.

The VACS index accurately predicted hospitalizations among HIV infected and uninfected women in our sample, consistent with other recent studies ^{13,25}. The VACS index may thus be a useful tool for predicting risk in uninfected women despite normalized CD4 counts, since it includes markers of renal and liver function. However, additional psychosocial and clinical factors independently predicted hospitalization in models that included VACS for both HIV infected and uninfected women. Women who reported a clinically relevant depressive symptom burden were 1.4-1.6 times more likely to be hospitalized, suggesting that using VACS in combination with risk assessment tools such as depression screening may better quantify overall risk. Depression disproportionately impacts people with HIV ²⁶, and is associated with inflammation ²⁷ and negative clinical outcomes ²⁸. Given the high prevalence of clinically significant depressive symptoms in our study, screening for and treating depression could have an important impact on women's health outcomes.

Approximately 60% of WIHS women reported history of sexual, physical, or emotional abuse, consistent with other literature showing high prevalence of physical and sexual abuse among HIV infected women ²⁹. Among HIV infected women, history of abuse was associated with an increased risk of hospitalization independently of the VACS Index and depression. Studies have consistently demonstrated negative consequences on HIV disease progression and health in general among patients with history of abuse and trauma, with long-term effects on physical and cognitive functioning, health care utilization, including hospitalizations, emergency room and outpatient visits ^{29,30}, and mortality ³¹ in HIV infected patients. It is unclear why history of abuse was not as strongly associated with hospitalization among HIV uninfected women in our study. This finding may reflect differences in sampling or self-selection factors among HIV infected and uninfected women, differences in cumulative exposures or specific types of abuse, or other unmeasured factors,

such as differences in care seeking patterns or reporting of abuse that impacted the relative associations we observed. Alternatively, the intersection of HIV infection and abuse may uniquely impact additional predisposing conditions, such as social isolation, that in turn impact risk of hospitalization and development of comorbidities.

Among HIV infected women, smoking was associated with an increased risk of hospitalization independently of the VACS Index, though a statistically significant association was not observed for HIV uninfected women. The reason for the difference by HIV status is unclear, but may be due to unique interactions of smoking and HIV and/or HIV therapy, or differences between groups in the distribution of other unmeasured confounders, such as care-seeking behaviors or other comorbidities. Given the high prevalence of smoking among women in our study smoking cessation remains a priority and may have particularly important effects for HIV infected women if health effects of smoking are exacerbated in the presence of HIV disease ³².

Substance use (recent and former) was associated with increased rates of hospitalization in univariable analysis for HIV infected and uninfected women, though not statistically significant in multivariable analysis. This is likely due to correlation with VACS Index scores, depression, other co-morbidities, or a combination of these. In contrast to the recent study by Agkun and colleagues ¹³ among male veterans, alcohol use was not strongly associated with hospitalization in our study. This may reflect differences in measurement of alcohol use and cutoff for hazardous levels, reporting bias, other unmeasured confounding, or true gender differences. Despite the lack of a strong association with hospitalization in our analysis, the confidence intervals included fairly large increases in risk for alcohol abuse. Substance and alcohol use are associated with lower adherence to HAART and adverse clinical outcomes in HIV infected and uninfected women ^{33,34} and remain important targets for clinical interventions.

For HIV infected and uninfected women, black race was associated with an increased risk of hospitalization independently of the VACS index and other clinical and psychosocial risk factors, though the effect for HIV infected women was attenuated over 5-year follow-up. Reasons for these disparities are not entirely clear, but may reflect a combination of socioeconomic hardship, experience of discrimination, and other structural adversities that increase vulnerability to negative health consequences ³⁵. Addressing factors contributing to racial disparities in access and care is a priority to reduce higher rates of hospitalization among these HIV infected and at-risk Black women.

As might be expected, hospitalization at the index visit was a strong predictor of subsequent hospitalizations, and a small but important proportion of women were hospitalized multiple times during the study. Repeat hospitalizations may reflect greater disease severity and may have uniquely deleterious effects on morbidity and mortality, quality of life, and associated healthcare costs. Understanding factors associated with repeated hospitalizations warrants further study.

Limitations

The WIHS has a broad geographic representation and demographic characteristics of the WIHS women reflect those of women living with HIV in the United States, but those retained in the study may be generally healthier than other women living with HIV due to repeated study assessments and ongoing clinical care; additionally, women who died or left the study prior to 2008 were not included. Our findings are not generalizable to HIV infected women not on HAART. Importantly, HIV uninfected WIHS participants are not representative of HIV uninfected women in the general population, due to eligibility criteria for enrollment in WIHS for HIV uninfected women¹⁷, although HIV infected and uninfected WIHS women represent vulnerable and often understudied populations.

Hospitalizations were self-reported and subject to recall bias and reasons for hospitalization were crudely categorized. We were unable to distinguish AIDS defining from non-AIDS defining hospitalizations or to identify the primary cause of hospitalization. Many of the surgeries and other procedures may be secondary to co-morbid conditions. There were also insufficient numbers of events in many of the hospitalization categories to examine multivariable predictors of cause-specific hospitalizations. Nonetheless, the rate of self-reported hospitalizations and the relative associations between VACS and all-cause hospitalizations in our study are similar in magnitude and direction to those reported in other studies^{13,25}.

Conclusions

Despite decreases in hospitalizations among HIV infected women since the widespread availability of HAART, we found persistently elevated rates of hospitalization among both HIV infected and uninfected WIHS women relative to rates in the general population. Our data suggest that higher rates of infection are the primary source of the disparity between HIV infected and uninfected women. We observed a 3-fold higher rate of infections resulting in hospitalization among HIV infected relative to HIV uninfected women, despite availability of HAART and improved CD4 counts. Further research is needed to understand differences in cause-specific predictors of hospitalization among HIV infected and uninfected women, and to quantify the contribution of clinical and psychosocial influences on women's health outcomes. In addition to improving clinical markers such as those captured in the VACS Index, addressing racial inequity in access and quality of care and prioritizing treatment for depression and smoking cessation may reduce morbidity among HIV infected and uninfected women.

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Figure 1.

Trends over Time in All-Cause Hospitalizations

Footnote: Across all visits, HIV positive women were more likely to be hospitalized ($p < 0.001$) controlling for time and repeated measures correlation in a generalized estimating equations logistic regression model. Among HIV positive women, hospitalizations declined over time (p for trend < 0.001); the trend among HIV negative women was not statistically significant ($p > 0.2$).

Table 1

Index Visit Characteristics by HIV Status

Characteristic at Index Visit	HIV Infected (n %)	HIV Uninfected n (%)	p-value
Total	1585 (100.0)	692 (100.0)	--
VACS Index Score			
0-23	732 (46.2)	547 (79.1)	<0.001
23-34	373 (23.5)	85 (12.3)	
35-50	272 (17.2)	49 (7.1)	
51	208 (13.1)	11 (1.6)	
Median (IQR); Range	23 (16-39); 0-106	10 (10-22); 0-86	
CESD			
16	558 (35.3)	218 (31.6)	0.082
<16	1022 (64.7)	473 (68.5)	
Current smoking			
Yes	607 (38.4)	353 (51.0)	<0.001
No	975 (61.6)	339 (49.0)	
Hazardous alcohol use			
Yes	276 (17.5)	211 (30.5)	<0.001
No	1306 (82.6)	481 (69.5)	
Transactional sex ever			
Yes	505 (31.9)	221 (31.9)	0.994
No	1077 (68.1)	471 (68.1)	
Transactional sex, recent			
Yes	16 (1.0)	30 (4.3)	<0.001
No	1563 (99.0)	661 (95.7)	
IDU ever			
Yes	354 (22.4)	140 (20.2)	0.260
No	1230 (77.6)	552 (79.8)	
CCH ever			
Yes	841 (53.1)	394 (56.9)	0.091
No	743 (46.9)	298 (43.1)	
Any IDU, recent			
Yes	19 (1.2)	14 (2.0)	0.132
No	1560 (98.8)	677 (98.0)	
Any CCH, recent			
Yes	117 (7.4)	104 (15.0)	<0.001
No	1465 (92.6)	588 (85.0)	
Hypertension, current			
Yes	578 (36.5)	245 (35.4)	0.628
No	1007 (63.5)	447 (64.6)	

Characteristic at Index Visit	HIV Infected (n %)	HIV Uninfected n (%)	p-value
Diabetes history			
Yes	306 (19.3)	150 (21.7)	0.194
No	1279 (80.7)	542 (78.3)	
Race/Ethnicity			
White	208 (13.1)	62 (9.0)	0.012
Black	897 (56.6)	430 (62.1)	
Hispanic	418 (26.4)	168 (24.3)	
Other race	62 (3.9)	32 (4.6)	
Abuse history			
Yes	762 (61.3)	341 (58.9)	0.327
No	481 (38.7)	238 (41.1)	
Recent abuse			
Yes	67 (5.7)	49 (9.1)	0.010
No	1100 (94.3)	488 (90.9)	
Hospitalized at index visit			
Yes	229 (14.5)	83 (12.0)	0.117
No	1356 (85.6)	609 (88.0)	
WIHS recruitment wave			
1994-95	842 (53.1)	296 (42.8)	<0.001
2001-2002	525 (33.1)	307 (44.4)	
2011-2012	218 (13.8)	89 (12.9)	

Abbreviations: CESD, Centers for Epidemiologic Studies – Depression; CCH, crack, cocaine, or heroin use; IDU, injection drug use; VACS, Veterans Aging Cohort Study, WIHS, Women's Interagency HIV Study

Table 2

Total Hospitalizations by HIV Status over 2 Years by Diagnostic Categories

	Visits among HIV infected women (N=5266)		Visits among HIV uninfected women (N=2263)	
	n	%	n	%
Visits where hospitalization was reported	673	12.8	235	10.4
Total times hospitalized since last visit	n	% of 673 visits	n	% of 235 Visits
1	480	71.3	184	78.3
2	121	18.0	39	16.6
3	72	10.7	12	5.1
Reason for hospitalization	n	% of 673 visits^a	n	% of 235 Visits^a
Surgery/procedures	148	22.0	55	23.4
Infection other than pneumonia	117	17.4	15	6.4
Pneumonia	111	16.5	9	3.8
Gastrointestinal disorders ^b	89	13.2	25	10.6
Cardiovascular problems	76	11.3	43	18.3
Lung problems (non-pneumonia)	58	8.6	21	8.9
Psychiatric/mental health issues	47	7.0	22	9.4
Central nervous system disorders	43	6.4	14	6.0
Injury/accident	39	5.8	21	8.9
Gynecologic procedures/surgery	24	3.6	12	5.1
Kidney problems	23	3.4	0	0.0
Liver problems ^c	21	3.1	5	2.1
Blood disorders	13	1.9	8	3.4
Endocrine disorders/diabetes	8	1.2	9	3.8
Cancer	7	1.0	2	0.9
Other illness	15	2.2	10	4.3

^aPercentages sum to more than 100% because multiple reasons for hospitalization could be provided at each visit.

^bIncludes stomach, intestinal, gallbladder, pancreatic issues

^cIncludes Hepatitis related issues

Table 3
Hospitalizations over 2-year follow-up by Patient Characteristics at Index Visit among HIV Infected and HIV Uninfected women

Characteristic at Index Visit	HIV Infected (on HAART)				HIV Uninfected			
	Total n (%)	First Events/Person-years	Incidence Rate per 100 person-years (95% CI)	Log-rank p-value	Total n (%)	First Events/Person-years	Incidence Rate per 100 person-years (95% CI)	Log-rank p-value
Total	1585 (100.0)	462/2308.6	20.01 (18.27-22.92)	--	692 (100.0)	184/1041.6	17.66 (15.29-20.41)	--
VACS Index Score								
0-23	732 (46.2)	163/1110.5	14.68 (12.59-17.11)	<0.001	547 (79.1)	130/840.7	15.46 (13.02-18.36)	<0.001
23-34	373 (23.5)	99/554.5	17.85 (14.66-21.74)		85 (12.3)	32/117.9	27.14 (19.19-38.37)	
35-50	272 (17.2)	90/395.4	22.76 (18.51-27.98)		49 (7.1)	15/67.8	22.11 (13.33-36.67)	
51	208 (13.1)	110/248.1	44.33 (36.77-53.44)		11 (1.6)	7/15.1	46.28 (22.06-97.07)	
On HAART since last visit								
Yes	1378 (86.9)	398/2008.7	19.81 (17.96-21.86)	0.627	--	--	--	--
No	207 (13.1)	64/300.0	21.34 (16.70-27.26)		--	--	--	--
CESD								
16	558 (35.3)	231/744.2	31.04 (27.29-35.31)	<0.001	218 (31.6)	74/314.7	23.51 (18.72-29.53)	0.002
<16	1022 (64.7)	228/1557.9	14.64 (12.85-16.66)		473 (68.5)	109/725.9	15.02 (12.45-18.12)	
Current smoking								
Yes	607 (38.4)	222/841.1	26.39 (23.14-30.10)	<0.001	353 (51.0)	99/531.4	18.63 (15.30-22.69)	0.395
No	975 (61.6)	237/1465.5	16.17 (14.24-18.37)		339 (49.0)	85/510.3	16.66 (13.47-20.60)	
Hazardous alcohol use								
Yes	276 (17.5)	88/395.6	22.25 (18.05-27.42)	0.203	211 (30.5)	55/322.5	17.05 (13.09-22.21)	0.739
No	1306 (82.6)	371/1911.0	19.41 (17.54-21.49)		481 (69.5)	129/719.1	17.94 (15.09-21.32)	
Transactional sex ever								
Yes	505 (31.9)	180/711.1	25.31 (21.87-29.30)	<0.001	221 (31.9)	75/321.1	23.36 (18.63-29.29)	0.004
No	1077 (68.1)	280/1595.0	17.55 (15.61-19.74)		471 (68.1)	109/720.5	15.13 (12.54-18.25)	
Transactional sex, recent								
Yes	16 (1.0)	8/20.0	40.09 (20.05-80.16)	0.041	30 (4.3)	10/43.9	22.78 (12.26-42.35)	0.395
No	1563 (99.0)	451/2280.9	19.77 (18.03-21.69)		661 (95.7)	173/996.7	17.36 (14.95-20.15)	

Characteristic at Index Visit	HIV Infected (on HAART)				HIV Uninfected			
	Total n (%)	First Events/Person-years	Incidence Rate per 100 person-years (95% CI)	Log-rank p-value	Total n (%)	First Events/Person-years	Incidence Rate per 100 person-years (95% CI)	Log-rank p-value
IDU ever								
Yes	354 (22.4)	137/484.4	28.28 (23.92-33.44)	<0.001	140 (20.2)	47/206.3	22.78 (17.11-30.32)	0.049
No	1230 (77.6)	325/1823.1	18.09 (15.99-19.87)		552 (79.8)	137/835.3	16.40 (13.87-19.39)	
CCH ever								
Yes	841 (53.1)	296/1184.2	25.00 (22.31-28.01)	<0.001	394 (56.9)	122/579.7	21.05 (17.62-25.13)	0.002
No	743 (46.9)	166/1123.4	14.78 (12.69-17.20)		298 (43.1)	62/461.9	13.42 (10.46-17.21)	
Any IDU, recent								
Yes	19 (1.2)	11/25.3	43.55 (24.12-78.64)	0.014	14 (2.0)	7/21.0	33.36 (15.91-69.99)	0.090
No	1560 (98.8)	448/2275.6	19.69 (17.95-21.60)		677 (98.0)	176/1019.6	17.26 (14.89-20.01)	
Any CCH, recent								
Yes	117 (7.4)	47/161.1	29.18 (21.92-38.83)	0.007	104 (15.0)	37/150.5	24.59 (17.82-33.94)	0.025
No	1465 (92.6)	412/2145.5	19.20 (17.44-21.15)		588 (85.0)	147/891.2	16.50 (14.03-19.39)	
Hypertension, current								
Yes	578 (36.5)	217/804.4	26.98 (23.62-30.82)	<0.001	245 (35.4)	101/340.8	29.63 (24.38-36.01)	<0.001
No	1007 (63.5)	245/1504.2	16.29 (14.37-18.46)		447 (64.6)	83/700.8	11.84 (9.55-14.69)	
Diabetes history								
Yes	306 (19.3)	122/422.9	28.85 (24.16-34.45)	<0.001	150 (21.7)	62/128.7	31.2 (24.3-40.0)	<0.001
No	1279 (80.7)	340/1885.7	18.03 (16.21-20.05)		542 (78.3)	122/842.9	14.5 (12.1-17.3)	
Race/Ethnicity								
White	208 (13.1)	54/302.5	17.85 (13.67-23.31)	0.016	62 (9.0)	15/96.4	15.56 (9.38-25.81)	0.015
Black	897 (56.6)	285/1277.4	22.31 (19.87-25.06)		430 (62.1)	131/630.6	20.77 (17.50-24.65)	
Hispanic	418 (26.4)	111/633.0	17.53 (14.56-21.12)		168 (24.3)	31/264.5	11.72 (8.24-16.66)	
Other race	62 (3.9)	12/95.7	12.54 (7.12-22.09)		32 (4.6)	7/50.1	13.97 (6.66-29.30)	
Abuse history^a (n=1,243)								
Yes	762 (61.3)	270/1082.3	24.95 (22.14-28.11)	<0.001	341 (58.9)	100/505.1	19.80 (16.27-24.08)	0.217
No	481 (38.7)	104/726.2	14.32 (11.82-17.35)		238 (41.1)	59/359.0	16.43 (12.73-21.21)	
Recent abuse^b (n=1,167)								

	HIV Infected (on HAART)					HIV Uninfected			
Characteristic at Index Visit	Total n (%)	First Events/Person-years	Incidence Rate per 100 person-years (95% CI)	Log-rank p-value	Total n (%)	First Events/Person-years	Incidence Rate per 100 person-years (95% CI)	Log-rank p-value	
Yes	67 (5.7)	24/92.2	26.02 (17.44-38.83)	0.326	49 (9.1)	10/73.8	13.54 (7.29-25.17)	0.228	
No	1100 (94.3)	336/1579.6	21.27 (19.11-23.67)		488 (90.9)	139/725.3	19.16 (16.23-22.63)		
Hospitalized at index visit									
Yes	229 (14.5)	122/270.5	45.11 (37.77-53.87)	<0.001	83 (12.0)	46/104.3	44.09 (33.03-58.87)	<0.001	
No	1356 (85.6)	340/2038.1	16.68 (15.00-18.55)		609 (88.0)	138/937.3	14.72 (12.46-17.40)		
WIHS recruitment wave									
1994-95	842 (53.1)	278/1212.1	22.94 (20.39-25.80)	0.006	296 (42.8)	98/432.3	22.67 (18.60-27.63)	<0.001	
2001-2002	525 (33.1)	133/785.5	16.93 (14.28-20.07)		307 (44.4)	59/483.3	12.21 (9.46-15.76)		
2011-2012	218 (13.8)	51/311.0	16.40 (12.46-21.58)		89 (12.9)	27/126.0	21.42 (14.69-31.24)		

Abbreviations: CESD, Centers for Epidemiologic Studies – Depression; CCH, crack, cocaine, or heroin use; HAART, highly active antiretroviral therapy; IDU, injection drug use; VACS, Veterans Aging Cohort Study, WIHS, Women's Interagency HIV Study

^aBased on non-missing observations, N=1243 for HIV positive women and N=579 for HIV negative women

^bBased on non-missing observations, N=1167 for HIV positive women and N=537 for HIV negative women

Table 4
Univariable and Multivariable Cox Regression: Relative Hazard of First Hospitalization over 2-year follow-up

	HIV Infected (on HAART)			HIV Uninfected		
	Univariable HR (95% CI)	p-value	Multivariable HR ^a (95% CI)	p-value	Univariable HR (95% CI)	Multivariable HR ^a (95% CI)
VACS at index visit (per 5 point increase)	1.12 (1.10-1.15)	<0.001	1.08 (1.06-1.11)	<0.001	1.13 (1.08-1.19)	1.08 (1.03-1.13)
CESD 16	2.15 (1.79-2.58)	<0.001	1.61 (1.30-1.99)	<0.001	1.63 (1.21-2.20)	1.38 (1.02-1.86)
Smoking	1.66 (1.38-1.99)	<0.001	1.26 (1.02-1.55)	0.018	1.17 (0.87-1.57)	--
Hazardous alcohol use	1.16 (0.92-1.47)	0.203	--	--	0.97 (0.71-1.32)	--
Transactional sex ever	1.45 (1.20-1.75)	<0.001	--	--	1.53 (1.14-2.05)	--
IDU history	1.60 (1.31-1.95)	<0.001	--	--	1.42 (1.02-1.98)	--
CCH ever	1.70 (1.41-2.06)	<0.001	--	--	1.67 (1.23-2.27)	--
CCH recent	1.52 (1.13-2.03)	0.006	--	--	1.54 (1.07-2.20)	--
Hypertension	1.67 (1.39-2.00)	<0.001	--	--	2.74 (2.05-3.67)	--
Diabetes ever	1.59 (1.30-1.96)	<0.001	1.63 (1.31-2.04)	<0.001	2.30 (1.69-3.14)	2.15 (1.57-2.95)
Abuse history	1.82 (1.44-2.29)	<0.001	1.52 (1.20-1.93)	0.001	1.28 (0.92-1.77)	--
HAART use since last visit	0.94 (0.72-1.22)	0.630	--	--	NA	NA
Time since HAART initiation	1.01 (0.99-1.04)	0.279	--	--	NA	NA
WHHS recruitment wave						
1994-95	1.0 (Ref)		--	--	1.0 (Ref)	--
2001-2002	0.74 (0.60-0.91)	0.004	--	--	0.50 (0.36-0.70)	--
2011-2012	0.74 (0.55-0.996)	0.047	--	--	1.00 (0.66-1.53)	--
Year of index visit	0.94 (0.87-1.02)	0.158	--	--	1.11 (0.998-1.24)	--
Hospitalization at index visit	2.84 (2.30-3.49)	<0.001	2.37 (1.87-2.99)	<0.001	3.43 (2.44-4.82)	3.10 (2.19-4.38)
Black race	1.34 (1.11-1.61)	0.003	1.28 (1.03-1.59)	0.028	1.62 (1.18-2.23)	1.61 (1.15-2.24)

Abbreviations: CESD, Centers for Epidemiologic Studies – Depression; CCH, crack, cocaine, or heroin use; IDU, injection drug use; VACS, Veterans Aging Cohort Study, WHHS, Women's Interagency HIV Study

^a Multivariable hazard ratios are adjusted for all variables for which estimates are presented.