Published in final edited form as:

Med Decis Making. 2014 August ; 34(6): 800–808. doi:10.1177/0272989X13507340.

Health Related Quality of Life in HIV-infected and at-risk Women: The Impact of Illicit Drug Use and Hepatitis C on a Community Preference Weighted Measure*

Brandon Aden, MD, MPH¹, Bohdan Nosyk, PhD^{2,3}, Eve Wittenberg, PhD⁴, and Bruce R. Schackman, PhD¹

¹Department of Public Health, Weill Cornell Medical College, New York, NY

²British Columbia Centre for Excellence in HIV/AIDS, Vancouver, British Columbia

³ Faculty of Health Sciences, Simon Fraser University

⁴Center for Health Decision Science, Harvard School of Public Health, Boston, MA

Abstract

Purpose—To assess the impact of illicit drug use and chronic hepatitis C virus (HCV) on health related quality of life (HRQoL) in women with HIV or at-risk for HIV infection.

Methods—Cross-sectional analysis of data from the Women's Interagency Health Study (WIHS) of women with HIV (n=2508) and at high risk of HIV infection (n=889) in the US. A Short-Form-6D (SF-6D) HRQoL measure derived from the Medical Outcomes Study–HIV (MOS–HIV) questionnaire, HIV infection status, CD4 cell count (a measure of immune status), antiretroviral treatment, current illicit drug use (heroin and/or cocaine), and HCV status were assessed at a recent study visit. We developed multivariate linear regression models adjusting for age, race/ethnicity, education, and testing for interactions.

Results—HIV-infected women with ≤ 200 CD4 cells/uL had lower mean HRQoL scores (0.69) than either HIV-infected women with >200 CD4 cells/uL (0.78) or HIV-uninfected women (0.80) ($p<0.01$). In multivariate analysis, illicit drug use, chronic HCV, and low CD4 count were independently associated with lower HRQoL. There was a differential effect of HCV and illicit drug use for HIV-infected women depending on CD4 cell count: HIV-infected women with >200 CD4 cells/uL had a significantly greater reduction in HRQoL associated with illicit drug use (-0.063) and chronic HCV (-0.036) than women with ≤ 200 CD4 cells/uL (-0.017 , -0.005 respectively).

Conclusion—Poorly-controlled HIV, illicit drug use, and chronic HCV are associated with lower HRQoL. Illicit drug use and chronic HCV have greater HRQoL impacts for HIV-infected

*Financial support for this study was provided in part by a grant from the National Institute on Drug Abuse R01 DA033424. The funding agreement ensured the authors' independence in designing the study, interpreting the data, writing, and publishing the report.

Current address and correspondence: Brandon Aden, MD, MPH, Department of Public Health, Weill Cornell Medical College, New York, NY 10065; phone: 646-962-8078; fax: 646-962-0281; bra2002@med.cornell.edu.

Portions of this manuscript were previously presented at the Society for Medical Decision Making Annual Meeting, October 17-20, 2012, Phoenix, AZ.

women with well-controlled HIV versus those with poorly-controlled HIV, which may affect clinical and policy priorities.

Keywords

HIV; HRQoL; Opiate Dependence; Health Utility; Illicit Drug use; HCV

INTRODUCTION

Health-related quality of life (HRQoL) measures have increasingly become part of the assessment of chronic disease treatment outcomes and are integral to health economic evaluation to guide treatment and resource allocation decisions. HIV infection, opioid dependence, and Hepatitis C Virus (HCV) infection are independently associated with poor HRQoL and lower health utility scores,(1-4) and these conditions are often co-occurring. Injection drug use is a primary risk factor for HIV infection; in the US, approximately 33% of all individuals with HIV/AIDS contracted the virus through injection drug use.(5, 6) Injection drug use is also the greatest risk factor for HCV infection.(7, 8) An estimated of 20% of all HIV infected persons in the US are co-infected with HCV and 5-10% of HCV infected persons are co-infected with HIV.(9)

The few studies that have explicitly examined HRQoL among individuals with these overlapping condition have used measures of health status (such as the SF-36 and SF-12) rather than health utility, and have not examined possible interactions among the health conditions in their effects on HRQoL.(10-12) We are not aware of any studies that have considered the independent and joint effects of all three conditions on HRQoL using a preference-based measure such as the Short-Form-6D (SF-6D). Our objective was to assess the impact of illicit drug use and chronic HCV infection on HRQoL among HIV-infected women and women at-risk for HIV infection in the US using SF-6D health utility scores derived from the Medical Outcomes Study–HIV (MOS-HIV) questionnaire. We evaluated the independent and joint effects of HIV disease status, heroin and/or cocaine use, and chronic HCV on HRQoL via statistical interaction terms.

METHODS

Patient Population

We analyzed data collected between 1994 and 2006 in the Women's Interagency HIV Study (WIHS), a prospective longitudinal cohort study of HIV-seropositive women and at-risk (assessed number of sexual partners, history of intravenous drug use) HIV-seronegative women in the United States.(13) Cohort enrollment began in 1994 at 6 sites (Bronx, Brooklyn, Washington DC, Chicago, Los Angeles and San Francisco) with a second wave of enrollment 2001-2002 for a total of 2794 HIV-infected and 975 HIV-uninfected women enrolled as of 2002.(14) Design, methodology and recruitment have been previously described.(13) Participant demographics were assessed at enrollment, including year of birth, race/ethnicity, and education level. HIV infection status (including CD4 cell count and treatment status if HIV-infected), HCV status, and self-reported measures of behavior (including illicit drug use), physical health, and mental health were assessed at 6 month

follow-up intervals. We used the public use data set(15) that includes data collected up until 2006. HRQoL, HIV status, substance use, and HCV status were measured at each 6 month visit, but we utilized only one response per participant for each of these measures. These responses were from the most recent study follow-up visit in 2006 or most recent visit prior to 2006 for subjects who disenrolled, died or were missing data at the 2006 visit.(15)

HRQoL Measure

Our measure of HRQoL was based on the SF-6D, a generic community preference-weighted health utility measure with defined algorithms for derivation from SF-36 and SF-12 measures.(16) The SF-6D condenses the eight dimensions of the SF-12 to six dimensions: physical functioning, role functioning, social functioning, pain, mental health and vitality. Each of these measures has 4 to 6 levels of functioning for a total of 18,000 possible health states. Using a standard gamble methodology, SF-6D scores were directly assessed for a sample of these health states from a representative sample of the UK population providing empirically-derived societal preference weights on a scale of 0-1. Health utility weights for the remaining states were derived using econometric methods.(17)

The WIHS study administered the MOS-HIV, a brief health status measure in the SF-36/SF-12 family that assesses eight subscales including physical functioning, role functioning, energy/fatigue, social functioning, cognitive functioning, pain, emotional well-being, and current health perception.(18) The MOS-HIV has been found to be a reliable and valid measure in HIV patient populations.(19-21) The MOS-HIV contains items identical, in both wording of the questions and responses, to those found in the SF-12UK version 1 that are utilized to define 5 of the 6 dimensions in the SF-12 to SF-6D conversion algorithm.(17) We derived SF-6D scores for role function, the remaining dimension, from two MOS-HIV items.[†] We then utilized the relevant survey items for the five other dimensions and applied the conversion algorithm for all six dimensions to obtain SF-6D scores. The two questions we utilized for the role function dimension were similar but not identical to wording for the two questions in the original SF-12 items; the responses were Yes/No for these role-function questions in both the MOS-HIV items and the SF-12 items. The same questions also appear in the HIV Cost and Services Utilization (HCSUS) study questionnaire and were previously used in the same way to conduct SF-6D analyses using HCSUS data.(1, 22, 23) Given this difference in wording we conducted sensitivity analyses to assess this approach. We re-categorized the 4-level role dimension for each individual by increasing and decreasing the dimension item response by 1 level and then re-calculating the SF-6D scores. We utilized Non-Bayesian methods for deriving the HRQoL score, which we then examined for floor effects.

Illicit Drug Use Measures

Illicit drug use was assessed via self-report, which is a commonly-used measure in other studies and generally found to have high reliability and validity.(24-26) Multiple measures of use were assessed, including reported frequency of use, routes of administration, and type

[†]MOS-HIV Items: 1) Does your health keep you from working at a job, doing work around the house or going to school? 2) Have you been unable to do certain kinds or amounts of work, housework, or schoolwork because of your health?

of substance used since last visit. We considered a positive response to any one of these questions related to the pre-selected substances of interest (heroin and/or cocaine) as indication of current use. We chose heroin and cocaine because of their route of administration, often intravenous, and associated risk of acquiring HIV and HCV infection. (5-8) Concurrent use of heroin and cocaine was frequent in this study population.(27)

HIV and HCV Measures

HIV status was determined based on serostatus at the time of the visit. For patients reported to be HIV-infected, CD4 cell count (a measure of immune status, 200 cells/uL are classified as having AIDS),(28) use of antiretroviral medications, and HIV viral load (a measure of viral burden that is affected by medication adherence) were also assessed at the most recent visit. Receipt of antiretroviral therapy was extracted from the medical chart and patients were defined as being on antiretroviral medication if it was recorded in the chart as being prescribed. Chronic HCV status was determined based on HCV antibody status and other laboratory values. A positive HCV antibody test result is an indicator of previous HCV infection, but not a marker of ongoing infection. We categorized women as having chronic HCV if their HCV antibody test was positive and the laboratory values at their most recent visit for aspartate transaminase (AST) and/or alanine transaminase (ALT), two measures of liver function, were at least 2 times the upper limit of normal values.

Analysis

We computed mean values and standard deviations for HRQoL scores for HIV-uninfected and HIV-infected women overall and stratified by age, race/ethnicity, education, heroin and cocaine use, chronic HCV status, year of most recent visit, and for HIV-infected women, CD4 cell count strata and whether or not they had a detectable HIV viral load. Differences in HRQoL scores were compared using t-test and ANOVA.

We then constructed multivariate linear regression models using ordinary least squares (OLS) modeling with robust standard errors to account for possible censoring of HRQoL scores at 1.(29) We assessed the independent effects of HIV, illicit drug use, chronic HCV controlling for demographic variables and year of last study visit. We also considered the joint effects of HIV and illicit drug use, HIV and chronic HCV, and illicit drug use and HCV. In order to explore the impact on HRQoL of both HIV infection and, among those with HIV infection, HIV clinical status, we constructed two sets of models: the first set included the full group of HIV-uninfected and HIV-infected women and the second included HIV-infected women only. For each group, we first developed models evaluating main effects by only including variables of interest (demographics, HCV status, and substance abuse) and then selecting for clinical variables related to HIV status including HIV infection, CD4 cell count, antiretroviral therapy, and HIV ribonucleic acid (RNA). We conducted stepwise model building and retained variables with p-values >0.05 only when there were interaction effects that included these variables; CD4 cell count greater than 200 cells/uL versus 200 cells/uL or lower was the only HIV clinical variable included in both final models. We then tested for statistical interactions between: (a) CD4 cell count and illicit drug use, (b) CD4 count and HCV status, and (c) illicit drug use and HCV status. Additionally, because changes in HIV treatment over time may have been associated with HRQoL we included

year of last visit (2006 or before 2006) in the models and we tested for interactions between HIV status and year of last visit. Similarly, we included a covariate indicating whether the individual died prior to next scheduled follow-up visit. The adjusted r-squared for the final models is 0.17. All analyses were conducted using SAS 9.2 (SAS Institute, Cary, NC).

RESULTS

Patient Characteristics

Data from 3,397 women enrolled in the WIHS study were included in the analysis after exclusion of 372 who were missing variables of interest. Demographic characteristics of HIV-uninfected women (n=889) and HIV-infected women (n=2,508) are presented in Table 1. Race/ethnicity was similar between the two groups; 58% (n=510 HIV uninfected; n=1445 HIV-infected) were black, 14% (n=122; 350) non-Hispanic white, and 9-10% (n=85; 215) Hispanic. HIV-infected women were older (42 years versus 39, $p = 0.001$), more likely to be categorized as having chronic HCV (34% vs. 19%, $p = 0.001$), less likely to report illicit drug use at last visit (11% vs. 14%, $p=0.02$), and more likely to have died after their most recent visit (25% vs. 5%, $p = 0.001$). Among HIV-infected women the mean CD4 cell count at last visit was 416 cells/uL (SD 313); 35% had an undetectable HIV viral load.

HRQoL Scores

The mean HRQoL score for the entire sample was 0.76 (SD 0.16) and was lower for HIV-infected women (0.75, SD 0.16) than HIV-uninfected women (0.80, SD 0.16) ($p<0.01$). The range of HRQoL scores reported for the cohort was 0.37 to 1.00 (12% with scores of 1.00, considered perfect health) (Appendix A). HRQoL scores declined with increasing age and decreasing level of education in both groups (Appendix B). Lower HRQoL scores were observed among current illicit drug using women regardless of HIV status; overall the mean HRQoL score was 0.77 (SD 0.16) for women who did not report current drug use compared to 0.69 (SD 0.15) for women who reported current use of heroin and/or cocaine ($p<0.01$). Women with chronic HCV also had lower HRQoL scores (overall 0.71 versus 0.79, $p<0.01$) regardless of HIV status. Among HIV-infected women lower HRQoL scores were observed among those with a CD4 count ≤ 200 cells/uL (0.69 versus 0.78, $p<0.01$) and detectable HIV viral load (0.74 versus 0.78, $p<0.01$).

Combined Impact of HIV, Illicit Drug Use, and Chronic HCV on HRQoL

In a multivariate model including both HIV-infected and HIV-uninfected women and controlling for demographics and year of survey, the impact of HIV status on HRQoL scores varied with CD4 cell counts (Table 2). HIV-infected women with CD4 cell counts ≤ 200 cells/uL had a significantly lower score than HIV-uninfected women (-0.03 , $p<0.001$); however, HIV-infected women with CD4 counts >200 cells/uL and HIV-uninfected women had HRQoL scores that were not statistically significantly different from each another. Chronic HCV was associated with a 0.03 lower HRQoL score and current use of heroin and/or cocaine was associated with a 0.05 lower score; both of these differences were significant ($p<0.001$).

Similar associations were observed in the multivariate model when incorporating interaction terms. In addition, the impact of illicit drug use and chronic HCV on HRQoL scores varied depending on HIV status and CD4 cell count, with the smallest impact on HIV-infected women with low CD4 cell counts (Table 2). For example, an HIV-infected woman with a CD4 count >200 cells/uL who reported current illicit drug use had a HRQoL score 0.06 lower than an HIV-infected woman with a CD4 count >200 cells/uL who did not report current illicit drug use. In contrast, an HIV-infected woman with a CD4 count <200 cells/uL who reported current illicit drug use had a HRQoL score 0.02 lower than her counterpart who did not report current illicit drug use (Figure 1). Similarly, chronic HCV had a differential impact depending on HIV infection status and disease severity (Figure 1). No significant interactions were observed between illicit drug use and HCV status or between year of survey and illicit drug use or HCV status.

Among HIV-infected women, CD4 count >200 cells/uL was independently associated with a higher HRQoL score (0.030, $p<0.001$), while current illicit drug use (-0.042 , $p<0.001$) and chronic HCV (-0.025 , $p<0.001$) were associated with lower HRQoL scores (Table 3). HIV RNA levels and antiretroviral treatment status were not included due to statistical non-significance. When interactions were included in the model, the negative impact of illicit drug use and chronic HCV on HRQoL score again depended on CD4 count. The impact of illicit drug use (-0.017 vs. -0.063) and chronic HCV (-0.005 vs. -0.036) was smaller for those with lower CD4 counts.

In sensitivity analyses when varying the role function dimension, there was no meaningful change in the independent or joint effects of HIV infection status, illicit drug use or chronic HCV in the multivariate models.

DISCUSSION

In this large, multicenter US cohort study of women with HIV infection or at-risk for HIV poorly-controlled HIV disease, illicit drug use and chronic HCV were independently associated with a significantly lower HRQoL that was also clinically important compared to reported estimated mean minimally important differences (MID) in SF-6D scores of 0.03-0.04.(30, 31) Average HRQoL was similar for HIV-uninfected women and HIV-infected women with well-controlled HIV. The HRQoL impact of illicit drug use and chronic HCV was also clinically significant for HIV-uninfected women and HIV-infected women whose HIV was well-controlled. However, the impact for both illicit drug use and chronic HCV among HIV-infected women with poorly controlled HIV was much smaller and did not meet clinical significance using MID criteria. In addition, having a follow-up visit in 2006 was associated with a higher HRQoL score. The higher HRQoL scores in this group could be because women with higher HRQoL were more likely to be retained in the study.

Our HRQoL score findings are consistent with reported SF-6D scores for comparable populations. Mean SF-6D scores in a representative national sample of women ranged from 0.80 (age 35-44) to 0.76 (age 55-64),(32) compared to overall score of 0.80 in this cohort of HIV-uninfected women with ages 18-73 (mean age 38). The mean HRQoL score for CD4

count 200 cells/uL (0.69) is comparable to the mean reported utility score for AIDS (0.70), while the mean score for CD4 count >200 cells/uL (0.78) falls within the range of reported utility scores for asymptomatic and symptomatic HIV (0.73-0.87).(1, 33) The HRQoL score for illicit drug use in our study (0.69) is also comparable to a previously reported mean SF-6D score for chronic heroin users in Canada (0.67).(34) The HRQoL score for chronic HCV in our study (0.71) is slightly higher than a previously reported mean SF-6D score for chronic HCV (0.67) in a clinic patient population referred for liver disease evaluation.(35)

This is the first study we are aware of to examine the combined effects of HIV, substance use and chronic HCV on HRQoL. From a clinical perspective, the analysis suggests that for HIV-infected urban women with co-morbid illicit drug use or chronic HCV, treating the HIV infection and getting it under control may have the greatest immediate impact on patients' HRQoL; and, that once this goal has been achieved treating the comorbid conditions will then have additional HRQoL benefit.

In our study, differences in HRQoL for illicit drug use and chronic HCV were associated with the severity of HIV disease. This finding suggests that models for these co-occurring conditions should take into account severity of HIV disease, which has important implications for evaluating the cost-effectiveness of treatment interventions. For example, integrated interventions that seek to address these multiple conditions could have different HRQoL benefits when evaluated using models that take into account HIV disease severity compared to models that do not consider HIV disease severity.(36) Whether a similar type of model that accounts for disease severity and interactions would be appropriate for other co-morbid conditions (e.g.-diabetes mellitus and hypertension) or other populations will require further exploration.

Our study has several limitations. First, the population examined included only women in urban settings who were predominately African American, although HRQoL scores were consistent with those reported in other relevant populations. While we were able to use data from 2006 for a little more than half of the patients, data for the remainder were from earlier years, and data from earlier years were more likely for HIV-infected women due to their higher death rate. We addressed this limitation by including year of assessment and subsequent death as additional variables in our models. We adapted the MOS-HIV data to obtain SF-6D scores for the role function dimension, although sensitivity analysis demonstrated no significant changes in outcome or conclusions due to this adaptation. We also did not fully capture other medical conditions associated with our variables of interest; for example, a variety of opportunistic infections that are associated with low CD4 cell counts. Finally, while the HIV uninfected women enrolled in the WIHS study had SF-6D scores similar to scores reported for women of similar ages in a national sample (0.76-0.80), (32) they were considered at-risk of HIV infection and are not representative of women nationally. Therefore, similarities in HRQoL between the HIV-uninfected women and the women with well-controlled HIV in this cohort could represent confounding and should not be interpreted as implying that HRQoL in women with well-controlled HIV is similar to HRQoL in HIV negative persons in the general population.

In summary, our study demonstrates the importance of HIV disease severity not only in terms of its impact on HRQoL, but also its impact on how other co-morbid conditions affect HRQoL. Further studies are needed both to assess HRQoL using preference-based measures in other populations with these co-morbid conditions and to measure the impact of interventions directed at these conditions on HRQoL improvement in diverse populations.

ACKNOWLEDGEMENTS

The authors thank Eryka Wentz and Lorie Benning for their assistance with coding for the variables in the WIHS dataset. Data in this manuscript were collected by the Women's Interagency HIV Study (WIHS) Collaborative Study Group with centers (Principal Investigators) at New York City/Bronx Consortium (Kathryn Anastos); Brooklyn, NY (Howard Minkoff); Washington DC, Metropolitan Consortium (Mary Young); The Connie Wofsy Study Consortium of Northern California (Ruth Greenblatt); Los Angeles County/Southern California Consortium (Alexandra Levine); Chicago Consortium (Mardge Cohen); Data Coordinating Center (Stephen Gange). The WIHS is funded by the National Institute of Allergy and Infectious Diseases (U01-AI-35004, U01-AI-31834, U01-AI-34994, U01-AI-34989, U01-AI-34993, and U01-AI-42590) and by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (U01-HD-32632). The study is co-funded by the National Cancer Institute, the National Institute on Drug Abuse, and the National Institute on Deafness and Other Communication Disorders. Funding is also provided by the National Center for Research Resources (UCSF-CTSI Grant Number UL1 RR024131). The contents of this publication are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health.

Appendix

Appendix A.

Histogram distribution of HRQoL Scores for WIHS Cohort

Appendix BHRQoL by Cohort Characteristics among HIV+ and HIV- at Risk Women[§]

	HIV negative (n=889)	HIV positive (n=2508)	All (n=3397)
	HRQoL mean (SD)	HRQoL mean (SD)	HRQoL mean (SD)
Overall	0.80 (0.16)	0.75 (0.16)	0.76 (0.16)
Age			
<30	0.84 (0.14)	0.81 (0.14)	0.82 (0.14)
30-39	0.82 (0.14)	0.77 (0.16)	0.78 (0.16)
40-49	0.77 (0.17)	0.74 (0.16)	0.75 (0.16)
>50	0.74 (0.16)	0.73 (0.16)	0.73 (0.16)
Race/Ethnicity			
Caucasian, non-hispanic	0.77 (0.15)	0.74 (0.16)	0.75 (0.16)
Caucasian, hispanic	0.81 (0.16)	0.81 (0.15)	0.81 (0.16)
Black	0.81 (0.16)	0.75 (0.16)	0.76 (0.16)
Asian/Pacific Islander/Native			
Alaskan/American	0.84 (0.14)	0.76 (0.15)	0.78 (0.15)
Other	0.79 (0.15)	0.75 (0.16)	0.76 (0.16)
Education			
Less than high school	0.79 (0.16)	0.77 (0.16)	0.78 (0.16)
High school graduate	0.81 (0.15)	0.78 (0.15)	0.79 (0.15)
Some college/associate degree	0.80 (0.15)	0.76 (0.16)	0.77 (0.16)
Bachelor degree/grad school	0.85 (0.14)	0.82 (0.13)	0.83 (0.14)
CD4 Count			
200		0.69 (0.15)	
>200		0.78 (0.16)	
HIV RNA			
Undetectable		0.78 (0.16)	
Detectable		0.74 (0.16)	
HCV Status			
Positive	0.72 (0.16)	0.71 (0.16)	0.71 (0.16)
Negative	0.82 (0.15)	0.78 (0.16)	0.79 (0.16)
Drug use			
Heroin and/or Cocaine	0.73 (0.15)	0.68 (0.14)	0.69 (0.15)
Neither heroin or cocaine	0.81 (0.15)	0.76 (0.16)	0.77 (0.16)
Year			
Pre 2006	0.78 (0.16)	0.71 (0.16)	0.72 (0.16)
2006	0.81 (0.15)	0.79 (0.15)	0.80 (0.15)
Outcome			
Alive	0.81 (0.15)	0.78 (0.16)	0.79 (0.15)
Dead	0.64 (0.14)	0.66 (0.14)	0.66 (0.14)

[§] All comparisons are statistically significant except Race/Ethnicity and Education for the HIV-negative group

REFERENCES

1. Schackman BR, Goldie SJ, Freedberg KA, Losina E, Brazier J, Weinstein MC. Comparison of health state utilities using community and patient preference weights derived from a survey of patients with HIV/AIDS. *Med Decis Making*. Jan-Feb;2002 22(1):27–38. [PubMed: 11833663]
2. Kauf TL, Roskell N, Shearer A, Gazzard B, Mauskopf J, Davis EA, et al. A predictive model of health state utilities for HIV patients in the modern era of highly active antiretroviral therapy. *Value Health*. Dec; 2008 11(7):1144–53. [PubMed: 18494750]
3. Chong CA, Gulamhussein A, Heathcote EJ, Lilly L, Sherman M, Naglie G, et al. Health-state utilities and quality of life in hepatitis C patients. *Am J Gastroenterol*. Mar; 2003 98(3):630–8. [PubMed: 12650799]
4. Pyne JM, Tripathi S, French M, McCollister K, Rapp RC, Booth BM. Longitudinal association of preference-weighted health-related quality of life measures and substance use disorder outcomes. *Addiction*. Mar; 2011 106(3):507–15. [PubMed: 21205046]
5. Alcabes P, Friedland G. Injection drug use and human immunodeficiency virus infection. *Clin Infect Dis*. Jun; 1995 20(6):1467–79. [PubMed: 7548494]
6. Risdahl JM, Khanna KV, Peterson PK, Molitor TW. Opiates and infection. *J Neuroimmunol*. Mar 15; 1998 83(1-2):4–18. [PubMed: 9610668]
7. Alter MJ, Kruszon-Moran D, Nainan OV, McQuillan GM, Gao F, Moyer LA, et al. The prevalence of hepatitis C virus infection in the United States, 1988 through 1994. *N Engl J Med*. Aug 19; 1999 341(8):556–62. [PubMed: 10451460]
8. Lauer GM, Walker BD. Hepatitis C virus infection. *N Engl J Med*. Jul 5; 2001 345(1):41–52. [PubMed: 11439948]
9. Sherman KE, Rousster SD, Chung RT, Rajcic N. Hepatitis C Virus prevalence among patients infected with Human Immunodeficiency Virus: a cross-sectional analysis of the US adult AIDS Clinical Trials Group. *Clin Infect Dis*. Mar 15; 2002 34(6):831–7. [PubMed: 11833007]
10. Batki SL, Canfield KM, Smyth E, Ploutz-Snyder R. Health-related quality of life in methadone maintenance patients with untreated hepatitis C virus infection. *Drug Alcohol Depend*. May 1; 2009 101(3):176–82. [PubMed: 19233573]
11. Korthuis PT, Zephyrin LC, Fleishman JA, Saha S, Josephs JS, McGrath MM, et al. Health-related quality of life in HIV-infected patients: the role of substance use. *AIDS Patient Care STDS*. Nov; 2008 22(11):859–67. [PubMed: 19025480]
12. Korthuis PT, Tozzi MJ, Nandi V, Fiellin DA, Weiss L, Egan JE, et al. Improved quality of life for opioid-dependent patients receiving buprenorphine treatment in HIV clinics. *J Acquir Immune Defic Syndr*. Mar; 2011 56(Suppl 1):S39–45. [PubMed: 21317593]
13. Barkan SE, Melnick SL, Preston-Martin S, Weber K, Kalish LA, Miotti P, et al. The Women's Interagency HIV Study. WIHS Collaborative Study Group. *Epidemiology*. Mar; 1998 9(2):117–25. [PubMed: 9504278]
14. WIHS Cohort Information. [10/2/2012]; Available from: <http://statepiaps.jhsph.edu/wihs/index-cohort-info.htm>
15. Women's Interagency HIV Study (WIHS) Dossier. [10/2/2012]; Available from: <http://statepiaps.jhsph.edu/wihs/invest-info/dossier.pdf>
16. Brazier JE, Roberts J. The estimation of a preference-based measure of health from the SF-12. *Med Care*. Sep; 2004 42(9):851–9. [PubMed: 15319610]
17. Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. *J Health Econ*. Mar; 2002 21(2):271–92. [PubMed: 11939242]
18. Bozzette SA, Hays RD, Berry SH, Kanouse DE, Wu AW. Derivation and properties of a brief health status assessment instrument for use in HIV disease. *J Acquir Immune Defic Syndr Hum Retrovirol*. Mar 1; 1995 8(3):253–65. [PubMed: 7859137]
19. Wu AW, Revicki DA, Jacobson D, Malitz FE. Evidence for reliability, validity and usefulness of the Medical Outcomes Study HIV Health Survey (MOS-HIV). *Qual Life Res*. Aug; 1997 6(6):481–93. [PubMed: 9330549]
20. Lubeck DP, Fries JF. Changes in quality of life among persons with HIV infection. *Qual Life Res*. Dec; 1992 1(6):359–66. [PubMed: 1299468]

21. Carretero MD, Burgess AP, Soler P, Soler M, Catalan J. Reliability and validity of an HIV-specific health-related quality-of-life measure for use with injecting drug users. *AIDS*. Dec; 1996 10(14): 1699–705. [PubMed: 8970691]
22. Health Related Quality of Life. [10/2/2012]; Available from: <http://www.rand.org/content/dam/rand/www/external/health/projects/hcsus/Base/b08.pdf>
23. Hays RD, Cunningham WE, Sherbourne CD, Wilson IB, Wu AW, Cleary PD, et al. Health-related quality of life in patients with human immunodeficiency virus infection in the United States: results from the HIV Cost and Services Utilization Study. *Am J Med*. Jun 15; 2000 108(9):714–22. [PubMed: 10924648]
24. Amato L, Davoli M, Perucci CA, Ferri M, Faggiano F, Mattick RP. An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research. *J Subst Abuse Treat*. [Review]. Jun; 2005 28(4):321–9.
25. Napper LE, Fisher DG, Johnson ME, Wood MM. The reliability and validity of drug users' self reports of amphetamine use among primarily heroin and cocaine users. *Addict Behav*. Apr; 2010 35(4):350–4. [PubMed: 20053503]
26. O'Farrell TJ, Fals-Stewart W, Murphy M. Concurrent validity of a brief self-report Drug Use Frequency measure. *Addict Behav*. Mar; 2003 28(2):327–37. [PubMed: 12573682]
27. Cohen MH, Grey D, Cook JA, Anastos K, Seaberg E, Augenbraun M, et al. Awareness of hepatitis C infection among women with and at risk for HIV. *J Gen Intern Med*. Dec; 2007 22(12):1689–94. [PubMed: 17924170]
28. Schneider E, Whitmore S, Glynn KM, Dominguez K, Mitsch A, McKenna MT. Revised surveillance case definitions for HIV infection among adults, adolescents, and children aged <18 months and for HIV infection and AIDS among children aged 18 months to <13 years--United States, 2008. *MMWR Recomm Rep*. Dec 5; 2008 57(RR-10):1–12. [PubMed: 19052530]
29. Pullenayegum EM, Tarride JE, Xie F, Goeree R, Gerstein HC, O'Reilly D. Analysis of health utility data when some subjects attain the upper bound of 1: are Tobit and CLAD models appropriate? *Value Health*. Jun-Jul;2010 13(4):487–94. [PubMed: 20230549]
30. Luo N, Johnson J, Coons SJ. Using instrument-defined health state transitions to estimate minimally important differences for four preference-based health-related quality of life instruments. *Med Care*. Apr; 2010 48(4):365–71. [PubMed: 20355266]
31. Walters SJ, Brazier JE. Comparison of the minimally important difference for two health state utility measures: EQ-5D and SF-6D. *Qual Life Res*. Aug; 2005 14(6):1523–32. [PubMed: 16110932]
32. Fryback DG, Dunham NC, Palta M, Hanmer J, Buechner J, Cherepanov D, et al. US norms for six generic health-related quality-of-life indexes from the National Health Measurement study. *Med Care*. Dec; 2007 45(12):1162–70. [PubMed: 18007166]
33. Tengs TO, Lin TH. A meta-analysis of utility estimates for HIV/AIDS. *Med Decis Making*. Nov-Dec;2002 22(6):475–81. [PubMed: 12458977]
34. Nosyk B, Sun H, Guh DP, Oviedo-Joekes E, Marsh DC, Brissette S, et al. The quality of eight health status measures were compared for chronic opioid dependence. *J Clin Epidemiol*. Oct; 2010 63(10):1132–44. [PubMed: 20236799]
35. Dan AA, Kallman JB, Srivastava R, Younoszai Z, Kim A, Younossi ZM. Impact of chronic liver disease and cirrhosis on health utilities using SF-6D and the health utility index. *Liver Transpl*. Mar; 2008 14(3):321–6. [PubMed: 18306356]
36. Altice FL, Kamarulzaman A, Soriano VV, Schechter M, Friedland GH. Treatment of medical, psychiatric, and substance-use comorbidities in people infected with HIV who use drugs. *Lancet*. Jul 31; 2010 376(9738):367–87. [PubMed: 20650518]

Figure 1.
Multivariate model Results: Incremental impact of HCV and Illicit Drug Use on HRQoL among HIV+ and at Risk Women

Table 1

Characteristics of HIV positive and HIV negative at-Risk Women

Characteristic	HIV negative (n=889) n (%)	HIV positive (n=2508) n (%)	All (n=3397) n (%)
	n (%)	n (%)	n (%)
Overall			
Age			
<30	194 (22)	179 (7)	373 (11)
30-39	282 (32)	767 (31)	1049 (31)
40-49	286 (32)	1044 (42)	1330 (39)
50+	127 (14)	518 (21)	645 (19)
Race/Ethnicity			
Caucasian, non-hispanic	122 (14)	350 (14)	472 (14)
Caucasian, Hispanic	85 (10)	215 (9)	300 (9)
Black	510 (58)	1445 (58)	1955 (58)
Asian/Pacific Islander/Native			
Alaskan/American	16 (2)	43 (2)	59 (2)
Other	154 (17)	449 (18)	603 (18)
Education			
Less than high school	217 (24)	646 (26)	863 (25)
High school graduate	212 (24)	522 (19)	734 (22)
Some college/associate degree	172 (19)	447 (25)	619 (18)
Bachelor degree/grad school	63 (7)	150 (6)	213 (6)
CD4 Count			
200 cells/uL		724 (29)	
>200 cells/uL		1784 (71)	
HIV RNA			
Undetectable		858 (35)	
Detectable		1564 (65)	
HCV Status			
Positive	172 (19)	832 (34)	1004 (30)
Negative	712 (81)	1642 (66)	2354 (70)
Drug use			
Heroin and/or cocaine	128 (14)	288 (11)	416 (12)
Neither heroin nor cocaine	761 (86)	2220 (89)	2981 (88)
Year			
Pre-2006	364 (41)	1202 (48)	1566 (46) [‡]
2006	525 (59)	1306 (52)	1831 (54)
Outcome			
Died	44 (5)	626 (25)	670 (20)

[‡] 666 deceased, 68 disenrolled, 832 missing data at most recent visit

Table 2

Multivariate Linear Models of HRQoL among HIV positive and HIV negative at-Risk Women

Model variable	Model 1A without Interactions		Model 1B with Interactions	
	Estimate	p-value	Estimate	p-value
Intercept	0.823		0.83	
Age	−0.023	<0.01	−0.022	<0.01
Black vs. white non-hispanic	0.020	0.01	0.021	0.01
White Hispanic vs. white non-hispanic	0.029	0.01	0.029	0.01
Native American/Asian vs. white non-hispanic	0.025	0.22	0.027	0.19
Other vs. white non-hispanic	0.011	0.23	0.013	0.17
High school vs. less than high school	0.009	0.20	0.009	0.20
Some college/associate degree vs. less than high school	−0.005	0.53	−0.005	0.52
College/Grad school vs. less than high school	0.044	<0.01	0.042	<0.01
2006 vs. pre-2006	0.031	<0.01	0.030	<0.01
Died subsequent to visit	−0.069	<0.01	−0.069	<0.01
HIV positive CD4 200 cells/uL vs. HIV negative	−0.029	<0.01	−0.052	<0.01
HIV positive CD4 >200 cells/uL vs. HIV negative	0.004	0.50	0.001	0.94
HCV positive vs. HCV negative	−0.030	<0.01	−0.047	<0.01
Heroin and/or cocaine use vs. no drug	−0.045	<0.01	−0.061	<0.01
HIV+ CD4 200 cells/uL * Heroin and/or cocaine use			0.044	0.02
HIV+ CD4 >200 cells/uL * Heroin and/or cocaine use			0.006	0.77
HIV+ CD4 200 cells/uL * HCV			0.044	<0.01
HIV+ CD4 >200 cells/uL * HCV			0.014	0.31

Table 3

Multivariate Linear Models of HRQoL in HIV positive Women

Model parameter	Model 2A without Interactions		Model 2B with Interactions	
	Estimate	p-value	Estimate	p-value
Intercept	0.78		0.77	
Age	-0.021	<0.01	-0.020	<0.01
Black vs. white non-hispanic	0.015	0.11	0.016	0.08
White Hispanic vs. white non-hispanic	0.036	0.01	0.035	0.01
Native American/Asian vs. white non-hispanic	0.019	0.43	0.022	0.36
Other vs. white non-hispanic	0.010	0.37	0.011	0.34
High school vs. less than high school	0.009	0.24	0.009	0.26
Some college/associate degree vs. less than high school	-0.009	0.29	-0.009	0.28
College/Grad school vs. less than high school	0.045	<0.01	0.043	<0.01
2006 vs. pre-2006	0.037	<0.01	0.036	<0.01
Died subsequent to visit	-0.062	<0.01	-0.061	<0.01
HCV positive vs. HCV negative	-0.025	<0.01	-0.005	0.70
Heroin and/or cocaine use vs. no drug	-0.042	<0.01	-0.017	0.23
CD4 >200 cells/uL vs. 200 cells/uL	0.030	<0.01	0.049	<0.01
CD4 >200 cells/uL * Heroin and/or cocaine use			-0.046	0.01
CD4 >200 cells/uL * HCV			-0.031	0.03