Published in final edited form as:

Antivir Ther. 2016 ; 21(8): 697–706. doi:10.3851/IMP3070.

Falls among Middle-Aged Women in the Women's Interagency HIV Study

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], **Amber L. WHEELER, MD**[6], **Kathleen WEBER, RN**[7], **Michelle FLORIS-MOORE, MD, MS**[8], **Hector H. BOLIVAR, MD**[9], **David E. VANCE, PhD**[10], **Wendy J. MACK, PhD**[11], **Elizabeth T. GOLUB, PhD**[12], **Marcia McDonnell HOLSTAD, PhD, FNP BC**[13], and **Michael T. YIN, MD**[14]

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

[2]Department of Statistics and Biostatistics, Rutgers University, Piscataway, NJ

[3]Department of Epidemiology and Community Health, New York Medical College, Valhalla, NY

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

[5]Department of Medicine, Georgetown University Medical Center, Washington, DC

[6]Department of Medicine, San Francisco VA Medical Center, San Francisco, CA

[7]Department of Medicine, John H. Stroger Jr. Hospital of Cook County, Chicago, IL

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

[9] Department of Medicine, University of Miami Health System, Miami, FL

[10]School of Nursing, The University of Alabama at Birmingham, Birmingham, AL

[11]Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA

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

[13]Office of Academic Advancement, Emory School of Nursing, Atlanta GA

[14]Department of Medicine, Columbia University Medical Center, NY, NY

Abstract

Objective—To determine the frequency and risk factors for falls among middle-aged HIV+ and HIV− women in the Women's Interagency HIV Study (WIHS).

Methods—We quantified self-report of any and multiple (≥2 falls) in the prior 6 months among 1,412 HIV+ and 650 HIV− women with mean age 48 years. Logistic regression was used to

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.

evaluate associations of demographics, behavioral factors, comorbid conditions, and medications with odds of any fall (vs. none) and multiple falls (vs. ≤1 fall).

Results—At least one fall was reported in 263 HIV+ (19%) vs. 119 HIV− (18%) women, and ≥2 falls reported in 133 HIV+ (9%) vs. 65 HIV− (10%) women. HIV infection was not associated with falls in multivariate analyses. Factors independently associated with any fall included age (aOR 1.71, 95% CI:1.17-2.49 age 50-59 vs. <39y; aOR 2.26, 95% CI:1.38-3.71 age ≥60 vs. <39), current marijuana use (aOR 2.19, 95% CI:1.53-3.13) depressive symptoms (aOR 1.57, 95% CI: 1.21-2.05 for CES-D ≥16), subjective cognitive complaints (aOR 2.19, 95% CI:1.56-3.08), neuropathy (aOR 1.59, 95% CI:1.19-2.13), obesity (aOR 1.39, 95% CI:1.08-1.80), number of CNS active agents (aOR 2.98, 95% CI:1.90-4.68 for ≥3 agents vs. 0) and WIHS site. Factors associated with ≥2 falls included age, marijuana use, number of CNS active agents, subjective cognitive complaints, depressive symptoms, neuropathy, and study site.

Conclusions—Falls were associated with factors affecting cognition, but not HIV status in this large cohort of women. Longitudinal studies are needed to determine the incidence and consequences of falls by HIV status as women age.

Keywords

Fall; HIV; aging; women; cognition

INTRODUCTION

Current paradigms suggest that aging may be accelerated in HIV-infected individuals [1], who are more likely to have conditions associated with both aging and falls, such as cognitive impairment [2, 3], frailty syndrome [4-6], and polypharmacy [7, 8] when compared to HIV-uninfected individuals. Slow gait and poor physical performance are common in HIV-infected persons [9, 10], and accelerated gait speed decline has been reported in older HIV-infected men [11]. Moreover, in predominantly male injection drug users, HIV infection status was associated with reduced physical performance, and both HIV and reduced physical performance predicted increased risk of death [12]. Low bone mineral density is prevalent in HIV-infected populations, [13] thus the occurrence of falls in HIV-infected older adults may confer a greater risk of osteoporotic fracture. Several published studies show 30-70% increased fracture rates among HIV-infected persons compared with uninfected persons [14-16]. We previously demonstrated a higher fracture incidence rate among HIV-infected compared with uninfected women in the Women's Interagency HIV Study (WIHS), and a greater increase in fracture rate over time for HIV-infected compared with uninfected women [17]. While few published data on falls in HIV-infected persons exist, middle-aged HIV-infected adults are reported to have unexpectedly high fall risk [18]. We conducted this study to determine the frequency of any fall and multiple (≥2) falls occurring in the prior 6 months, and determine risk factors associated with falls among HIV-infected and uninfected women participating in the Women's Interagency HIV Study (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 in 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 2067 participants who attended WIHS visit 40 (2014), this analysis includes the 2062 participants (1,412 HIV+ and 650 HIV− women) with data on falls available. WIHS methods and baseline cohort characteristics have been described previously [19]. HIV-uninfected women were recruited from groups at high risk for HIV infection. 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.

In 2014 (at semiannual visit 40), all WIHS participants were asked to report any history of fall within the prior 6 months. 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. To assess fear of falling (FOF), all participants were asked “Are you afraid of falling?” with possible responses of: not at all, a little, quite a bit, or very much.

Statistical Analyses

Medians, interquartile ranges, and proportions were derived to summarize study variables, depending upon whether they were continuous or categorical. The primary outcomes were: report of any fall compared with no fall, and among those who had a fall report of multiple falls (2 or more) compared with single fall. Logistic regression models determined factors associated with any fall (vs. none) and with multiple falls (vs. ≤1 fall). Bivariate analyses evaluating each predictor in association with the outcome were considered for HIV-infected and uninfected participants together, and for HIV-infected participants separately using univariate logistic regression. Multivariate stepwise logistic models (p to enter and remain = 0.05) with HIV status (the primary exposure of interest), age (a well-accepted predictor of falls) and WIHS site (Brooklyn, Washington D.C., San Francisco, Chicago, Southern sites, vs. reference site Bronx) forced into the model were fit. A separate multivariate model, restricted to HIV-infected women, was constructed using similar methodology, to evaluate 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. Candidate covariates for multivariate models included demographic factors, behavioral factors, comorbid conditions, central nervous System (CNS) active medications, and HIV-related factors, as follows: **Demographic factors** included: age (40-49, 50-59, and ≥60 vs. <39yrs [reference]), race/ethnicity (White, Black , vs. other), annual income of $12,000 or less; having graduated from high school; and year of WIHS enrollment (2001-2, 2011-14, vs. 1994-5). **Behavioral factors** included HIV transmission risk category (heterosexual, transfusion/unknown/other, vs. injection drug [IDU] [reference]); tobacco use (current smoker, former smoker, vs. never smoker [reference]); cocaine, crack, or heroin use (current, former, vs. never [reference]); injection drug 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, benzodiazepines/sedatives, and muscle relaxants. CNS active medications were cumulatively analyzed as the number of classes being “currently” used (categorized as 0, 1, 2, or ≥3; [reference group 0 classes]). **Comorbidities** were assessed at the same visit as the falls questionnaire and included the following medical conditions 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/m^2); 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) of ≥16) [21]; diabetes as previously operationalized in WIHS [22]; renal dysfunction (estimated glomerular filtration rate (eGFR) <60 using the Modification of Diet in Renal Disease calculation) [23]; 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) [24]; and hepatitis C virus infection (defined as positive HCV antibody with HCV RNA tested shortly after study entry).

Additional **HIV disease specific covariates** included: nadir CD4+ count (minimum CD4 measured at or prior to baseline) and current CD4+ count, current Log_{10} HIV RNA level, current suppressed (<20 c/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, neuropathy, or lipoatrophy in published literature: didanosine, stavudine, zidovudine, or efavirenz.

RESULTS

Participant characteristics

A total of 1,412 HIV-infected and 650 HIV-uninfected women completed the falls questionnaire 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, and to report current smoking, current use of marijuana, heroin, cocaine, or crack, and heavy alcohol consumption. Among the 1,412 HIV-infected women, 37% reported a prior ADI, 88% reported taking ART at the current visit, and 65% had suppressed HIV RNA viral load. The overall proportion of women reporting any fall was similar between HIV-infected and uninfected women, (18.6%, N=263/1,412 for HIV+ and 18.3%, N=119/650 for HIV− women, p= 0.12). Among WIHS participants reporting a fall, 31.9% (N=84) of HIV-infected and 36.1% (N=43) of HIV-uninfected women sought medical attention for an injury resulting from their fall (p=0.35), and 3.8% (N=10) of HIV-infected women and 9.2% (N=11) in HIV-uninfected women reported fracture (p=0.04).

Factors associated with falls in the Women's Interagency HIV Study Cohort

Univariate analyses of characteristics associated with no fall, single fall, and multiple falls are shown in Table 2. There was no difference in the occurrence of either single or multiple fall by HIV status, with single fall reported by 9% of HIV-infected and 8% of uninfected women, and multiple falls reported by 9% of HIV-infected women and 10% of uninfected women (overall p=0.75). Older age, behavioral factors (smoking, substance use, and alcohol use) and comorbidities (hypertension, depressive symptoms, subjective cognitive complaints, peripheral neuropathy, and obesity) were associated with reported falls (all $p<0.05$, Table 2). Each of the five classes of CNS active medications was associated with progressively greater occurrence of falls, as were consequently higher number of categories of CNS active medications used. Fear of falling (FOF) was positively associated with single and multiple falls. Among women who rated their FOF as “very much”, 13% had a single fall in the prior 6 months, and 25% had 2 or more falls, whereas among those with no FOF, 5% reported single fall and 4% reported ≥2 falls (overall $p <0.0001$). Among the subset of HIV-infected women, measures of HIV disease severity (including CD4+ nadir and prior ADI), current CD4+ count, current detectable HIV RNA viral load, and antiretroviral use were not associated with falls (Table 2). Unexpectedly, we found that falls differed by site, with at the lowest only about 10% of participants at the New York sites reporting sustaining a fall versus at the highest 30% of participants in San Francisco; therefore WIHS site was included in all multivariate models.

Multivariate analyses of factors associated with any fall

In multivariate analyses for the full cohort, age 50-59 was independently associated with higher odds of fall (adjusted Odds Ratio (aOR 1.71, 95% CI:1.17- 2.49 vs. <39), and women ≥60 years old had over double the odds of any fall compared with those < 39 years (aOR 2.26, 95% CI:1.38- 3.71) (**Table 3**). Use of greater numbers of CNS active medications was independently associated with increasing fall risk. Compared to use of no CNS active agents, use of two medication classes was associated with almost double the odds of falling, and use of three or more medication classes was associated with almost triple the odds of falling. Women with subjective cognitive complaints were independently over twice as likely to report falls than those reporting no cognitive difficulties (aOR 2.19, 95% CI:1.56- 3.08). Other factors independently associated with any fall included: WIHS site, current and past

marijuana use, depressive symptoms, peripheral neuropathy, and obesity (**Table 3**). HIV infection was not independently associated with fall risk (aOR 1.08, 95% CI: 0.82- 1.42).

Multivariate analyses of factors associated with multiple falls

In multivariate analyses of multiple falls compared with ≤1 fall among HIV-infected and uninfected women, independent risk factors were similar to those for any (vs. no) fall (**Table 3**), including older age, current or former marijuana use, use of CNS active medications, subjective cognitive complaints, depressive symptoms, peripheral neuropathy, and WIHS study site. In additional analyses comparing multiple falls with single falls, women reporting subjective cognitive complaints had almost double the adjusted odds of multiple vs. single falls than women who did not (aOR 1.75, 95% CI:1.05- 2.90), as did those with peripheral neuropathy (aOR 1.73, 95%CI:1.08- 2.77), (data not shown). Current crack, cocaine, or heroin use was independently associated with multiple (vs. single) falls (aOR 2.89, 95%CI: 1.32-6.34), whereas HIV infection, age, use of CNS active medications, depressive symptoms, obesity, and WIHS site were not (data not shown).

Multivariate analyses of factors associated with falls among HIV-infected women

Among HIV-infected women, those aged 60 or older had double the adjusted risk of any fall compared with women <39 years (aOR 2.00, 95%CI: 1.11-3.59) (data not shown). Other factors independently associated with any fall among HIV-infected women included WIHS site, current (aOR 1.93, 95%CI:1.26- 2.95) and past (aOR 2.92, 95%CI:1.69- 5.07) marijuana use, subjective cognitive complaints (aOR 2.31, 95% CI:1.53- 3.47), peripheral neuropathy (aOR 1.46, 95% CI:1.04- 2.06), depressive symptoms (aOR 1.49, 95% CI:1.08-2.04), and number of CNS active medications (aOR 1.55, 95% CI:1.08-2.23 for one (vs. no) class; aOR 2.14, 95% CI:1.40- 3.27 for 2 (vs. no) classes; aOR 2.79, 95% CI:1.63- 4.78 for ≥3 (vs. no classes). HIV-specific factors (data not shown) including measures of HIV disease severity (CD4 nadir and prior ADI), current CD4+ count, suppressed HIV RNA viral load, or antiretroviral use (including current ART use, as well as current and prior use of didanosine, stavudine, zidovudine, or efavirenz) were not associated with risk of any vs. no falls in multivariate analyses

Factors independently associated with risk of multiple falls (vs. ≤1 fall) among HIV-infected WIHS participants were similar to those in the complete WIHS cohort and included age 50-59 years, current and past marijuana use, subjective cognitive complaints, peripheral neuropathy, greater number of CNS active medications, and WIHS site (data not shown). Current HAART use was associated with half the risk of multiple falls (aOR 0.50, 95%CI: 0.30- 0.85); other HIV-specific factors were not associated with multiple falls (vs. ≤1 fall) in multivariate analyses. In models comparing risks for multiple vs. single falls, only heavy alcohol use (aOR 7.28, 95%CI: 1.91- 27.78), current marijuana use (aOR 3.19, 95%CI: 1.40- 7.28), peripheral neuropathy (aOR 2.17, 95%CI: 1.22- 3.86), and diabetes mellitus (aOR 2.04, 95%CI: 1.00-4.16) were associated with multiple falls among HIV-infected participants (data not shown).

DISCUSSION

This is the first study to examine the occurrence of falls and to compare fall frequency and risks in women with or at risk for HIV infection. We found that that HIV-infection was not associated with increased occurrence of either single or multiple falls, and among HIV infected women, measures of HIV-disease or treatment related characteristics did not confer additional risk or protection from falls.

Little data exist on fall risks and prevalence in HIV-infected populations, and in published and presented studies, estimates have varied widely. Among predominantly male HIV-infected HAART users with a mean age of 52 years, 30% reported one or more falls within 12 months and 18% reported recurrent falls, similar to overall fall rates reported among an older population (65 years or older) of general U.S. adults [18]. In that study, female gender, functional impairment, and multiple medical comorbidities and medications were significant predictors of more falls [18]. In a retrospective database review of medical records of 2,000 HIV-infected outpatients in Louisiana, only 32 falls were identified within 12 months, and polypharmacy (>5 medications), >3 medical comorbidities, and nonadherence to ART were associated with increased fall risk [25]. Similar to our study, a Multicenter AIDS Cohort Study (MACS) study of bone strength among men aged 50-79 years reported similar numbers of single fall and multiple falls over 2 years among HIV-infected and uninfected men (27% reported single fall for HIV+ and 23% for HIV-; multiple falls in 11% of HIV+ and 9% of HIV− men) [26].

It is well established that among older persons in the U.S., one-third fall annually [27, 28], with 10% of these falls resulting in injury requiring medical attention [27, 29]. By comparison among our 198 WIHS participants 60 years or older, about 25% reported having sustained a fall in the prior 6 months; however because we collected falls data over 6 months rather than 12 months, these numbers may represent an underestimation of annual rate of falls occurrence. Approximately one-third of woman having at least one fall had a fall that resulted in injury requiring medical attention, although the proportion of falls resulting in injury did not differ by HIV status.

We found that illicit drug use was also associated with more falls; marijuana use in particular was associated with both single and multiple falls. Our finding that current use of crack, cocaine, or heroin use was associated with multiple (vs. single falls) may in part explain the underlying reason for the increased incidence of fracture associated with cocaine use and injection drug use we previously reported in the WIHS cohort [17]. Among HIV-infected women, heavy alcohol use was also associated with multiple (vs. single) falls. Alcohol and/or illicit drug use may increase fall risk through over-sedation, dizziness, or impairment in gait, balance, judgment, or cognition. Combined alcohol and prescription medication use may also result in an increase in blood alcohol levels, altered metabolism of other medications, exacerbation of adverse effects of medications, decreased effectiveness of medications, or worsening of underlying conditions (including hypertension, diabetes, depression, seizures, and liver disease) [30]. Prescription opioid use has been associated with increased fall [31, 32] and fracture [32-35] risk, however fall or fracture risks associated with illicit opioid use or marijuana use among older persons have not been

evaluated to date. Our data suggest that marijuana use in particular may be an important consideration when evaluating fall risk in older populations.

Falls and fractures are considered as geriatric syndromes, clinical conditions with shared risk factors that are highly prevalent in the elderly, and associated with poor outcomes, including disability, frailty, reduced quality of life, loss of independence, and mortality [36, 37]. Many studies have described premature occurrence of medical comorbidities associated with aging in HIV-infected populations compared with the general population [1, 38, 39], including multimorbidity [1, 40], fracture [14-16], and frailty [4-6]. Because low BMD is prevalent in HIV-infected populations, falls may be more likely to result in fractures in this population. In a 10 year French national cohort study of treated HIV-infected patients with a median age of 36 years, 81% of the fractures that occurred were caused by sustaining a fall or other trauma; however no comparison group of uninfected persons was included [41]. Notably, we found an association between HAART use and reduced risk of multiple falls among HIV-infected women, which has not been previously reported. While we did not observe higher occurrence of falls among HIV-infected women, prospective longitudinal studies are need to determine whether falls result in greater likelihood of injury in HIV-infected than uninfected women, whether overall risk for fall-related injury increases disproportionately with age among HIV-infected vs. uninfected women, and whether HAART use reduces risk of recurrent falls among HIV-infected persons.

Ours is the first study of aging HIV-infected and uninfected women to characterize the fall-risk associated with number and type of medications. We found that concurrent use of multiple CNS active agents was associated with greater risk of falls. Many of these agents have anticholinergic activity, which has been associated with worse cognitive and functional performance as well as recurrent and injurious falls through gait and balance impairment among older adults [42, 43]. The associations between sedatives/hypnotics and anti-depressants with both falls and fall-related injuries has been well documented in elderly populations, as have those with antipsychotics, anticonvulsants, antihypertensives, and opioids [44-47]. Moreover, polypharmacy, often defined as the use of five or more prescribed medications, is a well-established risk factor for falls and fall-related injury, despite adjusting for fall risk inducing drugs or medical comorbidities [29, 48-50]. Although polypharmacy is common in HIV-infected populations and increases with age [7, 8]; the risk of harm associated with polypharmacy is greatly understudied in HIV-infected persons. Studies have shown increased fall risk associated with greater numbers of prescribed medications among HIV-infected persons; however these studies were limited by a lack of HIV-uninfected controls and few female participants [18, 26]. Identification of adverse effects associated with specific medication classes and polypharmacy is necessary in order to determine how best to mitigate risks and maximize benefits of each prescribed medication.

Unexpectedly, we found significant geographical differences in fall occurrence ranging from ~10% in the New York sites to 30% at San Francisco. Both New York City (NYC)-based WIHS sites in particular demonstrated reduced falls occurrence compared with other study sites. Although we are unable to explain these geographic differences in falls occurrence, we speculate that these differences may be in part due to the greater participant use of public

transportation and more time spent walking in NYC, compared with other sites in which driving may be a more frequent mode of transportation, however we are unable to test this theory. Additional possibilities include geographic variation of environmental factors, weather conditions or seasonality, or physical activity across sites.

Our study has several limitations. Fall ascertainment was based on participants' self-reportof events in the prior 6 months, which may result in underreporting of falls, particularly in older participants or those with cognitive impairment. Additionally, self-report of cognitive difficulty is a crude measure and is likely to capture only those with significant impairment, which is apparent to the participants themselves. We do not have complete data on measures of frailty, physical activity, or disability, nor on several factors associated with fall risk, such as vision problems, urinary incontinence, history of stroke or heart failure, polypharmacy, and orthostatic hypotension. We also do not have data on time of year when falls occurred, nor circumstances of fall, such as activity at the time of fall, conditions associated with fall (i.e. wet floor, icy sidewalk) or location (i.e. indoor vs. outdoor). Because this is a cross-sectional study, we are unable to ascertain temporal relationships between fear of falling, quality of life, and physical activity with fall, and in order to avoid biases associated with reverse-causality, we excluded these measures from analyses. Last, analyses of medication risks associated with falls may be subject to confounding by indication.

CONCLUSIONS

We found that the occurrence of self-reported falls is similar in HIV-infected and HIV-uninfected women with a mean age of 48, and that HIV-disease or treatment related characteristics were not associated with fall risk among those with HIV infection. We identified a number of modifiable risk factors for falls, including use of multiple CNS active medications and substance abuse, which could be important areas to target in falls prevention efforts as HIV-infected women age. Longitudinal studies are needed to determine whether the incidence and consequence of falls will be greater in HIV-infected than uninfected 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). Targeted supplemental funding for specific projects is also provided by the National Institute of Dental and Craniofacial Research (NIDCR), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute on Deafness and other Communication Disorders (NIDCD), and the NIH Office of Research on Women's Health. WIHS data collection is

also supported by UL1-TR000004 (UCSF CTSA) and UL1-TR000454 (Atlanta CTSA). 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. Guaraldi G, Orlando G, Zona S, et al. Premature Age-Related Comorbidities Among HIV-Infected Persons Compared With the General Population. Clin Infect Dis. 2011; 53(11):1120–6. [PubMed: 21998278]
2. Heaton RK, Clifford DB, Franklin DR Jr, et al. HIV-associated neurocognitive disorders persist in the era of potent antiretroviral therapy: CHARTER study. Neurology. 2010; 75(23):2087–2096. [PubMed: 21135382]
3. Tozzi V, Balestra P, Bellagamba R, et al. Persistence of neuropsychologic deficits despite long-term highly active antiretroviral therapy in patients with HIV-related neurocognitive impairment: prevalence and risk factors. J Acquir Immune Defic Syndr. 2007; 45(2):174–182. [PubMed: 17356465]
4. Piggott DA, Muzaale AD, Mehta SH, et al. Frailty, HIV infection, and mortality in an aging cohort of injection drug users. PLoS One. 2013; 8:e54910. [PubMed: 23382997]
5. Desquilbet L, Jacobson LP, Fried LP, et al. A frailty-related phenotype before HAART initiation as an independent risk factor for AIDS or death after HAART among HIV-infected men. J Gerontol A Biol Sci Med Sci. 2011; 66:1030–1038. [PubMed: 21719610]
6. Desquilbet L, Jacobson LP, Fried LP, et al. HIV-1 infection is associated with an earlier occurrence of a phenotype related to frailty. J Gerontol A Biol Sci Med Sci. 2007; 62:1279–1286. [PubMed: 18000149]
7. Greene M, Steinman MA, McNicholl IR, et al. Polypharmacy, drug-drug interactions, and potentially inappropriate medications in older adults with human immunodeficiency virus infection. J Am Geriatr Soc. 2014; 62:447–453. [PubMed: 24576251]
8. Edelman EJ, Gordon KS, Glover J, et al. The next therapeutic challenge in HIV: polypharmacy. Drugs Aging. 2013; 30:613–628. [PubMed: 23740523]
9. Greene M, Covinsky K, Astemborski J, et al. The relationship of physical performance with HIV disease and mortality. AIDS. 2014; 28:2711–9. [PubMed: 25493597]
10. Richert L, Dehail P, Mercie P, et al. High frequency of poor locomotor performance in HIV-infected patients. AIDS. 2011; 25:797–805. [PubMed: 21330905]
11. Schrack JA, Althoff KN, Jacobson LP, et al. Accelerated Longitudinal Gait Speed Decline in HIV-Infected Older Men. J Acquir Immune Defic Syndr. 2015; 70:370–6. [PubMed: 26102450]
12. Greene M, Covinsky K, Astemborski J, et al. The relationship of physical performance with HIV disease and mortality. AIDS. 2014; 28:2711–9. [PubMed: 25493597]
13. Brown TT, Qaqish RB. Antiretroviral therapy and the prevalence of osteopenia and osteoporosis: a meta-analytic review. AIDS. 2006; 20:2165–2174. [PubMed: 17086056]
14. Hansen AB, Gerstoft J, Kronborg G, et al. Incidence of low and high-energy fractures in persons with and without HIV infection: a Danish population-based cohort study. AIDS. 2012; 26(3):285–93. [PubMed: 22095195]
15. Young B, Dao CN, Buchacz K, Baker R, Brooks JT, HIV Outpatient Study (HOPS) Investigators. Increased rates of bone fracture among HIV-infected persons in the HIV Outpatient Study (HOPS) compared with the US general population, 2000-2006. Clin Infect Dis. 2011; 52(8):1061–8. [PubMed: 21398272]
16. Womack JA, Goulet JL, Gibert C, et al. Veterans Aging Cohort Study Project Team. Increased risk of fragility fractures among HIV infected compared to uninfected male veterans. PLoS One. 2011; 6(2):e17217. [PubMed: 21359191]
17. 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. J Acquir Immune Defic Syndr. 2015; 70:54–61. [PubMed: 26322667]

18. Erlandson KM, Allshouse AA, Jankowski CM, et al. Risk Factors for Falls in HIV-Infected Persons. J Acquir Immune Defic Syndr. 2012; 61(4):484–489. [PubMed: 23143526]
19. Bacon MC, von Wyl V, Alden C, et al. The Women's Interagency HIV Study: an Observational Cohort Brings Clinical Sciences to the Bench. Clin Diagn Lab Immunol. 2005; 12:1013–1019. [PubMed: 16148165]
20. Lamb SE, Jorstad-Stein EC, 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; 53:1618–1622. [PubMed: 16137297]
21. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Measur. 1977; 1:385–401.
22. Tien PC, Schneider MF, Cox C, et al. Association of HIV infection with Incident Diabetes Mellitus: Impact of using Hemoglobin A1C as a Criterion for Diabetes. J Acquir Immune Defic Syndr. 2012; 61(3):334–340. doi: 10.1097/QAI.0b013e31826bfc32. [PubMed: 22878421]
23. Levey AS, Bosch JP, Lewis JB, 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(6):461–70. [PubMed: 10075613]
24. Khalsa A, Karim R, Mack WJ, et al. Correlates of prevalent hypertension in a large cohort of HIV-infected women: Women's Interagency HIV Study. AIDS. 2007; 21(18):2539–41. [PubMed: 18025894]
25. Ruiz MA, Reske T, Cefalu C, Estrada J. Falls in HIV-infected patients: a geriatric syndrome in a susceptible population. J Int Assoc Provid AIDS Care. 2013; 12(4):266–9. [PubMed: 23719236]
26. Brown, TT., et al. Balance Confidence Predicts Falls Better Than Physical Function Testing in HIV + Men.. Abstract 786, Program and Abstracts of 22nd Conference on Retroviruses and Opportunistic Infections; Seattle, WA, USA. 2015 February 25;
27. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. N Engl J Med. 1988; 319(26):1701–1707. [PubMed: 3205267]
28. Centers for Disease Control and Prevention. Self-reported falls and fall-related injuries among persons aged ≥65 years—United States, 2006. MMWR Morb Mortal Wkly Rep. 2008; 57:225–229. [PubMed: 18322444]
29. Tinetti ME. Clinical practice. Preventing falls in elderly persons. N Engl J Med. 2003; 348:42–49. [PubMed: 12510042]
30. Moore AA, Whiteman EJ, Ward KT. Risks of combined alcohol/medication use in older adults. Am J Geriatr Pharmacother. 2007; 5(1):64–74. [PubMed: 17608249]
31. Söderberg KC, Laflamme L, Möller J. Newly initiated opioid treatment and the risk of fall-related injuries. A nationwide, register-based, case-crossover study in Sweden. CNS Drugs. 2013; 27(2): 155–61. [PubMed: 23345030]
32. Rolita L, Spegman A, Tang X, Cronstein BN. Greater number of narcotic analgesic prescriptions for osteoarthritis is associated with falls and fractures in elderly adults. J Am Geriatr Soc. 2013; 61(3):335–40. [PubMed: 23452054]
33. Ensrud KE, Blackwell T, Mangione CM, et al. Central nervous system active medications and risk for fractures in older women. Arch Intern Med. 2003; 163(8):949–57. [PubMed: 12719205]
34. Miller M, Stürmer T, Azrael D, Levin R, Solomon DH. Opioid analgesics and the risk of fractures in older adults with arthritis. J Am Geriatr Soc. 2011; 59(3):430–8. [PubMed: 21391934]
35. Teng Z, Zhu Y, Wu F, Zhu Y, Zhang X, Zhang C, Wang S, Zhang L. Opioids contribute to fracture risk: a meta-analysis of 8 cohort studies. PLoS One. 2015; 10(6):e0128232. doi: 10.1371/journal.pone.0128232. eCollection 2015. [PubMed: 26030421]
36. Inouye SK, Studenski S, Tinetti ME, Kuchel GA. Geriatric syndromes: clinical, research, and policy implications of a core geriatric concept. J Am Geriatr Soc. 2007; 55(5):780–91. [PubMed: 17493201]
37. Tinetti ME, Inouye SK, Gill TM, Doucette JT. Shared risk factors for falls, incontinence, and functional dependence: unifying the approach to geriatric syndromes. JAMA. 1995; 273(17):1348–1353. [PubMed: 7715059]

38. Goulet JL, Fultz SL, Rimland D, et al. Aging and infectious diseases: do patterns of comorbidity vary by HIV status, age, and HIV severity? Clin Infect Dis. 2007; 45:1593–601. [PubMed: 18190322]
39. Vance DE. Aging with HIV: bringing the latest research to bear in providing care. Am J Nurs. 2010; 110:42–7.
40. Kim DJ, Westfall AO, Chamot E, et al. Multimorbidity patterns in HIV-infected patients: the role of obesity in chronic disease clustering. J Acquir Immune Defic Syndr. 2012; 61:600–605. [PubMed: 23023101]
41. Collin F, Duval X, Le Moing V, et al. Ten-year incidence and risk factors of bone fractures in a cohort of treated HIV1-infected adults. AIDS. 2009; 23(8):1021–4. [PubMed: 19300202]
42. Pasina L, Djade CD, Lucca U, et al. Association of anticholinergic burden with cognitive and functional status in a cohort of hospitalized elderly: comparison of the anticholinergic cognitive burden scale and anticholinergic risk scale: results from the REPOSI study. Drugs Aging. 2013; 30(2):103–12. [PubMed: 23239364]
43. Zia A, Kamaruzzaman S, Myint PK, Tan MP. Anticholinergic burden is associated with recurrent and injurious falls in older individuals. Maturitas. Oct 23.2015 pii: S0378-5122(15)30068-2.
44. Huang AR, Mallet L, Rochefort CM, Eguale T, Buckeridge DL, Tamblyn R. Medication-related falls in the elderly: causative factors and preventive strategies. Drugs Aging. 2012; 29(5):359–76. [PubMed: 22550966]
45. Leipzig RM, Cumming RG, Tinetti ME. Drugs and falls in older people: a systematic review and meta-analysis, I: psychotropic drugs. J Am Geriatr Soc. 1999; 47(1):30–39. [PubMed: 9920227]
46. Leipzig RM, Cumming RG, Tinetti ME. Drugs and falls in older people: a systematic review and meta-analysis, II: cardiac and analgesic drugs. J Am Geriatr Soc. 1999; 47(1):40–50. [PubMed: 9920228]
47. Woolcott JC, Richardson KJ, Wiens MO, et al. Meta-analysis of the impact of 9 medication classes on falls in elderly persons. Arch Intern Med. 2009; 169(21):1952–60. [PubMed: 19933955]
48. Laflamme L, Monárrez-Espino J, Johnell K, Elling B, Möller J. Type, number or both? A population-based matched case-control study on the risk of fall injuries among older people and number of medications beyond fall-inducing drugs. PLoS One. 2015; 10(3):e0123390. doi: 10.1371/journal.pone.0123390. eCollection 2015. [PubMed: 25815483]
49. Lai SW, Liao KF, Liao CC, Muo CH, Liu CS, Sung FC. Polypharmacy correlates with increased risk for hip fracture in the elderly: a population-based study. Medicine (Baltimore). 2010; 89(5): 295–9. [PubMed: 20827106]
50. Tinetti ME, Kumar C. The patient who falls: “It's always a trade-off”. JAMA. 2010; 303(3):258–66. [PubMed: 20085954]

Table 1

Characteristics of Women's Interagency HIV Study Participants

Characteristic	HIV-infected (N=1412)	HIV-uninfected (N=650)	P value*
Age (years)			< 0.0001
<39	236 (16.7%)	164 (25.2%)	
40-49	509 (36.1%)	220 (33.9%)	
50-59	531 (37.6%)	204 (31.4%)	
≥60	136 (9.6%)	62 (9.5%)	
WIHS Site			<0.0001
Bronx / Manhattan	237 (16.8%)	125 (19.2%)	
Brooklyn	238 (16.9%)	90 (13.9%)	
Washington DC	204 (14.5%)	86 (13.2%)	
Chicago	211 (14.9%)	75 (11.5%)	
San Francisco	207 (14.7%)	102 (15.7%)	
Southern sites	315 (22.3%)	172 (26.5%)	
Race			0.28
White	224 (16.0%)	86 (13.4%)	
Black	1002 (71.6%)	479 (74.5%)	
Other	173 (12.%)	78 (12.1%)	
HIV transmission risk category			< 0.0001
Injection Drug Use	233 (16.7%)	88 (13.7%)	
Heterosexual risk	577 (41.5%)	181 (28.2%)	
Transfusion risk/ Unknown/other	582 (41.8%)	373 (58.1%)	
Smoking status			< 0.0001
Never	455 (32.2%)	176 (27.1%)	
Past	421 (29.8%)	159 (24.5%)	
Current	536 (38.0%)	315 (48.5%)	
Cocaine, crack or heroin use			< 0.0001
Never	667 (47.24%)	289 (44.5%)	
Past	662 (46.9%)	283 (43.5%)	
Current	83 (5.9%)	78 (12.0%)	
Marijuana use			0.0003
Never	476 (33.7%)	207 (31.9%)	
Past	690 (48.9%)	281 (43.2%)	
Current	246 (17.4%)	162 (24.9%)	
Recent alcohol use			< 0.0001
None	765 (54.8%)	286 (44.5%)	
Light (< 3 drinks/wk)	475 (34.0%)	220 (34.2%)	
Moderate (3-13 drinks/wk)	57 (4.1%)	36 (5.6%)	

Characteristic	HIV-infected (N=1412)	HIV-uninfected (N=650)	P value*
Heavy (≥14 drinks/wk)	99 (7.1%)	101 (15.7%)	
Comorbidities			
Hepatitis C Virus infection	172 (12.2%)	46 (7.1%)	0.0005
Diabetes Mellitus	265 (18.8%)	131 (20.3%)	0.43
Hypertension	683 (48.4%)	320 (49.2%)	0.72
Renal dysfunction (eGFR <60)	153 (11.0%)	42 (6.5%)	0.002
Depressive symptoms (CESD ≥16)	440 (31.5%)	203 (31.6%)	0.96
Subjective cognitive complaints	162 (11.5%)	81 (12.5%)	0.52
Peripheral neuropathy	291 (20.6%)	91 (14.0%)	0.0003
Obesity (≥30kg/m^2)	650 (47.1%)	373 (58.9%)	< 0.0001
Current use of CNS active medications by category			
Anticonvulsants	188 (13.3%)	58 (8.9%)	0.004
Antidepressants	385 (27.3%)	115 (17.7%)	< 0.0001
Antipsychotics	143 (10.1%)	78 (12.0%)	0.20
Benzodiazepines and other sedatives	174 (12.3%)	80 (12.3%)	0.99
Muscle relaxants	55 (3.9%)	44 (6.8%)	0.005
Categories of CNS active medication used			0.014
0	833 (59.0%)	430 (66.2%)	
1	319 (22.6%)	113 (17.4%)	
2	174 (12.3%)	69 (10.6%)	
≥3	86 (6.1%)	38 (5.9%)	
Reported fear of falling			0.93
Not at all	876 (62.0%)	408 (62.8%)	
A little	296 (21.0%)	131 (20.2%)	
Quite a bit	102 (7.2%)	44 (6.8%)	
Very much	138 (9.8%)	67 (10.3%)	
Number of falls within 6 months			0.75
0	1149 (81.4%)	531 (81.7%)	
1	130 (9.2%)	54 (8.3%)	
≥2	133 (9.4%)	65 (10.0%)	
HIV disease related characteristics			
AIDS defining illness ever	517 (36.6%)	N/A	
Current CD4+ cell count (cells/μl), median (IQR)	589 (385-808)	N/A	
Nadir CD4+ cell count (cells/μl), median (IQR)	274 (146-462)	N/A	
Suppressed HIV RNA viral load (<20c/mL)	907 (65.4%)	N/A	
Current ART use	1240 (87.8%)	N/A	
Efavirenz use		N/A	
Never	764 (54.1%)	N/A	
Current/former	648 (45.9%)	N/A	

Characteristic	HIV-infected (N=1412)	HIV-uninfected (N=650)	P value*
Zidovudine Use		N/A	
Never	691 (48.9%)	N/A	
Current/former	721 (51.1%)	N/A	
Didanosine use		N/A	
Never	1065 (75.4%)	N/A	
Current/former	347 (24.6%)	N/A	
Stavudine use		N/A	
Never	988 (70.0%)	N/A	
Current/former	424 (30.0%)	N/A	

* Compares HIV− to HIV+ with independent samples t-test or Wilcoxon test for continuous variables and with Chi-square test for categorical variables

Table 2

Factors Associated with Falls in the Women's Interagency HIV Study

	No Fall (N=1680)	Single Fall (N=184)	Multiple Falls (N=198)	P value *
HIV status				0.75
HIV-uninfected	531 (31.6%)	54 (29.3%)	65 (32.8%)	
HIV-infected	1149 (68.4%)	130 (70.7%)	133 (67.2%)	
Age (years)				0.0001
<39	346 (20.6%)	32 (17.4%)	22 (11.1%)	
40-49	614 (36.5%)	48 (26.1%)	67 (33.8%)	
50-59	571 (34.0%)	77 (41.8%)	87 (43.9%)	
≥60	149 (8.9%)	27 (14.7%)	22 (11.1%)	
WIHS Site				<0.0001
Bronx / Manhattan	324 (19.3%)	20 (10.9%)	18 (9.1%)	
Brooklyn	299 (17.8%)	12 (6.5%)	17 (8.6%)	
Washington DC	235 (14.0%)	28 (15.2%)	27 (13.6%)	
San Francisco	218 (13.0%)	29 (15.8%)	39 (19.7%)	
Chicago	216 (12.9%)	48 (26.1%)	45 (22.7%)	
Southern sites	388 (23.1%)	47 (25.5%)	52 (26.3%)	
Race				0.55
White	251 (15.1%)	26 (14.3%)	33 (16.9%)	
Black	1208 (72.6%)	129 (70.9%)	144 (73.8%)	
Other	206 (12.4%)	27 (14.8%)	18 (9.2%)	
HIV transmission risk category				0.0001
Injection Drug Use	237 (14.3%)	38 (21.1%)	46 (23.6%)	
Heterosexual risk	607 (36.6%)	72 (40.0%)	79 (40.5%)	
Transfusion risk/Unknown/Other	815 (49.1%)	70 (38.9%)	70 (35.9%)	
Smoking status				0.0009
Never	544 (32.4%)	45 (24.5%)	42 (21.2%)	
Past	476 (28.3%)	49 (26.6%)	55 (27.8%)	
Current	660 (39.3%)	90 (48.9%)	101 (51.0%)	
Cocaine, crack or heroin use				< 0.0001
Never	822 (48.9%)	74 (40.2%)	60 (30.3%)	
Past	743 (44.2%)	97 (52.7%)	105 (53.0%)	
Current	115 (6.8%)	13 (7.1%)	33 (16.7%)	
Marijuana use				<0.0001
Never	598 (35.6%)	47 (25.5%)	38 (19.2%)	
Past	787 (46.8%)	91 (49.5%)	93 (47.0%)	
Current	295 (17.6%)	46 (25.0%)	67 (33.8%)	
Recent alcohol use				0.028

	No Fall (N=1680)	Single Fall (N=184)	Multiple Falls (N=198)	P value*
None	870 (52.3%)	90 (49.5%)	91 (46.9%)	
Light	562 (33.8%)	72 (39.6%)	61 (31.4%)	
Moderate	76 (4.6%)	7 (3.8%)	10 (5.2%)	
Heavy	155 (9.3%)	13 (7.1%)	32 (16.5%)	
Comorbidities				
Hepatitis C Virus infection	167 (9.9%)	26 (14.1%)	25 (12.6%)	0.13
Diabetes Mellitus	310 (18.5%)	37 (20.1%)	49 (24.7%)	0.10
Hypertension	779 (46.4%)	104 (56.5%)	120 (60.6%)	<0.0001
Renal dysfunction (eGFR <60)	149 (9.0%)	21 (11.5%)	25 (12.9%)	0.14
Depressive symptoms (CESD ≥ 16)	450 (27.1%)	85 (46.7%)	108 (55.4%)	<0.0001
Subjective cognitive complaints	142 (8.5%)	36 (19.6%)	65 (32.8%)	< 0.0001
Peripheral neuropathy	257 (15.3%)	48 (26.1%)	77 (38.9%)	<0.0001
Obesity (≥30kg/m^2)	815 (49.6%)	106 (59.2%)	102 (53.4%)	0.039
Current use of CNS active medications by category				
Anticonvulsants	159 (9.5%)	37 (20.1%)	50 (25.3%)	<0.0001
Antidepressants	346 (20.6%)	72 (39.1%)	82 (41.4%)	<0.0001
Antipsychotics	145 (8.6%)	34 (18.5%)	42 (21.2%)	<0.0001
Benzodiazepines/sedatives	179 (10.7%)	37 (20.1%)	38 (19.2%)	<0.0001
Muscle relaxants	63 (3.8%)	12 (6.5%)	24 (12.1%)	< 0.0001
Number of categories of CNS active medication used				<0.0001
0	1114 (66.3%)	78 (42.4%)	71 (35.9%)	
1	327 (19.5%)	49 (26.6%)	56 (28.3%)	
2	168 (10.0%)	35 (19.0%)	40 (20.2%)	
3	57 (3.4%)	15 (8.2%)	24 (12.1%)	
4	12 (0.7%)	7 (3.8%)	7 (3.5%)	
5	2 (0.1%)	0	0	
Reported fear of falling				<0.0001
Not at all	1170 (69.6%)	65 (35.3%)	49 (24.7%)	
A little	307 (18.3%)	65 (35.3%)	55 (27.8%)	
Quite a bit	77 (4.6%)	27 (14.7%)	42 (21.2%)	
Very much	126 (7.5%)	27 (14.7%)	52 (26.3%)	
HIV disease related characteristics (N=1412)				
AIDS defining illness ever	412 (35.9%)	47 (36.2%)	58 (43.6%)	0.21
Current CD4+ count (cells/μl), median (IQR)	585 (389-808)	639 (356-804)	590 (382-824)	0.93
Nadir CD4+ count (cells/μl), median (IQR)	270 (144-456)	295 (154-485)	303 (156-483)	0.44
Suppressed HIV RNA viral load (<20c/mL)	389 (34.5%)	41 (31.5%)	49 (38.3%)	0.52
Current ART use	1016 (88.4%)	115 (88.5%)	109 (82.0%)	0.094
Didanosine use				0.25
Never	858 (74.7%)	100 (76.9%)	107 (80.5%)	

	No Fall (N=1680)	Single Fall (N=184)	Multiple Falls (N=198)	P value*
Former	274 (23.8%)	30 (23.1%)	26 (19.5%)	
Current	17 (1.5%)	0	0	
Stavudine use				
Never	795 (69.2%)	93 (71.5%)	100 (75.2%)	0.60
Former	351 (30.5%)	37 (28.5%)	33 (24.8%)	
Current	3 (0.3%)	0	0	
Zidovudine use				0.17
Never	547 (47.6%)	72 (55.4%)	72 (54.1%)	
Former	534 (46.5%)	54 (41.5%)	57 (42.9%)	
Current	68 (5.9%)	4 (3.1%)	4 (3.0%)	
Efavirenz use				0.76
Never	625 (54.4%)	72 (55.4%)	67 (50.4%)	
Former	263 (22.9%)	28 (21.5%)	37 (27.8%)	
Current	261 (22.7%)	30 (23.1%)	29 (21.8%)	

* Comparison between groups using Chi-Square test for categorical variables and Wilcoxon test for continuous variable

Table 3

Predictors of Any Fall (vs. No Falls) and Multiple (≥2) Falls (vs. ≤1 Fall) in the Women's Interagency HIV Study

	Any Fall Multivariate OR (95% CI)	Multiple Falls Multivariate OR (95% CI)
HIV infection	1.08 (0.82, 1.42)	0.84 (0.60, 1.18)
Age (years)		
<39	Reference	Reference
40-49	1.18 (0.81, 1.74)	1.69 (0.99, 2.86)
50-59	1.71 (1.17, 2.49)**	1.96 (1.16, 3.31)**
≥60	2.26 (1.38, 3.71)*	2.08 (1.05, 4.10)*
Marijuana use		
Never	Reference	Reference
Past	1.55(1.13, 2.14)**	1.73 (1.11, 2.68)**
Current	2.19 (1.53, 3.13)***	2.60 (1.64, 4.13)***
Categories of CNS active medications		
0	Reference	Reference
1	1.59 (1.17, 2.15)**	1.61 (1.08, 2.40)*
2	1.98 (1.38, 2.84)***	1.81 (1.14, 2.85)**
≥3	2.98 (1.90, 4.68)***	2.68 (1.57, 4.57)***
Depressive symptoms (CESD ≥ 16)	1.57 (1.21, 2.05)***	1.56 (1.10, 2.19)**
Subjective cognitive complaints	2.19 (1.56, 3.08)***	2.45 (1.66, 3.62)***
Peripheral neuropathy	1.59 (1.19, 2.13)***	1.89 (1.33, 2.70)***
Obesity (≥30kg/m^2)	1.39 (1.08, 1.80)*	-

Comparison group for analyses of any fall represents participants reporting no fall; comparison group for analyses of multiple (≥) falls represents participants reporting no fall or single fall. All models are adjusted for WIHS site.

* p<= 0.05

** p<= 0.01

*** p<= 0.001