
Predictors of Hospitalization for HIV-Positive Women and Men Drug Users, 1996-2000

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S Y N O P S I S

Objective: This study sought to determine whether health outcomes differed by gender in a cohort of African American, Hispanic American, and white drug users.

Methods: The authors studied hospitalization rates and discharge diagnoses in the HERO Study, an ongoing prospective study of drug users that included HIV-positive and HIV-negative opiate users. The data are from 1996-2000, when highly active antiretroviral therapy (HAART) was available.

Results: Women had higher rates of hospitalization than men independent of HIV status, and there was no association between ethnicity and hospitalization. Being a woman was an independent risk factor for HIV and non-HIV-related hospitalization.

Conclusion: Health disparities between men and women extend to HIV.

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INTRODUCTION

Disparities in health status and the utilization of health care services continue to exist between women and men and between minority groups and whites.¹ The HIV epidemic, which has disproportionately affected white homosexual and bisexual men largely of the middle class as well as African American and Hispanic men and women drug users of the lowest economic status, has provided stark evidence of differential access and adherence to highly active antiretroviral therapy (HAART).²⁻⁵ Use of HAART has resulted in a dramatic decline in HIV-related morbidity and hospitalizations,⁶ but drug users in many settings are less likely to receive HAART than men who acquired HIV via sex with men, and they are more likely to be hospitalized.^{3,5,7} The lower socioeconomic status of drug users, including lower education, lower income, and inferior or no health insurance, confounds these comparisons and limits assessment of the effects of race, ethnicity, and gender.⁸ Consequently, little is known about the effects of these factors on health outcomes attributable to the use of HAART by drug users. Factors such as drug treatment and type and route of illicit drug administration may be related to the health status of drug users and resultant hospitalization, whereas socioeconomic status is more uniform.⁹⁻¹²

METHODS

Starting in July 1986, drug users attending a long-term methadone treatment program at Montefiore Hospital in the Bronx, New York City, were enrolled in a prospective study of HIV disease progression and temporal trends in drug-use behaviors called the HERO Study (HIV Epidemiologic Research Study on Outcomes). All enrollees underwent a standardized interview, in English or Spanish, that elicited information on sociodemographic characteristics, medical history, and drug and alcohol use. Venipuncture was performed for HIV antibody and CD4+ count.³ Research visits were conducted semiannually by interviewers who were not methadone program staff. Participants were followed whether or not they continued attending the methadone treatment program. Hospitalizations were monitored, and inpatient medical records were abstracted on standardized forms. All information was confidential. The study was approved by the institutional review board of Montefiore Hospital.

Cohort members who had one or more research visits between January 1, 1996, and December 31, 2000,

were included in this analysis. Information from the first research interview was used for baseline data. Hospitalizations were categorized according to discharge diagnoses and were linked to demographic characteristics, HIV infection, drug-use variables, CD4+ count, and whether or not HAART was used. HAART was defined as the use of three or more approved antiretroviral medications that included one or more nucleosides plus a nonnucleoside and/or protease inhibitor.

We calculated the cumulative follow-up time between 1996 and 2000, which we used to determine crude rates of hospitalization for a given group. Two-tailed chi-square tests were used to examine associations between covariates such as drug use, CD4+ count, and HAART with gender and hospitalization among HIV-positive participants. Poisson regression was used to examine independent factors associated with the number of hospital admissions per year for HIV-positive and HIV-negative participants during follow-up. Separate models were constructed for HIV-positive participants for analysis of risk factors for all hospitalizations and for hospitalizations related to HIV-related diagnoses. A log link function was used to model the mean number of hospitalizations (or hospitalization rate) as a linear function of the explanatory variables. The log of the follow-up time was included to adjust for different follow-up times. Repeated hospitalizations may not be independent, and the variability among counts may exceed the nominal (or expected) variability. To correct this overdispersion, we used a correction term, suggested by McCullagh and Nelder, the ratio of the Pearson chi-square to its associated degree of freedom.¹³

RESULTS

During 1996-2000, 1,039 HERO Study participants were followed, 37.0% (n = 384) of whom were infected with HIV (table 1). HIV-positive and HIV-negative participants were comparable in terms of gender and age, with a median age of 38 for women and 40 for men. The sample was predominantly of Puerto Rican descent. The prevalence of HIV infection was 48.3% among African Americans, 37.6% among Hispanic Americans, and 27.1% among whites. HIV-positive participants were significantly more likely to be receiving public assistance and not to have graduated from high school. The distribution of demographic characteristics was similar when examined by gender, with the exception of receiving public assistance, which was reported by 88.9% of women and 77.9% of men ($p < .0001$).

Among HIV-positive participants, CD4+ counts were higher in women: 29.8% of HIV-positive women had

Table 1. Characteristics of HIV-positive and HIV-negative HERO Study participants, 1996-2000

Characteristic	HIV-positive n = 384 n (%)	HIV-negative n = 649 n (%)	P value
Sex			
Women	155 (40.4)	277 (42.7)	ns
Men	229 (59.6)	372 (57.3)	
Ethnicity			
African American	84 (21.9)	90 (13.9)	<.0001
Hispanic	259 (67.5)	430 (66.3)	
White	38 (9.9)	122 (18.8)	
Other	3 (0.7)	7 (1.0)	
Age			
<35 years	89 (23.2)	171 (26.3)	ns
35-45 years	218 (56.8)	336 (51.8)	
>45 years	77 (20.0)	142 (21.9)	
Receive public assistance:			
Yes	367 (95.6)	487 (75.0)	<.00001
No	17 (4.4)	162 (25.0)	
Education			
<12 years	222 (58.3)	338 (52.3)	<.00001
12 years	991 (23.9)	169 (26.2)	
>12 years	68 (17.8)	139 (21.5)	
CD4+ count			
<200	119 (31.6)		na
200-500	151 (40.1)		
>500	107 (28.4)		
Use of HAART ^a			
Yes	48 (17.8)		na
No	222 (82.2)		

na = not applicable.

ns = not significant.

^aLimited to 270 people with CD4+ counts of 500 or more.

counts below 200, 33.8% had counts of 200-500, and 36.4% had counts greater than 500 ($p = .01$). Among HIV-positive men, 32.7% had counts below 200, 44.3% had counts of 200-500, and 23.0% had counts greater than 500 ($p = .01$). There was no relationship between gender or ethnicity and use of HAART, even when the sample was limited to people whose CD4+ count reached 500 at their first visit in 1996 or at the last visit before December 31, 2000. The percentage reporting HAART use increased from 17.1% in 1996 to 29.5% in 2000.

Drug-using behaviors were examined by HIV status to avoid the confounding effect of being HIV-positive as a result of drug-using behaviors (table 2). The

proportion of participants who reported current needle use did not differ by HIV infection status. More HIV-negative participants used heroin than HIV-positive participants (22.6% versus 17.7%; $p = .06$), but cocaine use was unrelated to HIV infection. HIV-negative status was also associated with drinking alcohol: 44.8% of HIV-negative participants and 34.4% of HIV-positive participants drank at least once a day ($p = .01$). When drug-use behaviors were stratified by gender and HIV status, men without HIV were more likely to be using heroin and to be drinking more heavily than HIV-negative women. Methadone treatment was significantly associated with HIV status ($p = .01$); there was no difference by gender.

Table 2. Substance abuse behaviors by HIV status and gender

Behavior	Use	HIV-positive		p value	HIV-negative		p value
		Women n = 155 n (%)	Men n = 229 n (%)		Women n = 277 n (%)	Men n = 372 n (%)	
Drug injection	Yes	5 (3.2)	17 (7.4)	0.08	11 (4.0)	24 (6.5)	0.16
	No	150 (96.8)	212 (92.6)		266 (96.0)	348 (93.6)	
Heroin use	Yes	25 (16.1)	43 (18.8)	0.50	51 (18.4)	96 (25.8)	0.03
	No	130 (83.9)	186 (81.2)		226 (81.6)	276 (74.2)	
Cocaine use	Yes	30 (19.3)	41 (17.9)	0.72	44 (15.9)	66 (17.7)	0.53
	No	125 (80.7)	188 (82.1)		233 (84.1)	306 (82.3)	
Alcohol use (daily)	Yes	42 (27.1)	90 (60.7)	0.01	119 (43.0)	172 (46.2)	0.001
	No	113 (72.9)	139 (39.3)		158 (57.0)	200 (53.8)	
Prescription methadone use	Yes	131 (84.5)	206 (90.0)	0.11	250 (90.2)	330 (88.7)	0.5
	No	24 (15.5)	23 (10.0)		27 (9.8)	42 (11.3)	

Among the 384 HIV-positive participants, 193 were hospitalized between 1996 and 2000. The total number of hospitalizations was 662, with a cumulative follow-up time of 1,101.7 years. The cumulative follow-up time for 90 of 155 women with HIV was 461.4 years, during which time there were 321 hospitalizations; 107 of 229 HIV-positive men had 341 hospitalizations, with 640.3 years of follow-up. The crude rate of hospitalization among HIV-positive women was 69.6 per 100 person-years of observation and 53.3 per 100 person-years in HIV-positive men. There was no difference in hospitalization rates by race or ethnicity. In contrast, 210 of 277 HIV-negative participants had 492 hospitalizations, accounting for 2,456.4 years of follow-up; 93 women had 249 hospitalizations, accounting for 1,083.4 years of follow-up; and 107 men had 243 hospitalizations, accounting for 1,372.9 years of follow-up. For people without HIV, the hospitalization rate

was 23.0/100 person-years for women and 17.7/100 person-years for men.

Table 3 displays the hospitalization rates stratified by HIV status and gender for selected diagnostic categories likely related to HIV or drug use. Rates of bacterial pneumonia, other bacterial infections, and liver disease were lower in drug users without HIV. Psychiatric admissions were similar across the four strata. Bacterial pneumonia was the most frequent diagnosis and was more common in women than men for people with and people without HIV. HIV/AIDS (largely opportunistic infections) and liver disease were more common among men. There was no significant difference between people taking HAART and those not taking HAART in terms of the proportion who had had at least one hospitalization.

We performed multivariate analysis using Poisson regression models to assess predictors of

Table 3. Hospitalization rates by HIV status and gender (number of events per 100 years of follow-up)

Sex and HIV status	HIV/AIDS	Bacterial pneumonia	Other bacterial infections	Liver disease	Psychiatric admissions
HIV+ women	9.8	16.3	10.0	3.5	5.0
HIV+ men	8.7	10.3	8.4	5.0	3.3
HIV- women	na	2.9	3.4	0.6	3.0
HIV- men	na	1.3	2.7	1.7	3.2

na = not applicable.

Table 4. Poisson regression analysis of predictors of hospitalizations

Variable	Relative risk ratio	Parameter estimate	Standard error	95% CL	P value
Model of HIV+ and HIV- drug users and any hospitalization					
HIV+ (vs. HIV-)	2.64	0.97	0.133	2.04, 3.43	<0.0001
Women (vs. men)	1.34	0.29	0.132	1.04, 1.74	0.03
Recent drug injection (vs. none)	1.86	0.62	0.245	1.15, 3.00	<0.01
Age (per year)	1.04	0.04	0.009	1.02, 1.06	<0.0001
Receive public assistance (yes vs. no)	2.88	1.06	0.300	1.60, 5.19	0.0004
Model of HIV+ drug users and any hospitalization ^a					
Women (vs. men)	1.49	0.40	0.187	1.03, 2.15	0.03
CD4+ count <200 (vs. ≥500)	2.25	0.81	0.246	1.39, 3.65	0.001
CD4+ count 200-500 (vs. ≥500)	1.50	0.41	0.247	0.93, 2.43	0.10
Recent drug injection (vs. none)	1.95	0.67	0.329	1.02, 3.71	0.04
Age/year	1.03	0.03	0.014	1.00, 1.06	0.05
Model of HIV+ drug users and HIV-related hospitalizations ^{a,b}					
Women (vs. men)	1.57	0.45	0.236	0.99, 2.49	0.06
CD4+ count <200 (vs. ≥500)	5.85	1.77	0.402	2.66, 12.85	<0.0001
CD4+ count 200-500 (vs. >500)	3.21	1.17	0.410	1.44, 7.17	0.004

^aReceiving public assistance not significant.
^bRecent drug injection and age not significant.

hospitalization with relative risk ratios (RRR) that describe the incidence of hospitalization in a subgroup relative to the incidence in the reference group. Table 4 displays the final models for the predictors of the number of hospitalizations per year for the entire cohort and for HIV-positive participants alone. A third model of the predictors of HIV-related hospitalization was limited to the HIV-positive participants. Women were at significantly higher risk for hospitalization independent of HIV status and recent injection-drug use (RRR = 1.34; 95% confidence interval [CI], 1.04-1.74) and when limited to HIV-positive participants and controlling for CD4+ count (RRR = 1.49; 95% CI, 1.03-2.15). HAART use was not associated with hospitalization. Neither race, ethnicity, nor level of education was associated with hospitalization in any of the three models. Among recent substance abuse behaviors, only injection of drugs in the past six months was significantly related to any hospitalization among all participants (RRR = 1.86; 95% CI, 1.15-3.00) and when limited to those who were HIV-positive (RRR = 1.95; 95% CI, 1.02-3.71). Daily alcohol use and use of cocaine, heroin, or both by any route of administration were not associated with hospitalization in any model. Drug treatment with

methadone was not independently associated with frequency of hospitalization.

DISCUSSION

This study describes antiretroviral use and high-risk behavior for men and women drug users among a cohort of African American, Hispanic American, and white drug users during a time when effective treatment for HIV was available. It examines how these factors relate to hospitalization for HIV and other diseases. Many studies have shown that HIV-positive drug users are less likely to receive HAART,^{4,12} less likely to suppress viral load if on treatment,⁷ and more likely to be hospitalized than HIV-positive individuals without a history of intravenous drug use.^{5,14-16} Women have also been identified as being at a high risk for these adverse outcomes, as well as for hospitalization.^{5,14} These findings have emerged largely from studies of HIV clinic populations and Medicaid insurance claim data, however, or from hospital discharge diagnosis trends rather than from defined study populations.

Our study addressed risk factors for hospitalization among men and women who were addicted to narcotics and were participating in a well-established prospective

study of HIV disease progression.^{3,17} It found that women were one-third more likely than men to be hospitalized for HIV- and non-HIV-related diagnoses (RRR = 1.34). Among HIV-positive participants, women were 50% more likely than men to be hospitalized. Women experienced about 60% more HIV-related hospitalizations than men (RRR = 1.57; $p = .06$). Although the level of significance of this result was borderline, women remained at higher risk, controlling for CD4+ count, a powerful predictor of HIV-associated opportunistic infections that require hospitalization and the major cause of hospitalization in this model.¹⁸

Our study did not address emergency department utilization. Markson and colleagues examined New York State Medicaid claims and found higher repeated emergency department use by women and injection-drug users with HIV infection than among men and noninjectors with HIV infection. This could partly explain the higher hospitalization rate by women in our study.⁹

Our rates of hospitalization were 69 per 100 person-years for women and 53 per 100 person-years for men. Tashima recently analyzed hospitalization rates in a prospective study of HIV in women (HER Study) in which rates of 3-3.4 per 100 person-months coincided with the early HAART era and were higher for women who injected drugs.¹⁹ These rates correspond roughly to 36-40 per 100 person-years. While this rate is somewhat lower than the rate we found in women, by design one-half of the HIV-positive participants in the HER Study were current or former drug users. In contrast, our study was limited to drug users. Our rates may have been affected by the cohort study design, in which participants enrolled before 1996 were included in follow-up time from 1996 to 2000. These participants may have aged and have had more advanced HIV infection when they contributed time to our analysis participants in comparison to a more recently assembled cohort. Alternatively, older and sicker people may have died.

Gebo and colleagues found that among HIV-positive clinic patients followed from 1995 to 1998, women were significantly more likely to be hospitalized than men (adjusted OR = 1.45). Their results are similar to ours.¹⁴ In Gebo's study and in others, HAART was associated with a decline in hospitalization.^{14,16,19,20} In contrast, in our study, HAART use was not a predictor of hospitalization. The proportion of participants in

our study on HAART was only 17.1% in 1996 and 29.5% by 2000, with no difference in use between men and women. Our study participants had a history of extensive use of an antiretroviral medication, which may have dampened their willingness to use HAART. Those in our study who reported use of HAART had previously been treated with a mean of 2.7 antiretroviral medicines.²¹ Adherence to HAART in our population was also low, with only about one-half of prescribed doses confirmed by electronic monitoring devices. Women had lower levels of adherence than men.²¹

These findings echo those from a prospective study in Vancouver, British Columbia, where HAART is widely available and free. In that study, women drug users were two to three times as likely as men drug users not to be treated with HAART.²² Although many of our participants attended methadone programs with on-site HIV care, for others, reluctance by providers to treat people with a history of drug use may also account for the low level of HAART use and the lack of a significant relationship between HAART use and hospitalization.^{3,5,10}

All participants in our study had a history of injection-drug use as a risk factor for acquiring HIV, although less than 10% of participants had injected drugs in the six months before their first interview in 1996. Injection-drug use significantly increased the risk of non-HIV-related hospitalization. The higher rates of hospitalization among the HIV-positive participants suggest a lower threshold for hospitalization by health care personnel when a drug user is HIV-positive. The frequent hospitalization of drug injectors and HIV and hepatitis C alcohol users may indicate future hospitalizations for liver disease.²³ Finally, as people with HIV live longer, diseases associated with aging may increase, changing the pattern of hospitalization accordingly.

Women were hospitalized more often than men independent of HIV status, and there was no association between ethnicity and hospitalization. Being a woman was an independent risk factor for HIV and non-HIV-related hospitalization. This finding points to an increase in morbidity relative to men and indicates that health disparities that exist for women in other diseases extend to HIV.^{24,25} Our study did not find that HAART use in 1996 predicted a lower rate of hospitalization. Further study is required to determine whether differential patterns of HAART use and other factors led to this health disparity for women drug users with HIV.

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