Title

Longitudinal Study of Falls among HIV-Infected and Uninfected Women: The Role of Cognition

Journal

Antiviral Therapy, 23(2)

ISSN

1359-6535

Authors

Sharma, Anjali
Hoover, Donald R
Shi, Qiuhu
et al.

Publication Date

2018-02-01

DOI

10.3851/imp3195

Peer reviewed

HHS Public Access

Author manuscript

Antivir Ther. Author manuscript; available in PMC 2019 January 01.

Published in final edited form as:

Antivir Ther. 2018 ; 23(2): 179–190. doi:10.3851/IMP3195.

Longitudinal Study of Falls among HIV-infected and Uninfected Women: the Role of Cognition

Anjali SHARMA, MD, MS[1], **Donald R. HOOVER, PhD**[2], **Qiuhu SHI, MS, PhD**[3], **Susan HOLMAN, RN, MS**[4], **Michael W. PLANKEY, PhD**[5], **Phyllis C. Tien, MD**[6,7], **Kathleen M. WEBER, MS**[8], **Michelle FLORIS-MOORE, MD, MS**[9], **Hector H. BOLIVAR, MD**[10], **David E. VANCE, PhD**[11], **Elizabeth T. GOLUB, PhD**[12], **Marcia McDonnell HOLSTAD, PhD, FNP-BC**[13], and **Michael T. YIN, MD**[14]

[1]Albert Einstein College of Medicine, Bronx, NY

[2]Rutgers University, Piscataway, NJ

[3]New York Medical College, Valhalla, NY

[4]State University of New York Downstate Medical Center, Brooklyn, NY

[5]Georgetown University Medical Center, Washington, DC

[6]San Francisco VA Medical Center, San Francisco, CA

[7]University of California San Francisco, San Francisco, CA

[8]Cook County Health and Hospitals System/Hektoen Institute of Medicine, Chicago, IL

[9]University of North Carolina School of Medicine, Chapel Hill, NC

[10]University of Miami Health System, Miami, FL

[11]The University of Alabama at Birmingham, Birmingham, AL

[12]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

[13]Emory School of Nursing, Atlanta GA

[14]Columbia University Medical Center, NY, NY

Abstract

Background—Although fracture rates are higher in HIV+ than HIV− women, whether HIV infection increases risk of falls is unclear. We determined the longitudinal occurrence and risk factors for falls in the Women's Interagency HIV Study (WIHS), and explored associations with cognitive complaints.

Corresponding author: Anjali Sharma, MD, MS, Department of Medicine, Albert Einstein College of Medicine, 1300 Morris Park Ave, Block Building #305, Bronx, NY 10461, Tel. 718-430-2067, Fax. 718-839-7977, anjali.sharma@einstein.yu.edu.

Conflicts of Interest

For all authors, there are no conflicts of interest.

Methods—Recent (prior 6 months) self-reported falls were collected in 1816 (1250 HIV+; 566 HIV−) women over 24 months. Generalized estimating equation models using stepwise selection determined odds of any fall (vs. none).

Results—HIV+ women were older than HIV− women (median 49 vs. 47yrs, p=0.0004), more likely to report neuropathy (20% vs. 16%, p=0.023), and had greater central nervous system (CNS) medication use. At least one fall was reported in 41% HIV+ vs. 42% HIV− women, including ≥2 falls in 25% HIV+ and 24% HIV− (overall p =0.30). Cognitive complaints were associated with falls among HIV+ [odds ratio (OR) 2.38; 95% CI: 1.83–3.09] and HIV− women (OR 3.43; 95% CI: 2.37–4.97); in adjusted models, cognitive complaints remained significant only in HIV− women [adjusted (aOR) 2.26; 95%CI: 1.46, 3.48)]. Factors associated with any fall in adjusted analyses included: depressive symptoms and neuropathy (both HIV+ and HIV−); age, marijuana use, multiple CNS medications, and hepatitis C virus infection (HIV+ only); and cognitive complaints, quality of life, hypertension, and obesity (HIV− only).

Conclusions—Middle-aged HIV+ and HIV− women had similar fall rates. Among HIV+ women, factors affecting cognition such as age, depressive symptoms, marijuana use, and multiple CNS medications were important predictors of falls, however cognitive complaints were not.

Keywords

Fall; HIV; aging; women; cognition

INTRODUCTION

Over half of HIV-infected persons in the United States are ≥ 50 years old, with growing numbers surviving into older age due to the success of widely available highly active antiretroviral therapy (HAART).[1] It has been suggested that HIV accelerates aging via established pathways of the aging process, or alternatively, that HIV accentuates aging as an additional risk factor for chronic disease conditions.[2] Persons surviving with HIV infection are experiencing an excess burden of comorbid conditions typically associated with advanced age, including geriatric syndromes such as falls, frailty, and functional impairment, occurring on average 15–20 years earlier than in the general population.[3–11] Additionally, because low bone mineral density is prevalent in HIV+ populations,[12] occurrence of falls in aging HIV-infected persons may confer a greater risk of osteoporotic fracture. We previously demonstrated that HIV-infected women had higher 10-year fracture incidence rates than did uninfected women in the Women's Interagency HIV Study (WIHS).[13]

While published data on falls among HIV-infected populations are limited, an unexpectedly high prevalence of falls has been reported in middle-aged HIV-infected adults on antiretroviral therapy, and greater fall risk was observed in women compared with men.[14] Although in a cross-sectional analysis conducted in the WIHS, we found a similar occurrence of self-reported falls in HIV-infected and HIV-uninfected women with a mean age of 48 years, we identified a number of factors affecting cognition that were associated with increased risk of falls, including use of multiple central nervous system (CNS) active medications, substance abuse, and subjective cognitive complaints.[15] In elderly HIV-uninfected persons, subjective memory complaints can be an early sign of cognitive

impairment that are not consistently associated with objective deficits on neuropsychological testing, yet often predict future cognitive decline.[16,17] Recently, among elderly uninfected women in the United Kingdom, baseline subjective memory complaints predicted increased risk of falls and upper limb fractures over the following two years.[18] Therefore, the objective of this study is to examine the rate of falls over time and determine whether risk factors for falls differ between middle-aged HIV+ and HIV− women, and further, to evaluate the relationship between subjective cognitive complaints and falls among HIV+ and HIV− women in the WIHS.

METHODS

Study Population

The WIHS is an ongoing, multicenter prospective cohort study of the natural and treated history of HIV infection in women, that initially enrolled HIV-infected and uninfected women in 1994–95 at six sites nationally (Bronx/Manhattan NY, Brooklyn NY, Chicago IL, Washington DC, San Francisco CA, and Los Angeles, CA), with additional enrollment in 2001–02 and 2011–12. In 2014–15, the WIHS closed its Los Angeles site and added four southern U.S. sites: Atlanta GA, Chapel Hill NC, Miami FL, and Birmingham AL/Jackson MI. Of the 2,062 participants who completed the falls history questionnaire at visit 40, 1,816 (1,250 HIV+ and 566 HIV−) are included in the current analysis based upon having data on falls available from visit 40 and the next three semiannual visits. WIHS methods and baseline cohort characteristics have been described previously.[19] HIV-uninfected women were recruited from groups at risk for HIV infection.[19] At semiannual visits, participants complete physical examinations, provide biological specimens, and undergo extensive assessment of clinical, behavioral, and demographic characteristics via face to-face interviews. Informed consent was obtained using procedures approved by committees on human research at each of the collaborating institutions.

Beginning in 2014 (visit 40), all WIHS participants were asked to report any history of fall within the prior 6 months. In subsequent semi-annual study visits, participants were asked if they had sustained a fall since the last visit. Fall was defined as: “an unexpected event, including a slip or trip, in which you lost your balance and landed on the floor, ground or lower level, or hit an object like a table or chair” and participants were further instructed that “Falls that result from a major medical event (for example, a stroke or seizure) or an overwhelming external hazard (for example, hit by a truck or pushed) should not be included.”[20] Participants reporting any fall were asked: i) if they had either “1” or “2 or more” falls in the prior 6 months, ii) if they sought medical attention for any of these falls, and iii) whether any of these falls resulted in fracture.

Statistical Analyses

Medians, interquartile ranges, and proportions summarized study variables accordingly, depending upon whether they were continuous or categorical. Chi-square tests compared proportions of categorical or categorized variables between HIV-infected and HIV-uninfected women and proportions with at least one fall in the prior six months at a single visit (for visits 40–43). Bivariate analyses evaluated each predictor in association with this

outcome for HIV-infected and uninfected participants together and separately using univariate logistic regression. The primary outcome was report of any (i.e. at least one) fall during the prior six months compared with no fall. As the associations between each of the predictors and any fall in the prior six months were the same at each of the visits (40 – 43), all four visits were pooled together and logistic regression models for prediction of falls were fit. Generalized estimating equations (GEE) with logit link and (as covariates were time invariant) unstructured covariance structure handled collinearity between repeated measures form the same subjects. A multivariable GEE model of independent prediction of having at least one fall in the 6 months prior to each of the 4 visits pooled was fit using stepwise selection with SAS default criteria to enter and remain in the model.

HIV status (the primary exposure of interest), age (a well-accepted predictor of falls) and WIHS site were forced into these models. Because enrollment for the southern WIHS sites had only recently begun and started concurrently, participant numbers were too small for individual evaluation of southern sites and they were combined in analyses. Separate multivariable models stratified by HIV status were constructed similarly; models restricted to HIV-infected women additionally evaluated the contribution of measures of HIV disease-specific characteristic on fall risk. All p-values reported are two sided from chi-square (for unadjusted proportions), Wilcoxon (for unadjusted continuous variables), and Wald tests (for logistic regression).

Our primary exposure of interest was HIV status. Covariates were time invariant being measured at the last visit prior to the first self-reported assessment of falls (referred to as the index visit) to avoid potential for reverse causality. Candidate covariates for multivariable models included demographic factors, behavioral factors, comorbid conditions, central nervous system (CNS) active medications, and HIV-related factors, as follows: **Demographic factors** included: age per 10 years, race/ethnicity (White, Hispanic/Other, vs. Black), annual household income of $12,000 or less; having graduated from high school; and year of WIHS enrollment (2001–2, 2011–14, vs. 1994–5). **Substance use** included tobacco use (current smoker, former smoker, vs. never smoker [reference]); cocaine, crack, and/or heroin use (current, former, vs. never [reference]); marijuana use (current, former, vs. never [reference]); and recent (6 month) alcohol use: heavy (≥14 drinks/wk), moderate (3–13 drinks/wk), or light (<3 drinks/wk) vs. none [reference]). **CNS active medication classes** included anticonvulsants, antidepressants, antipsychotics, sedatives (including benzodiazepines, barbiturates, and non-benzodiazepine sleep aids), and muscle relaxants. CNS active medications were cumulatively analyzed as the number of classes being “currently” used at index visit (categorized as 0, 1, 2, or ≥3; [reference group 0 classes]). **Comorbid conditions** were assessed at the index visit, prior to administration of the falls questionnaire, and included the following medical conditions, symptoms, or pre-clinical indices associated with falls in published literature: peripheral neuropathy (self-report of numbness, tingling, or burning sensations in arms, legs, hands or feet lasting for more than two weeks); obesity (body mass index (BMI) >30 kg/m2); subjective cognitive complaints (defined as self-report over the prior 6 months of either major problems with memory or concentration that interfered with normal everyday activities and lasted for more than two weeks, or self-report of confusion, getting lost in a familiar place or inability to perform

routine mental tasks); depressive symptoms (defined as Center for Epidemiology Studies Depression (CES-D) total score of ≥16);[21] quality of life summary score (per 10 units calculated using the scores from six domains, i.e. physical functioning, role functioning, energy/fatigue, social functioning, pain and emotional well-being) based on an established algorithm using a shortened version of the Medical Outcome Study (MOS)-HIV;[22,23] diabetes mellitus as previously operationalized in WIHS;[24] renal dysfunction (estimated glomerular filtration rate (eGFR) <60 ml/min using the Modification of Diet in Renal Disease calculation);[25] hypertension (self-report of hypertension in addition to diastolic blood pressure 90 mmHg or greater, systolic blood pressure 140 mmHg or greater, or current receipt of antihypertensive medication);[26] and Hepatitis C Virus (HCV) infection (defined as positive HCV antibody with HCV RNA detectable tested shortly after study entry).

Additional **HIV disease specific covariates** included: nadir CD4+ count (lowest CD4 measured in cells per mm^3 prior to index) and current CD4+ count, current Log_{10} HIV RNA level, current suppressed (<20 copies/mL) HIV RNA, prior AIDS-defining illness (ADI), current antiretroviral therapy (ART) use, and current and prior use of the following antiretrovirals associated with CNS side effects or neuropathy in published literature: didanosine, stavudine, zidovudine, or efavirenz.

To evaluate associations between subjective cognitive complaints and odds of having at least one any fall (vs. none), we created hierarchical models stratified by HIV serostatus that first evaluated (1) subjective cognitive complaints and odds of having at least one fall (unadjusted), and then sequentially adjusted for: (2) demographics, (3) comorbid conditions, (4) substance abuse and CNS active agents, (4) HIV-specific factors for HIV-infected women.

RESULTS

Participant characteristics

A total of 1,250 HIV-infected and 566 HIV-uninfected women completed the falls questionnaire at all four study visits and are included in the current analyses (Table 1). HIV-infected women were older and more likely to be HCV-infected, have renal dysfunction, and report symptoms of peripheral neuropathy. HIV-infected women were less likely than uninfected women to be obese, or to report current smoking, current use of marijuana, heroin, cocaine, or crack, and heavy alcohol consumption. Among the 1,250 HIV-infected women, 37% reported a prior ADI, 88% reported taking ART at the index visit, and 63% had suppressed HIV RNA viral load.

The overall proportion of women reporting any fall over the entire 24 months was similar between HIV-infected and uninfected women (41%, N=512/1,250 for HIV+ and 42%, N=239/566 for HIV− women). There was no difference in the occurrence of either single or multiple falls in this time period by HIV status, with single fall reported by 16% of HIV-infected and 18% of uninfected women, and multiple falls reported by 25% of HIV-infected women and 24% of uninfected women (overall p=0.30). At least one fall was reported in 23.5% vs. 24.0% at one visit, 9.8% vs. 11.3% at two visits, 4.7% vs. 3.7% at three visits, and 3.0% vs. 3.2% at all four visits, among HIV+ and HIV− women respectively (overall

p=0.73, Figure 1). Among all participants reporting a fall over 24 months, 38% (N=194/512) of HIV-infected and 45% (N=107/239) of uninfected women with at least one fall sought medical attention for a fall-related injury (p=0.08); 6% of HIV-infected women (N=31/512) and uninfected women (N=14/239) reported sustaining a fracture resulting from a fall.

Predictors of Any Fall in the Women's Interagency HIV Study

Univariate analyses of index visit characteristics associated with any fall in the prior six months, measured during the subsequent two-year observation period in HIV-infected and uninfected women are shown in Table 2. Among HIV-infected women, older age, white race (vs. other), lower income, earlier year of study enrollment, study site, substance use (including past and current smoking, marijuana use, cocaine, crack, or heroin use, and heavy alcohol use), higher number of CNS active medications classes used, and comorbid conditions (hypertension, diabetes, renal dysfunction, HCV coinfection, depressive symptoms, lower quality of life, subjective cognitive complaints, and peripheral neuropathy) were associated with reported falls in the prior six months (all $p<0.05$, Table 2). Prior AIDS defining illness was associated with greater odds of falling (aOR 1.55, 95%CI: 1.26–1.89, $p<0.0001$); other HIV-related factors were not associated with falls (Table 2). Among HIV-uninfected women, older age, substance use (current smoking, past or current crack, cocaine or heroin use, and current marijuana use), higher number of CNS active medication classes used, and comorbid conditions (hypertension, renal dysfunction, depressive symptoms, lower quality of life, subjective cognitive complaints, peripheral neuropathy, and obesity) were associated with reported falls in the prior six months (all $p<0.05$, Table 2).

Multivariable analyses of characteristics associated with any fall during the study period in HIV-infected and uninfected women are shown in Table 3. Among HIV-infected women, older age, WIHS site, current marijuana use, higher number of categories of CNS active medications, HCV coinfection, depressive symptoms, and peripheral neuropathy remained associated with greater odds of sustaining at least one fall (all $p<0.05$, Table 3). Prior AIDS defining illness was no longer statistically associated with falls in multivariable analyses. In sensitivity analyses limited to HIV-infected women, factors associated with multiple falls (vs. single fall) in multivariable models included age (AOR 1.00, 95%CI: 1.00–1.00, p=0.002), Hispanic/other race vs Black (AOR 0.45, 95%CI: 0.23–0.88, p=0.019), use of ≥3 classes of CNS active medications vs none (AOR 3.29, 95% CI: 1.54–7.05, p=0.002), neuropathy (AOR 1.61, 95%CI: 1.01–2.55, p= 0.045), and depressive symptoms (AOR1.84, 95%CI: 1.15–2.94, p= 0.011 for CESD ≥ 16 vs <16), in addition to study site (data not shown). Among uninfected women, factors remaining statistically associated with falls included reduced quality of life, hypertension, depressive symptoms, subjective cognitive complaints, peripheral neuropathy, and obesity (all $p<0.05$, Table 3).

Relationship between Subjective Cognitive Complaints and Falls

In unadjusted analyses, HIV-infected women who reported cognitive complaints had over double the odds of falling as did those who did not have these cognitive complaints (aOR 2.38, 95% CI: 1.83–3.09, $p<0.0001$) and among uninfected women, report of cognitive complaints was associated with over triple the odds of falling (aOR 3.43, 95% CI: 2.37–4.97, $p<0.0001$), (Table 4). Among HIV-infected women, after additional adjustment for

demographics risk factors, cognitive complaints remained associated with falls (aOR 2.05, 95% CI: 1.56–2.70, p<0.0001). However after additional adjustment for comorbidities, cognitive complaints were no longer statistically associated with falls (aOR 1.31, 95%CI: 0.98–1.75, p=0.066) (Table 4). Additional adjustment for substance use, CNS active medications, and prior AIDS further attenuated the association between subjective cognitive complaints and falls in HIV-infected women (aOR 1.25, 95%CI: 0.93–1.68, p=0.14). In unadjusted analyses, uninfected women with subjective cognitive complaints had over three times the odds of falls as did those without cognitive complaints (aOR 3.43 95%CI: 2.37–4.97, p<0.0001). Among uninfected women, subjective cognitive complaints remained associated with increased odds of falling after sequentially adjusting for demographics (aOR 3.18, 95%CI: 2.11–4.78, p<0.0001). While still statistically significant, this association was attenuated with the addition of comorbid conditions (aOR 2.17, 95%CI: 1.41–3.34, p=0.0004), however unlike in the HIV-infected women, the association between cognitive complaints and falls was strengthened after accounting for substance use and number of CNS active agents (aOR 2.26, 95%CI: 1.46–3.48, p=0.0002) (Table 4).

DISCUSSION

We conducted the first longitudinal study to examine occurrence of and risk factors for falls in HIV-infected and uninfected women. We found an unexpectedly high occurrence of falls among middle-age HIV-infected and sociodemographically similar uninfected women in the WIHS. Over 40% of women reported sustaining one or more falls over a two-year period, despite a median cohort age of only 48 years. The overall occurrence of falls did not differ by HIV status, and among HIV-infected women, HIV-disease and treatment related characteristics did not confer additional risk or protection from falls.

Although we are unaware of any published longitudinal data on falls among HIV-infected populations, several cross-sectional studies have reported a high prevalence of falls in HIV-infected populations.[14,15,27] In studies of predominantly male HIV-infected adults, 24–30% of participants reported at least one fall in the previous year,[14,27] which was similar to the occurrence of falls in community dwelling persons aged 65 years older in the general U.S. population.[28] Other cross sectional studies have found that HIV-infected women have greater risk of falls compared with HIV-infected men, after accounting for other fall risk factors.[14,27] We recently reported a 19% prevalence of self-reported falls within the previous 6 months among HIV-infected women in the WIHS cohort, which did not differ from the prevalence observed in the uninfected women. However, the HIV uninfected women in WIHS differ from the general population since they have similar demographic and HIV acquisition risk characteristics to the HIV-infected women including poverty, unemployment, low educational attainment, unstable housing, and history of substance abuse, and risky sexual behaviors.[15]

Among elderly community dwelling U.S. persons, 18–24% of falls result in injury requiring medical attention.[29,30] Despite their younger age, 38% of HIV-infected and 45% of uninfected women who sustained at least one fall sought medical attention for a fall related injury, suggesting that these falls are not only frequent and premature, but are also relatively severe. Among both HIV status groups, 6% of women with a recent fall reported a resulting

fracture, which is slightly lower than the 10% estimates among elderly persons (age 65 and older).[31] The WIHS cohort is primarily comprised of middle aged, racial minority women with high BMI and low number of post-menopausal person years, making these findings noteworthy. In an earlier WIHS publication, after ten years of follow-up, HIV-infected women had greater fracture incidence compared to uninfected women; and over time fracture rates increased disproportionately with age among HIV-infected vs. uninfected women.[13]

Taken together, our data show that middle-aged HIV-infected and demographically matched uninfected women experience falls and associated injury rates approaching that of much older community dwelling residents in the general population. As WIHS women age, transition through menopause, and experience a greater burden of comorbid conditions that disproportionately affect racial minority women, we anticipate that falls and associated injury rates will also increase disproportionately in HIV-infected vs. uninfected women, similar to what we what we have already begun to observe with fractures.

Our study explored the association between subjective cognitive complaints and fall risk. Subjective cognitive complaints[32] have been associated with actual cognitive impairment,[33,34] depression,[35] increased risk of dementia,[36] and future cognitive decline,[34,35,37] although they are only weakly associated with neuropsychological testing.[38] In clinical care, subjective cognitive complaints often prompt concerns about dementia and initiation of dementia workup and testing. Moreover, the presence of subjective cognitive complaints are part of the diagnostic criteria for mild cognitive impairment (MCI)[39] and the Motoric Cognitive Risk Syndrome (MCR),[40] a pre-dementia syndrome characterized by both slow gait and subjective cognitive complaints. Among community-dwelling older people, MCR was recently associated with an increased risk of future falls and was a stronger predictor of falls than either of its individual components;[41] however, we did not have these measures in our study. In a study designed to provide normative data on timed gait conducted in predominantly young men with AIDS and HIV-uninfected and HIV-infected asymptomatic controls, Robertson et al found that slow gait was associated with advanced HIV disease (symptomatic HIV and AIDS), as well as with lower neuropsychological test scores and AIDS dementia.[42] To date, the relationship between cognition or gait speed, either in combination as part of MCR, or independently, has not been evaluated previously in aging HIV-infected populations, but could be helpful in defining the impact of cognition on falls in future studies.

Although cognitive complaints were associated with over twice the odds of falling in unadjusted analyses of HIV-infected women, this association was no longer significant after adjusting for comorbidities. Among uninfected women, while the association between cognitive complaints and fall risk was attenuated after inclusion of comorbidities, the association between cognition and falls remained significant even after taking medical comorbidities into account. These data suggest that medical comorbidities may be confounders and/or mediators for the association between cognitive complaints and falls, particularly in HIV-infected women. Moreover, comorbidities such as HCV coinfection may play a more important role in cognition among HIV-infected women, whereas among uninfected women, cognition may have more of an independent effect on fall risk.

Depressive symptoms were significant risk factors for falls in both HIV status groups. We found that HIV-infected women with depressive symptoms had 1.70 times greater odds of sustaining a fall during the prior six months, and uninfected women had 1.61 times greater odds of falling, compared to those with lower CESD scores. This is consistent with results from systematic review of studies conducted in persons age 60 years or older in the general population in which measures of depressive symptoms from various scales (such as the Geriatric Depression Scale, CES-D, and others), were found to be significant predictors of prospective falls, with a pooled odds ratio of 1.46 (95% CI: 1.27–1.67, $p < 0.001$).[43]

Although depression has been prospectively shown to be a risk factor for falls, the mechanisms remain unclear but may be mediated by decreased cognitive function, such as impaired attention/executive function and memory, or by anti-depressive medications, and/or by decreased physiologic response, including reduced muscle strength and nerve conduction, slow reaction time, or poor balance.[44] Greater depressive symptoms have been prospectively associated with 4 year decline in physical performance including change in standing balance, walking speed, and ability to rise from a chair, [45] as well as with subsequent self-reported physical disability.[46–48] Our findings suggest that depression is a strong predictor of falls among high risk middle-aged women, regardless of HIV status, despite adjusting for substance abuse and CNS active medication use or cognitive complaints. Additional research is needed to understand the mechanisms by which depressive symptoms directly or indirectly increase the risk of falls among HIV-infected and uninfected aging women and to determine if HIV and treatment longevity confer greater fall and fracture risk with increasing age or post-menopausal status.

Our study has several limitations. Fall ascertainment was based on participants' self-report, which may result in under estimation of falls, particularly in older participants or those with cognitive impairment or in falls that result in minimal injury. Additionally, subjective cognitive complaints are contingent on self-report of cognition, non-specific, overlap with depressive symptoms, and may not identify less subtle or early cognitive impairment. We do not have complete data on measures of gait speed, frailty, physical activity, or comprehensive multifactorial falls risk assessments. We also do not have data on circumstances of fall, such as activity at the time of fall, conditions associated with fall, or indoor vs. outdoor location, nor the environmental conditions of the home or neighborhood. We also do not have detailed data on sleep quantity and quality which may impact both cognitive function and physical performance. Complete data on prescribed and non-prescribed opioids, which have been associated with falls in uninfected populations, are not currently available in WIHS. Further, associations between CNS active medications and risk of falls may be subject to confounding by indication. Last, our findings may not generalize to men, other racial/ethnic groups, or less marginalized women with better socioeconomic conditions.

CONCLUSIONS

In this longitudinal study of predominantly middle-aged low income minority women, HIV-infected women did not report a greater frequency of falls than uninfected women at high risk for HIV infection. Fall occurrence was similar and quite high for both HIV status groups

with 41% of women reporting at least one fall over a two year time period, exceeding rates observed among community dwelling adults who are much older. Among HIV infected women, cognitive complaints were associated with falls, but the effect was attenuated by adjustment for comorbid illnesses. Further research is also needed in order to elucidate the underlying mechanism of these falls, as well as identify potential targets for therapeutic interventions to prevent falls in HIV-infected and at-risk women as they age.

Acknowledgments

Source of Funding:

Data in this manuscript were collected by the Women's Interagency HIV Study (WIHS). The contents of this publication are solely the responsibility of the authors and do not represent the official views of the National Institutes of Health (NIH). WIHS (Principal Investigators): UAB-MS WIHS (Michael Saag, Mirjam-Colette Kempf, and Deborah Konkle-Parker), U01-AI-103401; Atlanta WIHS (Ighovwerha Ofotokun and Gina Wingood), U01-AI-103408; Bronx WIHS (Kathryn Anastos), U01-AI-035004; Brooklyn WIHS (Howard Minkoff and Deborah Gustafson), U01-AI-031834; Chicago WIHS (Mardge Cohen and Audrey French), U01-AI-034993; Metropolitan Washington WIHS (Mary Young), U01-AI-034994; Miami WIHS (Margaret Fischl and Lisa Metsch), U01-AI-103397; UNC WIHS (Adaora Adimora), U01-AI-103390; Connie Wofsy Women's HIV Study, Northern California (Ruth Greenblatt, Bradley Aouizerat, and Phyllis Tien), U01-AI-034989; WIHS Data Management and Analysis Center (Stephen Gange and Elizabeth Golub), U01-AI-042590; Southern California WIHS (Joel Milam), U01-HD-032632 (WIHS I – WIHS IV). The WIHS is funded primarily by the National Institute of Allergy and Infectious Diseases (NIAID), with additional co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), the National Cancer Institute (NCI), the National Institute on Drug Abuse (NIDA), and the National Institute on Mental Health (NIMH). 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. This research was also supported by National Institutes of Health K23AR06199301 (AS).

References

1. HIV/AIDS Surveillance Report. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2007. at http://www.cdc.gov/hiv/pdf/statistics_2007_HIV_Surveillance_Report_vol_19.pdf
2. Pathai S, Bajillan H, Landay AL, High KP. Is HIV a model of accelerated or accentuated aging? The journals of gerontology Series A, Biological sciences and medical sciences. 2014; 69:833–42.
3. Greene M, Justice AC, Lampiris HW, Valcour V. Management of human immunodeficiency virus infection in advanced age. Jama. 2013; 309:1397–405. [PubMed: 23549585]
4. Greene M, Covinsky KE, Valcour V, et al. Geriatric Syndromes in Older HIV-Infected Adults. Journal of acquired immune deficiency syndromes (1999). 2015; 69:161–7. [PubMed: 26009828]
5. Guaraldi G, Orlando G, Zona S, et al. Premature age-related comorbidities among HIV-infected persons compared with the general population. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2011; 53:1120–6. [PubMed: 21998278]
6. Effros RB, Fletcher CV, Gebo K, et al. Aging and infectious diseases: workshop on HIV infection and aging: what is known and future research directions. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2008; 47:542–53. [PubMed: 18627268]
7. Goulet JL, Fultz SL, Rimland D, et al. Aging and infectious diseases: do patterns of comorbidity vary by HIV status, age, and HIV severity? Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2007; 45:1593–601. [PubMed: 18190322]
8. Kim DJ, Westfall AO, Chamot E, et al. Multimorbidity patterns in HIV-infected patients: the role of obesity in chronic disease clustering. Journal of acquired immune deficiency syndromes (1999). 2012; 61:600–5. [PubMed: 23023101]
9. El-Sadr WM, Lundgren J, Neaton JD, et al. CD4+ count-guided interruption of antiretroviral treatment. The New England journal of medicine. 2006; 355:2283–96. [PubMed: 17135583]
10. Deeks SG, Phillips AN. HIV infection, antiretroviral treatment, ageing, and non-AIDS related morbidity. BMJ (Clinical research ed). 2009; 338:a3172.

11. Kuller LH, Tracy R, Belloso W, et al. Inflammatory and coagulation biomarkers and mortality in patients with HIV infection. PLoS medicine. 2008; 5:e203. [PubMed: 18942885]
12. Brown TT, Qaqish RB. Antiretroviral therapy and the prevalence of osteopenia and osteoporosis: a meta-analytic review. AIDS (London, England). 2006; 20:2165–74.
13. Sharma A, Shi Q, Hoover DR, et al. Increased Fracture Incidence in Middle-Aged HIV-Infected and HIV-Uninfected Women: Updated Results From the Women's Interagency HIV Study. Journal of acquired immune deficiency syndromes (1999). 2015; 70:54–61. [PubMed: 26322667]
14. Erlandson KM, Allshouse AA, Jankowski CM, et al. Risk factors for falls in HIV-infected persons. Journal of acquired immune deficiency syndromes (1999). 2012; 61:484–9. [PubMed: 23143526]
15. Sharma A, Hoover DR, Shi Q, et al. Falls among middle-aged women in the Women's Interagency HIV Study. Antiviral therapy. 2016
16. Abdulrab K, Heun R. Subjective Memory Impairment. A review of its definitions indicates the need for a comprehensive set of standardised and validated criteria. European psychiatry : the journal of the Association of European Psychiatrists. 2008; 23:321–30. [PubMed: 18434102]
17. Gauthier S, Reisberg B, Zaudig M, et al. Mild cognitive impairment. Lancet (London, England). 2006; 367:1262–70.
18. Al-Sari UA, Tobias JH, Archer H, Clark EM. Do subjective memory complaints predict falls, fractures and healthcare utilization? A two-year prospective study based on a cohort of older women recruited from primary care. International journal of geriatric psychiatry. 2016
19. Bacon, MCvWV., Alden, C., et al. The Women's Interagency HIV Study: an Observational Cohort Brings Clinical Sciences to the Bench. Clin Diagn Lab Immunol. 2005; 12:1013–9. [PubMed: 16148165]
20. Lamb SEJ-SE, Hauer K, et al. Prevention of Falls Network E, Outcomes Consensus G. Development of a common outcome data set for fall injury prevention trials: the Prevention of Falls Network Europe consensus. J Am Geriatr Soc. 2005; 53:1618–22. [PubMed: 16137297]
21. LSR. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Measur. 1977; 1:385–401.
22. Bozzette SAHR, Berry SH, Kanouse DE, Wu AW. Derivation and properties of a brief health status assessment instrument for use in HIV disease. Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology. 1995; 8:253–65. [PubMed: 7859137]
23. Liu C, Weber K, Robison E, Hu Z, Jacobson LP, Gange SJ. Assessing the effect of HAART on change in quality of life among HIV-infected women. AIDS research and therapy. 2006; 3:6. [PubMed: 16549012]
24. Tien PCSM, Cox C, et al. Association of HIV infection with Incident Diabetes Mellitus: Impact of using Hemoglobin A1C as a Criterion for Diabetes. Journal of acquired immune deficiency syndromes (1999). 2012; 61:334–40. [PubMed: 22878421]
25. Levey AS, Lewis BJJB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999; 130:461–70. [PubMed: 10075613]
26. Khalsa AKR, Mack WJ, et al. Correlates of prevalent hypertension in a large cohort of HIV-infected women: Women's Interagency HIV Study. AIDS (London, England). 2007; 21:2539–41.
27. Erlandson KM, Plankey MW, Springer G, et al. Fall frequency and associated factors among men and women with or at risk for HIV infection. HIV medicine. 2016; 17:740–8. [PubMed: 27028463]
28. Tinetti ME. Clinical practice. Preventing falls in elderly persons. The New England journal of medicine. 2003; 348:42–9. [PubMed: 12510042]
29. Reinsch S, MacRae P, Lachenbruch PA, Tobis JS. Attempts to prevent falls and injury: a prospective community study. The Gerontologist. 1992; 32:450–6. [PubMed: 1427246]
30. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. The New England journal of medicine. 1988; 319:1701–7. [PubMed: 3205267]
31. Gillespie LD, Gillespie WJ, Robertson MC, Lamb SE, Cumming RG, Rowe BH. Interventions for preventing falls in elderly people. The Cochrane database of systematic reviews. 2003:Cd000340. [PubMed: 14583918]

32. Mendonca MD, Alves L, Bugalho P. From Subjective Cognitive Complaints to Dementia: Who is at Risk?: A Systematic Review. American journal of Alzheimer's disease and other dementias. 2016; 31:105–14.
33. Rouch I, Anterion CT, Dauphinot V, et al. Cognitive complaints, neuropsychological performance and affective disorders in elderly community residents. Disability and rehabilitation. 2008; 30:1794–802. [PubMed: 18608410]
34. Dufouil C, Fuhrer R, Alperovitch A. Subjective cognitive complaints and cognitive decline: consequence or predictor? The epidemiology of vascular aging study. J Am Geriatr Soc. 2005; 53:616–21. [PubMed: 15817007]
35. Reid LM, MacLullich AMJ. Subjective Memory Complaints and Cognitive Impairment in Older People. Dementia and Geriatric Cognitive Disorders. 2006; 22:471–85. [PubMed: 17047326]
36. Mitchell AJ, Beaumont H, Ferguson D, Yadegarfar M, Stubbs B. Risk of dementia and mild cognitive impairment in older people with subjective memory complaints: meta-analysis. Acta psychiatrica Scandinavica. 2014; 130:439–51. [PubMed: 25219393]
37. Kaup AR, Nettiksimmons J, LeBlanc ES, Yaffe K. Memory complaints and risk of cognitive impairment after nearly 2 decades among older women. Neurology. 2015; 85:1852–8. [PubMed: 26511452]
38. Derouesné C, Dealberto MJ, Boyer P, et al. Empirical evaluation of the 'Cognitive Difficulties Scale' for assessment of memory complaints in general practice: A study of 1628 cognitively normal subjects aged 45–75 years. International journal of geriatric psychiatry. 1993; 8:599–607.
39. Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's & dementia : the journal of the Alzheimer's Association. 2011; 7:270–9.
40. Verghese J, Wang C, Lipton RB, Holtzer R. Motoric cognitive risk syndrome and the risk of dementia. The journals of gerontology Series A, Biological sciences and medical sciences. 2013; 68:412–8.
41. Callisaya ML, Ayers E, Barzilai N, et al. Motoric Cognitive Risk Syndrome and Falls Risk: A Multi-Center Study. Journal of Alzheimer's disease : JAD. 2016; 53:1043–52.
42. Robertson KR, Parsons TD, Sidtis JJ, et al. Timed Gait test: normative data for the assessment of the AIDS dementia complex. Journal of clinical and experimental neuropsychology. 2006; 28:1053–64. [PubMed: 16840235]
43. Kvelde T, McVeigh C, Toson B, et al. Depressive Symptomatology as a Risk Factor for Falls in Older People: Systematic Review and Meta-Analysis. Journal of the American Geriatrics Society. 2013; 61:694–706. [PubMed: 23617614]
44. Kvelde T, Pijnappels M, Delbaere K, Close JCT, Lord SR. Physiological and Cognitive Mediators for the Association Between Self-reported Depressed Mood and Impaired Choice Stepping Reaction Time in Older People. The Journals of Gerontology: Series A. 2010; 65A:538–44.
45. Penninx BW, Guralnik JM, Ferrucci L, Simonsick EM, Deeg DJ, Wallace RB. Depressive symptoms and physical decline in community-dwelling older persons. Jama. 1998; 279:1720–6. [PubMed: 9624025]
46. Broadhead WE, Blazer DG, George LK, Tse CK. Depression, disability days, and days lost from work in a prospective epidemiologic survey. Jama. 1990; 264:2524–8. [PubMed: 2146410]
47. Gallo JJ, Rabins PV, Lyketsos CG, Tien AY, Anthony JC. Depression without sadness: functional outcomes of nondysphoric depression in later life. J Am Geriatr Soc. 1997; 45:570–8. [PubMed: 9158577]
48. Bruce ML, Seeman TE, Merrill SS, Blazer DG. The impact of depressive symptomatology on physical disability: MacArthur Studies of Successful Aging. American journal of public health. 1994; 84:1796–9. [PubMed: 7977920]

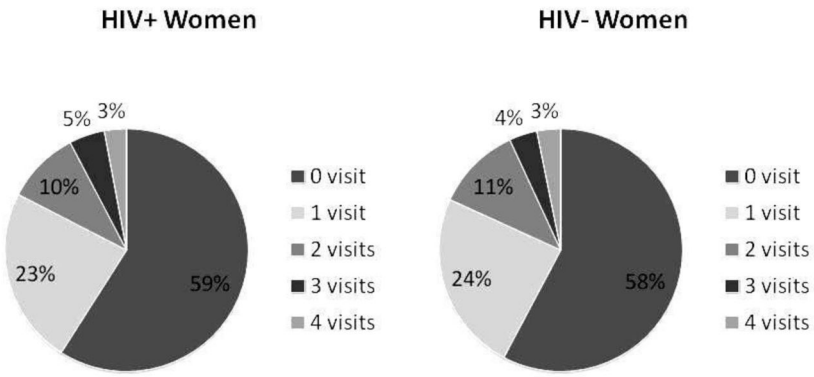

Figure 1.
Percentage of Women Reporting at Least One Fall at Each Visit

Table 1

Characteristics of 1,816 HIV+ and HIV− WIHS Participants at Index Visit

Characteristic	HIV-infected (N=1250)	HIV-uninfected (N=566)	P value*
Age, years, median (IQR)	48.9 (42.8–54.6)	47.1 (39.9–53.8)	0.0004
Education level high school or greater	811 (65.3%)	388 (68.9%)	0.13
Annual Income ≥$12,000/yr	596 (48.5%)	285 (51.8%)	0.20
Enrollment year			0.002
94–95	459 (37.3%)	166 (29.9%)	
01–02	311 (25.2%)	179 (32.2%)	
11–14	462 (37.5%)	211 (38.0%)	
WIHS Site			
Bronx/Manhattan	216 (17.3%)	111 (19.6%)	0.14
Brooklyn	226 (18.1%)	87 (15.4%)	
Washington DC	180 (14.4%)	81 (14.3%)	
Chicago	168 (13.4%)	81 (14.3%)	
San Francisco	174 (13.9%)	59 (10.4%)	
Southern sites	286 (22.9%)	147 (26.0%)	
Race			0.24
White	191 (15.4%)	70 (12.4%)	
Black	905 (72.8%)	428 (75.9%)	
Hispanic/Other	148 (11.9%)	66 (11.7%)	
Injection Drug Use			0.52
Never	1035 (83.1%)	477 (84.3%)	
Past/Current	211 (16.9%)	89 (15.7%)	
Smoking status			<0.0001
Never	417 (33.4%)	155 (27.4%)	
Past	369 (29.5%)	135 (23.9%)	
Current	464 (37.1%)	276 (48.8%)	
Cocaine, crack, or heroin use			0.004
Never	658 (52.8%)	267 (47.2%)	
Past	492 (39.5%)	230 (40.6%)	
Current	96 (7.7%)	69 (12.2%)	
Marijuana use			0.025
Never	486 (39.0%)	193 (34.1%)	
Past	524 (42.1%)	237 (41.9%)	
Current	236 (18.9%)	136 (24.0%)	
Recent alcohol use			<0.0001
None	687 (55.3%)	243 (43.1%)	
Light (< 3 drinks/wk)	420 (33.8%)	199 (35.3%)	
Moderate (3–13 drinks/wk)	52 (4.2%)	48 (8.5%)	

Characteristic	HIV-infected (N=1250)	HIV-uninfected (N=566)	P value*
Heavy (≥14 drinks/wk)	84 (6.8%)	74 (13.1%)	
Postmenopausal status *	494 (39.9%)	171 (30.3%)	<0.0001
Quality of Life Rating, median (IQR)	8 (7–9)	8 (6–9)	0.0005
Comorbidities			
Hepatitis C Virus infection	147 (11.8%)	44 (7.8%)	0.01
Diabetes Mellitus	261 (21.0%)	129 (22.8%)	0.38
Hypertension	633 (50.8%)	278 (49.1%)	0.51
Renal dysfunction (eGFR <60)	117 (9.5%)	34 (6.0%)	0.015
Depressive symptoms (CESD ≥16)	356 (28.6%)	172 (30.5%)	0.42
Peripheral neuropathy	253 (20.2%)	89 (15.7%)	0.023
Obesity (≥30kg/m^2)	591 (47.9%)	328 (58.8%)	<0.0001
Subjective cognitive complaints	144 (11.5%)	57 (10.1%)	0.36
CNS active medication currently used			
Anticonvulsants	175 (14.0%)	59 (10.4%)	0.035
Antidepressants	359 (28.7%)	116 (20.5%)	0.0002
Antipsychotics	140 (11.2%)	73 (12.9%)	0.30
Benzodiazepines and other sedatives	161 (12.9%)	60 (10.6%)	0.17
Muscle relaxants	56 (4.5%)	37 (6.5%)	0.066
Number of current CNS active medication types			0.002
0	717 (57.4%)	373 (65.9%)	
1	276 (22.1%)	92 (16.3%)	
2	180 (14.4%)	62 (11.0%)	
≥3	77 (6.2%)	39 (6.9%)	
Reported fear of falling			0.91
Not at all	775 (62.2%)	358 (63.3%)	
A little	265 (21.3%)	112 (19.8%)	
Quite a bit	86 (6.9%)	40 (7.1%)	
Very much	120 (9.6%)	56 (9.9%)	
Fall status at any time during study			0.30
No fall	738 (59.0%)	327 (57.8%)	
One fall	194 (15.5%)	104 (18.4%)	
More than one fall	318 (25.4%)	135 (23.9%)	
HIV disease related characteristics			
AIDS defining illness ever	425 (34.0%)	N/A	N/A
Current CD4+ cell count (cells/μl), median (IQR)	588 (385–781)	N/A	N/A
Nadir CD4+ cell count (cells/μl), median (IQR)	280 (161–411)	N/A	N/A
Suppressed HIV RNA viral load (<20c/mL)	777 (63.4%)	N/A	N/A
Current ART use	1100 (88.3%)	N/A	N/A

Postmenopausal status * is defined by self-reported amenorrhea at 2 consecutive visits for women aged >=45 years old and no resumption of menses

Table 2

Unadjusted Predictors of Any Fall within Six Months in the Women's Interagency HIV Study

	HIV-infected Women Unadjusted OR (95% CI)	P value	HIV-uninfected Women Unadjusted OR (95% CI)	P value
Age (per 10 years)	1.41 (1.26, 1.57)	0.0000	1.24 (1.07, 1.44)	0.0035
Race (REF: Black)				
White	1.39 (1.08, 1.78)	0.011	0.98 (0.64, 1.51)	0.94
Hispanic/Other	1.02 (0.77, 1.35)	0.90	0.81 (0.50, 1.30)	0.38
Annual Household Income ≥$12,000	0.63 (0.52, 0.77)	0.0000	0.95 (0.70, 1.27)	0.71
Enrollment Cohort (REF: 94–95)				
01–02	0.55 (0.42, 0.72)	0.0000	0.75 (0.51, 1.10)	0.14
11–14	0.81 (0.65, 1.01)	0.065	1.32 (0.93, 1.86)	0.12
WIHS Site (REF: Bronx/Manhattan)				
Brooklyn	0.59 (0.40, 0.87)	0.007	0.64 (0.37, 1.12)	0.12
Washington DC	1.47 (1.04, 2.08)	0.028	1.23 (0.75, 2.01)	0.40
Chicago	1.81 (1.27, 2.57)	0.0009	1.45 (0.85, 2.47)	0.17
San Francisco	2.77 (1.98, 3.87)	0.0000	2.13 (1.31, 3.48)	0.002
Southern sites	1.34 (0.98, 1.84)	0.070	1.48 (0.95, 2.31)	0.082
Smoking status (REF: Never)				
Past	1.56 (1.20, 2.02)	0.0007	1.38 (0.88, 2.15)	0.16
Current	1.55 (1.21, 1.99)	0.0005	1.68 (1.16, 2.44)	0.006
Cocaine, crack, or heroin use (REF: Never)				
Past	1.50 (1.21, 1.84)	0.0002	1.43 (1.04, 1.96)	0.026
Current	2.84 (2.03, 3.99)	0.0000	2.06 (1.34, 3.15)	0.0009
Marijuana use (REF: Never)				
Past	1.45 (1.15, 1.82)	0.001	1.20 (0.85, 1.68)	0.30
Current	2.32 (1.76, 3.04)	0.0000	1.77 (1.20, 2.61)	0.004
Recent alcohol use (REF: None)				
Light (< 3 drinks/wk)	1.12 (0.90, 1.39)	0.32	0.87 (0.62, 1.23)	0.43
Moderate (3–13 drinks/wk)	1.17 (0.68, 2.04)	0.57	1.15 (0.69, 1.94)	0.59
Heavy (≥14 drinks/wk)	1.63 (1.13, 2.36)	0.009	1.26 (0.83, 1.90)	0.28
Current # of CNS active medication classes used (REF: 0)				
1	1.93 (1.52, 2.45)	<0.0001	1.85 (1.30, 2.64)	0.0006
2	2.37 (1.80, 3.11)	<0.0001	2.16 (1.32, 3.53)	0.002
≥3	4.30 (3.01, 6.14)	<0.0001	2.99 (1.81, 4.94)	<0.0001
Quality of Life Summary Rating (0–10 scale)	0.85 (0.81, 0.90)	<0.0001	0.80 (0.74, 0.86)	<0.0001
Hepatitis C Virus infection	1.89 (1.44, 2.48)	<0.0001	1.27 (0.80, 2.03)	0.32
Diabetes Mellitus	1.49 (1.18, 1.87)	0.0007	1.19 (0.85, 1.66)	0.32
Hypertension	1.62 (1.33, 1.97)	<0.0001	1.97 (1.47, 2.64)	<0.0001

	HIV-infected Women Unadjusted OR (95% CI)	P value	HIV-uninfected Women Unadjusted OR (95% CI)	P value
Renal dysfunction (eGFR <60)	1.79 (1.34, 2.39)	0.0001	1.67 (1.01, 2.78)	0.047
Depressive symptoms (CESD ≥ 16)	2.47 (2.02, 3.04)	<0.0001	2.56 (1.91, 3.43)	<0.0001
Peripheral neuropathy	2.26 (1.82, 2.82)	<0.0001	2.46 (1.74, 3.48)	<0.0001
Obesity (≥30kg/m^2)	1.06 (0.87, 1.30)	0.54	1.43 (1.06, 1.93)	0.018
Subjective cognitive complaints	2.38 (1.83, 3.09)	<0.0001	3.43 (2.37, 4.97)	<0.0001
AIDS defining illness ever	1.55 (1.26, 1.89)	<0.0001	N/A	N/A
Current CD4+ cell count (per 100 cells/μl)	0.99 (0.96, 1.02)	0.58	N/A	N/A
Nadir CD4+ cell count (per 100 cells/μl)	0.99 (0.95, 1.04)	0.71	N/A	N/A
Log_{10} HIV RNA viral load	1.03 (0.94, 1.12)	0.58	N/A	N/A
Current HAART use	0.95 (0.71, 1.28)	0.73	N/A	N/A

Table 3

Multivariable Analyses of Any Fall within Six Months in the Women's Interagency HIV Study

	HIV-infected Women Multivariable OR (95% CI)	P value	HIV-uninfected Women Multivariable OR (95% CI)	P value
Age (per 10 years)	1.29 (1.11, 1.49)	0.0009	1.12 (0.92, 1.37)	0.27
Race (REF: Black)				
White	1.16 (0.88, 1.53)	0.30	0.90 (0.57, 1.42)	0.64
Hispanic/Other	1.08 (0.78, 1.50)	0.65	0.73 (0.43, 1.25)	0.26
Annual Income ≥$12,000	0.81 (0.65, 1.01)	0.059	1.37 (0.98, 1.91)	0.065
Enrollment year (REF: 94–95)				
01–02	0.91 (0.67, 1.23)	0.53	1.09 (0.70, 1.69)	0.71
11–14	1.02 (0.71, 1.47)	0.90	1.21 (0.74, 1.96)	0.45
WIHS Site (REF: Bronx/Manhattan)				
Brooklyn	0.75 (0.50, 1.12)	0.16	0.80 (0.44, 1.45)	0.46
Washington DC	1.66 (1.16, 2.39)	0.0059	1.29 (0.77, 2.18)	0.34
Chicago	1.74 (1.20, 2.52)	0.0036	1.48 (0.83, 2.64)	0.19
San Francisco	2.19 (1.55, 3.09)	<0.0001	1.64 (0.95, 2.82)	0.074
Southern sites	1.52 (0.98, 2.36)	0.062	1.11 (0.57, 2.17)	0.75
Smoking status (REF: Never)				
Past	1.15 (0.85, 1.56)	0.36	0.95 (0.58, 1.58)	0.85
Current	0.98 (0.72, 1.33)	0.88	0.97 (0.60, 1.56)	0.89
Cocaine, crack or heroin use (REF: Never)				
Past	0.88 (0.65, 1.18)	0.38	1.06 (0.67, 1.68)	0.81
Current	1.33 (0.90, 1.97)	0.16	1.02 (0.58, 1.79)	0.95
Marijuana use (REF: Never)				
Past	1.32 (0.99, 1.77)	0.062	1.32 (0.83, 2.11)	0.24
Current	1.68 (1.21, 2.34)	0.002	1.57 (0.95, 2.60)	0.082
Current alcohol use (REF: None)				
Light (< 3 drinks/wk)	1.15 (0.91, 1.44)	0.24	0.96 (0.67, 1.39)	0.84
Moderate (3–13 drinks/wk)	0.85 (0.49, 1.47)	0.55	1.00 (0.58, 1.72)	0.99
Heavy (≥14 drinks/wk)	1.05 (0.70, 1.55)	0.83	0.98 (0.60, 1.58)	0.93
Categories of CNS active medications (REF: 0)				
1	1.31 (1.02, 1.68)	0.035	1.14 (0.76, 1.72)	0.53
2	1.41 (1.04, 1.90)	0.027	1.40 (0.85, 2.30)	0.18
≥3	2.37 (1.60, 3.50)	<0.0001	1.14 (0.63, 2.08)	0.66
Quality of Life Summary Rating (scale 0–10)	0.97 (0.92, 1.03)	0.29	0.90 (0.82, 0.98)	0.020
Hepatitis C Virus infection	1.40 (1.04, 1.88)	0.027	1.20 (0.70, 2.06)	0.51
Diabetes Mellitus	1.16 (0.91, 1.49)	0.24	0.78 (0.53, 1.14)	0.20
Hypertension	1.03 (0.82, 1.29)	0.82	1.59 (1.12, 2.25)	0.010
Renal dysfunction (eGFR <60)	1.08 (0.79, 1.46)	0.64	1.64 (0.92, 2.92)	0.091

	HIV-infected Women Multivariable OR (95% CI)	P value	HIV-uninfected Women Multivariable OR (95% CI)	P value
Depressive symptoms (CESD ≥16)	1.70 (1.33, 2.16)	<0.0001	1.61 (1.12, 2.32)	0.01
Peripheral neuropathy	1.44 (1.12, 1.84)	0.004	1.63 (1.10, 2.41)	0.015
Obesity (≥30kg/m^2)	1.18 (0.95, 1.47)	0.14	1.56 (1.08, 2.23)	0.017
Subjective cognitive complaints	1.25 (0.93, 1.68)	0.14	2.26 (1.46, 3.48)	0.0002
AIDS defining illness ever	1.16 (0.90, 1.50)	0.26	N/A	N/A

Multivariable GEE model of independent prediction of at least one fall in the 6 months prior to each of the 4 visits pooled was fit using stepwise selection with SAS default criteria to enter and remain in the model. All models are adjusted for age and study site.

Table 4

Relationship between Subjective Cognitive Complaints and Odds of Any Fall in WIHS

	HIV-infected Women		HIV-uninfected Women	
	Multivariable OR (95% CI)	**P value**	**Multivariable OR (95% CI)**	**P value**
Model 1: Subjective Cognitive Complaints	2.38 (1.83, 3.09)	<0.0001	3.43 (2.37, 4.97)	<0.0001
Model 2: Adjusted for Model 1 + **Demographics** *	2.05 (1.56, 2.70)	<0.0001	3.18 (2.11, 4.78)	<0.0001
Model 3: Adjusted for Model 2 + **Comorbidities** †	1.31 (0.98, 1.75)	0.066	2.17 (1.41, 3.34)	0.0004
Model 4: Adjusted for Model 3 + **Substance Use & CNS Active Medications** ‡	1.27 (0.95, 1.70)	0.11	2.26 (1.46, 3.48)	0.0002
Model 5: Adjusted for Model 4 + **Prior AIDS** §	1.25 (0.93, 1.68)	0.14	N/A	N/A

* Demographics: age per 10 years, race/ethnicity, annual household income; high school education or more; and year of WIHS enrollment.

† Comorbidities: peripheral neuropathy; obesity (BMI>30 kg/m^2); CESD≥16; quality of life summary score; diabetes mellitus; renal dysfunction (eGFR <60 ml/min); hypertension; and HCV infection

‡ Substance Use: tobacco use; cocaine, crack, and/or heroin use; marijuana use; and alcohol use (heavy, moderate, light, or none); CNS Active medications included anticonvulsants, antidepressants, antipsychotics, benzodiazepines/sedatives, and muscle relaxants and were analyzed as the number of classes being used at index visit (0, 1, 2, or ≥3).

§ History of any prior AIDS-defining illness