POLYPHARMACY IS ASSOCIATED WITH FALLS IN WOMEN WITH AND WITHOUT HIV

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Abstract

Background: Aging in people with HIV is associated with increased risk of developing synergistic conditions such as neurocognitive impairment, polypharmacy, and falls. We assessed associations between polypharmacy (use of 5 or more non-ART medications), use of neurocognitive-adverse effects (NCAE) medications, and odds of falls in women with HIV (WWH) and without HIV (HIV−).

Methods: Self-reported falls and medication use data were contributed semiannually by 1872 (1315 WWH, 557 HIV−) Women's Interagency HIV Study (WIHS) participants between 2014 and 2016. Polypharmacy and NCAE medication use were evaluated separately and jointly in multivariable models to assess their independent contributions to single and multiple falls risk.

Results: The proportion of women who reported any fall was similar by HIV status (19%). WWH reported both greater polypharmacy (51 % vs 41%; p<0.001) and NCAE medication use (44% vs 37%; p=0.01) than HIV− women. Polypharmacy conferred elevated odds of single fall (adjusted odds ratio (aOR) 1.67, 95% CI: 1.36–2.06; p<0.001) and multiple falls (aOR 2.31, 95% CI: 1.83–2.93; p<0.001); results for NCAE medications and falls were similar. Both polypharmacy and number of NCAE medications remained strongly and independently associated with falls in multivariable models adjusted for HIV serostatus, study site, sociodemographics, clinical characteristics, and substance use.

Conclusions: Polypharmacy and NCAE medication use was greater among WWH compared to HIV− and both were independently and incrementally related to falls. De-prescribing and avoidance of medications with NCAEs may be an important consideration for reducing fall risk among WWH and sociodemographically similar women without HIV.

Keywords

INTRODUCTION

Widespread use of effective antiretroviral therapy (ART) in people with HIV (PWH) in the United States (U.S.) has led to dramatic improvements in survival. Life expectancy of PWH on ART is now similar to that of the general population[1–4]. Currently, over half of PWH in the U.S. are over 50 years of age[5]. Among PWH, aging is accompanied by an increased risk of developing multiple comorbidities[6,7], as well as medications to treat those conditions. Indeed, compared to persons without HIV, older PWH may face a disproportionate burden of age-associated conditions[6,7] including falls[8–10], and risk factors for falls such as neurocognitive impairment (NCI)[11–14]. In the general population, older women are at greater risk for falls compared to older men, although reasons for these differences remain unclear[15–17]. We previously reported similar prevalence and incidence of falls between women with and without HIV in the Women's Interagency HIV Study (WIHS), and identified several factors associated with increased risk of falls, including use of multiple central nervous system (CNS) active medications[18,19]. Overall, frequency of falls occurs decades earlier for PWH; specifically, rates for falls among middle-aged PWH (45–65 years old) are similar to that of adults in the general population aged 65 years and older[19–23], and women with HIV appear to be at greater risk for falls than men with HIV despite accounting for other falls-related risk factors[22].

Polypharmacy, often defined as use of five or more medications (other than ART), is prevalent among PWH, with estimates ranging between 37–44% in previous studies[24,25]. Polypharmacy often occurs at younger ages in PWH[26,27]. Older PWH may have increased vulnerability to medication side effects than uninfected persons [28–30], and polypharmacy has been associated with an increased risk for falls among older PWH [20,22,23]. Associations between polypharmacy and risk of falls are not well studied among PWH, or among older women with HIV,HIV, despite their increased risk for both polypharmacy and associated adverse effects. The objective of our study was to evaluate the risk of falls in women with HIV compared with women without HIV who have similar demographics and comorbidities.

In addition to polypharmacy itself, certain medications including anticholinergics[31–34], opioids[35], anxiolytics[36], and anticonvulsants may confer greater risk for falls because of their neurocognitive adverse neurocognitive effects (NCAE)[37]. Indeed, we have previously shown that some specific medications are associated with increased falls among middle-aged and older PWH[22]. Many NCAE medications are frequently prescribed to PWH[29,38], who are more also likely to have NCI than their seronegative counterparts[39,40]. NCAE medications may therefore have an even greater effect on falls risk among older PWH who are already at high risk for falls[39,40]. We hypothesized that polypharmacy and specific classes of medications, particularly NCAE, would confer additional fall risk in women with HIV (WWH) and women without HIV.

METHODS

Study Population

The Women's Interagency HIV Study (WIHS), a prospective multicenter cohort, enrolled women with and without HIV infection initially at six U.S. sites (Bronx/Manhattan

NY, Brooklyn NY, Chicago IL, Washington DC, San Francisco CA, and Los Angeles, CA) in 4 waves: 1994–95, 2001–02, and 2011–12. In 2013, the WIHS closed its Los Angeles site and added 4 southern U.S. sites: Atlanta, GA; Chapel Hill, NC; Miami, FL; and Birmingham, AL/Jackson, MS. WIHS methods and cohort characteristics have been described previously[41,42]. WIHS[43] participants completed face-to-face interviews and physical examinations and provided biological specimens at semiannual visits. The institutional review boards of all participating sites approved the WIHS study protocol, and all participants provided written informed consent.

Falls Ascertainment

From 2014 through 2016, 1,872 (1,315 WWH and 557 HIV– women) contributed 4,911 and 2,063 total person-visits respectively) including semiannual falls questionnaires in which they reported the number of falls they had sustained in the prior 6 months as either 0, 1, or 2+. A 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, excluding falls resulting from a major medical event (for example, a stroke or seizure) or an overwhelming external hazard (for example, hit by a truck or pushed)"[19]. Participants reporting any fall were asked if they sought medical attention for an injury resulting from any of these falls. All visits (up to four per person) with available falls data were included in repeated measures analyses. The first visit where a participant answered the falls questionnaire was defined as the index visit.

Medication Assessments

At each WIHS visit, participants reported ART and non-ART medications taken currently and since the last visit (~6 months). Total medication count included herbal drugs, topical and ophthalmic medications, over-the-counter remedies, as well as short courses of drugs. If a medication contained two or more pharmacologically active agents, each substance was counted individually in the analysis. Supplements that have multiple ingredients were counted as one. Herbals were also counted as one regardless of the mixture. To assess polypharmacy, the total number of medications excluding ART at each visit was quantified. Polypharmacy was defined as use of 5 or more non-ART medications taken since participants' last visit, with 5–9 medications defining moderate polypharmacy and 10 or more medications indicating high polypharmacy[44]. The total number of medications with known NCAE properties[45], were summed and categorized as 0, 1, or 2+. These medications included opioids, anticonvulsants, anticholinergics, anxiolytics, antihistamines, gastrointestinal agents (H2 blockers, antiemetics, antidiarrheals), beta-blockers, antidepressants, antipsychotics, and muscle relaxants.

Statistical Analyses

The following variables previously found to be related to falls risk in WIHS[19] were examined in relation to our predictor and outcome measures; participant **sociodemographics**: age at visit (roughly quartiles   43, 44–50, 51–56,   57 years), race/ethnicity (White including Hispanic, Black including Hispanic, Other), annual income $12K, and high school education or greater; **clinical characteristics**: peripheral

neuropathy symptoms, obesity (BMI 30 kg/m²), depressive symptomatology by Center for Epidemiologic Studies Depression Scale (CES-D) 16[46], diabetes mellitus as previously operationalized in WIHS[47], renal dysfunction (estimated glomerular filtration rate (eGFR) 60 ml/min using the Modification of Diet in Renal Disease calculation)[48], hypertension (self-reported hypertension with systolic blood pressure 140 mmHg, diastolic blood pressure 90 mmHg, and/or current use of an antihypertensive medication)[49], hepatitis C virus (HCV) infection (HCV antibody positive with detectable RNA), self-reported cognitive complaints (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 2 weeks, or self-report of confusion, getting lost in a familiar place or inability to perform routine mental tasks)[23]; **substance use behaviors** classified as (current, former, never): tobacco use, marijuana, crack/cocaine/heroin; recent alcohol use classified as none, light (<3 drinks/wk), moderate (3–13 drinks/wk), and heavy (14 drinks/wk); and **HIV disease characteristics**: prior AIDS defining illness, protease inhibitor (PI) use since last visit, and integrase strand transfer inhibitor (INSTI) use since last visit. These variables were all time-updated in the statistical analyses. Prior analyses in this cohort did not find associations of falls in WWH with nadir CD4+ count, current CD4+ count, current $\log_{10}$ HIV RNA level, current suppressed (<80 copies/mL) HIV RNA, current/prior AIDS-defining illness (ADI), or other ART use with falls[19]. These variables were therefore not included in the present study.

Chi-square tests were used to compare participant characteristics by number of falls (0, 1, 2+) reported during 6 months prior to index visit and by HIV serostatus. Logistic regression models applied to all visits combined, separately compared single fall (i.e., 1 vs. 0), multiple falls (i.e., 2+ vs. 0) and injurious falls in the prior 6 months to no falls. These models accounted for HIV status and WIHS site which were part of the sampling frame but are otherwise unadjusted. Separate binary logistic regression models comparing 1 vs. 0 falls and 2+ vs. 0 falls were fit here and elsewhere. Our primary exposures of interest were the degree of polypharmacy (0–4, 5–9, or 10+ medications) and total number of NCAE medications (0, 1, or 2+). Multivariable models with adjusted odds ratios (aOR) were created to evaluate polypharmacy and NCAE medications separately, on risk of single fall, multiple falls, and injurious falls. These models were sequentially adjusted by successively including covariates as follows: **model A** adjusted for HIV serostatus and WIHS clinic site, **model B** additionally adjusted for participant sociodemographics, **model C** additionally adjusted for clinical characteristics, **model D** additionally adjusted for substance use behaviors, **model E** additionally adjusted for both total polypharmacy and NCAE medication use in order to fix potential confounding from each other (Tables 3 and 4 for all participants). Among WWH only, model E additionally adjusted for HIV disease-related characteristics (Supplementary Material, Tables S1 and S2) and **model F** (Tables S1 and S2) was also fit with both total polypharmacy and NCAE medication use to adjust for potential confounding from each other. All repeated person visits for each participant were used in logistic regression analyses incorporating generalized estimating equations with study subject as the cluster, a logit link and independence working correlation structure to obtain cross sectional regression parameter estimates[50,51]. Analysis was done using SAS 9.4 (Cary, NC). Statistical significance was p 0.05.

RESULTS

Participant Characteristics

At the index visit, WWH were older (mean age 49 vs 47 years, p<0.001) and more likely to have HCV-coinfection, renal dysfunction, and report symptoms of peripheral neuropathy than HIV− women (Table 1). HIV− women were more likely than WWH to be obese and to report current tobacco use, recent marijuana, heroin, cocaine, or crack use, as well as alcohol consumption. Among WWH at the index visit, median CD4+ T cell count was 580 cells/µl; 37% had prior AIDS-defining illness, 90% reported current ART, and 63% had suppressed HIV RNA viral load (<20 copies/mL).

The proportion of women who reported any fall in the prior 6 months was similar for WWH and HIV− women (19% in both groups, p=0.99). A single fall was reported by 9.0% of WWH and 9.2% of HIV− women; recurrent falls were reported by 9.7% of WWH vs 9.5% of HIV− women (overall p=0.98), while injurious falls were reported by 6.5% of WWH and 7.2% of HIV− women (p=0.06). Overall, WWH reported significantly greater polypharmacy (51% of WWH compared to 41% of HIV− women, p<0.001) and use of any NCAE medication compared to HIV− women (44% of WWH vs 37% of HIV− women, p=0.01). The higher use of NCAE medications in WWH was mainly driven by a higher proportion of WWH reporting use of antidepressants (Table 2).

Polypharmacy as a Predictor of Falls

In analyses adjusting for HIV-serostatus and study site only, compared to those without polypharmacy (0–4 non-ART medications), women with moderate polypharmacy (5–9 medications) had significantly higher odds of single fall (aOR 1.67, 95% CI: 1.36–2.06; p<0.001), multiple falls (aOR 2.31, 95% CI: 1.83– 2.93; p<0.001) and injurious falls (aOR 2.26, 95% CI: 1.74– 2.92; p<0.001) (Table 3, **model A**). Severe polypharmacy (10 medications) further increased the odds of both single fall (aOR 2.74, 95% CI:2.18– 3.44, p< 0.001), multiple falls (aOR 4.83, 95% CI:3.69–6.33, p< 0.001) and injurious falls (aOR 4.14, 95% CI: 3.09– 5.55; p<0.001) (Table 3, **model A**). These results were attenuated after adjusting for demographics, clinical characteristics, and substance use behaviors; however, they remained statistically significant in fully adjusted models; those with moderate polypharmacy were associated with greater odds of a single fall (aOR 1.52, 95% CI: 1.22–1.90; p<0.001), multiple falls (aOR 1.71, 95% CI: 1.34– 2.19; p<0.001) and falls with injury (aOR 1.85, 95% CI: 1.39– 2.45; p<0.001). Severe polypharmacy was associated with even higher odds of single fall (aOR 2.08; 95% CI: 1.60–2.69; p<0.001), multiple falls (aOR 2.69; 95% CI: 2.00– 3.62; p<0.001) and falls with injury (aOR 2.43, 95% CI: 1.74– 3.37; p<0.001) (Table 3, **model D**). Similar results were observed in models restricted to WWH, in whom use of multiple non-ARV medications were significantly associated with greater odds of both single and multiple falls in fully adjusted models ().

Total NCAE Medication Burden as a Predictor of Falls

In separate analyses adjusting for HIV-serostatus and study site only, women who used one NCAE medication had significantly higher odds of having a single fall (aOR 1.70, 95% CI: 1.36–2.11; p<0.001), multiple falls (aOR 2.13, 95% CI: 1.64– 2.77; p<0.001) and injurious

falls (aOR 1.70, 95% CI: 1.28– 2.26; p<0.001); use of two or more NCAE medications further increased the odds of single fall (aOR 2.25, 95%CI: 1.80–2.81; p<0.001), multiple falls (OR 4.38, 95% CI: 3.41– 5.62; p<0.001) and injurious falls (aOR 2.96, 95% CI: 2.26– 3.88; p<0.001) (Table 4, **model A**). In fully adjusted models these associations were attenuated, but use of a single NCAE medication remained associated with greater odds of both a single fall (aOR 1.46, 95%CI: 1.16–1.83; p=0.0013) and multiple falls (aOR 1.60, 95% CI: 1.23– 2.10; p<0.001) while association with injurious falls was no longer significant (aOR 1.29, 95% CI: 0.95– 1.75; p=0.11) (Table 4, **model D**). Use of multiple NCAEs remained associated with increases in the odds of single fall (aOR 1.66, 95%CI: 1.30–2.11; p<0.001), multiple falls (aOR 2.37, 95% CI: 1.81– 3.11; p<0.001) and falls with injury (aOR 1.79, 95% CI: 1.32– 2.42; p<0.001) (Table 4, **model D**). Similar findings were observed among WWH, in whom use of multiple NCAE medications were significantly associated with greater odds of both single and multiple falls in fully adjusted models (Supplemental Table 2).

Polypharmacy and NCAE Medications Together as Predictors of Falls

Polypharmacy remained significantly associated with single, multiple, and injurious falls, even after adjustment for NCAE medications, demographics, clinical characteristics, and substance use behaviors. In these fully adjusted models, moderate polypharmacy was associated with a single fall (aOR 1.39, 95%CI: 1.10–1.76; p=0.0053), multiple falls (aOR 1.43, 95% CI: 1.10–1.86; p=0.007) and falls with injury (aOR 1.72, 95% CI: 1.27– 2.31; p=0.0004) (Table 3, **model E**). Severe polypharmacy further increased odds of single fall (aOR 1.81; 95%CI: 1.36–2.41; p<0.001), multiple falls (aOR 1.94; 95% CI: 1.40–2.70; p<0.001) and falls with injury (aOR 2.09, 95% CI: 1.45– 3.01; p<0.0001) (Table 3, **model E**). Similarly, use of multiple NCAE medications remained associated with odds of both single and multiple falls, after adjusting for polypharmacy, demographics, clinical characteristics, and substance use behaviors, but associations with injurious falls was no longer significant. Use of one NCAE medication was associated with single fall (aOR 1.29, 95%CI: 1.02–1.63; p=0.03), and multiple falls (aOR 1.41, 95% CI: 1.06–1.88; p=0.02). Use of two or more NCAEs was non-significantly associated with single fall (aOR 1.29, 95%CI: 0.99–1.68; p=0.06) and significantly associated with multiple falls (aOR 1.79, 95% CI: 1.33– 2.41; p<0.001) (Table 4, **model E**). Similar findings were observed among WWH (Supplemental Table 2).

DISCUSSION

This is the first study to evaluate the effect of both polypharmacy and NCAE-specific medications on falls risk among women with and without HIV, after accounting for other falls risk covariates. Polypharmacy was a strong, independent predictor for both single/ multiple falls and falls with injury, with higher polypharmacy associated with higher odds of self-reported falls. Moreover, use of NCAE medications conferred higher odds of single or multiple falls among WWH and HIV– women, independent of the total number of medications used (i.e., polypharmacy). Although WWH in our cohort were older, more likely to report symptoms of peripheral neuropathy, had greater NCAE medication use, and more polypharmacy, they did not report greater occurrence of single, recurrent, or

injurious falls than did HIV– women. This could reflect a greater access to medical care and possibly falls prevention measures compared to HIV– women or residual confounding from substance use and alcohol consumption (more frequent among HIV– women) that had further detrimental effects on risk of falls.

Among older persons without HIV, polypharmacy has been associated with numerous adverse events including worsened physical and psychological health and increased risk of falls[52–56]. More recently, among HIV+ and seronegative individuals in the US Veterans Affairs Healthcare System, polypharmacy has been associated with hospitalization and mortality independently of HIV status[57], as well as with additional geriatric syndromes including frailty[58] and fractures[28]. Because PWH have an increased likelihood of experiencing polypharmacy [24,44,59] and drug-drug interactions[60], there is a need for dedicated efforts aimed at rational prescribing and consideration of de-prescribing when medically appropriate, particularly with increasing age.

Beyond polypharmacy, we hypothesized that specific classes of medications, particularly NCAE, would have additional falls risk. Indeed, our findings highlight the contribution of NCAE medications on falls risk among WWH and HIV– women, even after accounting for polypharmacy. Similar results for NCAE medications (albeit not adjusted for polypharmacy) were observed in a cohort of PWH, with a significant association between recurrent falls and beta-blockers, antidepressants, antipsychotics, and sedative/hypnotics [22]. Similarly, in the MACS cohort, antidepressants were a significant predictor of recurrent falls in men with and without HIV[20]. NCAE medications are often prescribed to PWH, presumably to treat HIV and non-HIV related comorbidities. However, these medications can be problematic in PWH if impairment in cognition and physical functioning is associated in these individuals[61–63]. NCI is shown to increase susceptibility to falls and subsequent adverse outcomes in older PWH, such as fracture, hospitalization, disability, and mortality[64]. These observations should sensitize physicians to evaluate the benefits versus the potential harms of specific drugs in fragile populations and motivate efforts towards a targeted deprescribing of NCAE medications, particularly when other falls risk factors are not modifiable.

Our study has several strengths. The WIHS is representative of the U.S. HIV epidemic among women, which includes women with and without HIV with similar demographic and behavioral characteristics to WWH, allowing meaningful comparisons by HIV serostatus. WIHS is a phenotypically well-characterized cohort including demographics, substance use, and medical history, as well as detailed characterization of medications taken. The richness of the data collected enables us to prospectively evaluate self-reported falls and to analyze associations with number and type of medications taken.

This study also has some limitations. Falls ascertainment was based on participants' self-report of events in the prior 6 months, which may underestimate or on the contrary over-report frequency of falls, particularly in the most vulnerable participants with cognitive impairment who may not be able to accurately recount falls prevalence. Medication usage was also based on participant self-report, which likely underestimates the number of NCAE medications taken, e.g., if over the counter and as needed drugs are not systematically reported, or if participants are unable to recall all their medications since the last visit.

Data on duration or dose was not collected, thus we were unable to evaluate potential pharmacologic drug-drug interactions that may accentuate adverse neurocognitive effects of medications. Lastly because our study includes only women, findings may not be generalizable to men.

In conclusion, we observed that both total polypharmacy and greater number of NCAE medications were independent predictors of increased odds of falls among middle-aged women with and without HIV. Additional studies are needed to determine the extent to which medication simplification, targeted de-prescribing, and avoidance of medications with overlapping neurocognitive toxicities may reduce falls risk among aging WWH and HIV– women.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Conflicts of Interest and Source of Funding:

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Table 1.

Women's Interagency HIV Study Participant Characteristics at Index Visit

Characteristic, N (%)	HIV+ (N=1,315)	HIV− (N=557)	P Value
Number of falls since last visit			0.98
No fall	1069 (81.3)	453 (81.3)	
One fall	118 (9.0)	51 (9.2)	
More than one fall	128 (9.7)	53 (9.5)	
Injurious falls	86 (6.5)	40 (7.2)	0.6
Age, years, median (IQR)	49 (43,55)	47 (40,54)	<0.001
Education level high school or greater	872 (66.4)	382 (68.7)	0.32
Annual Income $12,000/yr	624 (49.4)	285 (53.8)	0.09
WIHS Site			0.06
Bronx/Manhattan, NY	234 (17.8)	126 (22.6)	
Brooklyn, NY	239 (18.2)	95 (17.1)	
Washington DC	215 (16.3)	93 (16.7)	
San Francisco, CA	232 (17.6)	106 (19.0)	
Chicago, IL	215 (16.3)	82 (14.7)	
Southern sites	180 (13.7)	55 (9.9)	
Race			0.22
White	226 (17.2)	78 (14.0)	
Black	917 (69.7)	400 (71.8)	
Other	172 (13.1)	79 (14.2)	
Smoking status			<0.001
Never	395 (30.7)	127 (23.3)	
Current	480 (37.3)	256 (47.0)	
Former	413 (32.1)	162 (29.7)	
Crack, Cocaine, or Heroin use			<0.001
Never	562 (42.8)	210 (37.7)	
Current	77 (5.9)	60 (10.8)	
Former	674 (51.3)	287 (51.5)	
Marijuana use			<0.001
Never	383 (29.1)	121 (21.7)	
Current	230 (17.5)	151 (27.1)	
Former	701 (53.3)	285 (51.2)	
Alcohol consumption [*]			<0.001
Abstainer/None	717 (55.7)	241 (44.2)	
Light (< 3 drinks/week)	427 (33.2)	198 (36.3)	
Moderate (3–13 drinks/week)	50 (3.9)	28 (5.1)	
Heavy (14 drinks/week)	93 (7.2)	78 (14.3)	

Characteristic, N (%)	HIV+ (N=1,315)	HIV– (N=557)	P Value
Hepatitis C virus seropositive	246 (18.8)	66 (11.9)	<0.001
Diabetes Mellitus	294 (22.4)	135 (24.2)	0.38
Hypertension	619 (47.1)	258 (46.3)	0.77
Renal disease [†]	137 (10.8)	31 (5.8)	<0.001
Depressive symptoms [††]	363 (28.6)	147 (27.3)	0.59
Peripheral neuropathy	262 (19.9)	75 (13.5)	<0.001
Obesity [‡]	569 (45.3)	296 (55.7)	<0.001
Cognitive complaints	152 (11.6)	57 (10.2)	0.41
ART use at index visit	1182 (89.9)	N/A	N/A
Undetectable HIV RNA viral load [**]	783 (62.5)	N/A	N/A
Nadir CD4+ cell count (cells/µl), median (IQR)	257(135,428)	N/A	N/A
CD4+ cell count at index visit (cells/µl), median (IQR)	580 (372,776)	N/A	N/A
Prior AIDS defining illness ever	480 (36.5)	N/A	N/A

[*]
Alcohol use: light (< 3 drinks/wk), moderate (3–13 drinks/wk), (14 drinks/wk)

[†]Estimated Glomerular Filtration Rate <60 mL/min by MDRD (Modification of Diet in Renal Disease) equation defined as GFR (mL/min/1.73 m2) = $175 \times (Scr)-1.154 \times (Age)-0.203 \times (0.742$ if female$) \times (1.212$ if African American$)$

[‡]Body Mass Index 30kg/m^2

[††]Center for Epidemiologic Studies Depression Scale (CES-D) 16

[**]
<20copies/mL

Table 2.

Participant Medication Use by HIV Serostatus

Reported Number of Medications Used, N (%)	HIV+ (N=1,315)	HIV− (N=557)	P-Value
Total non-antiretroviral medications			0.0002
0–4	648 (49.3)	329 (59.1)	
5–9	433 (32.9)	161 (28.9)	
10+	234 (17.8)	(12.0)	
Neurocognitive adverse effect (NCAE) medications			0.01
0	732 (55.7)	349 (62.7)	
1	288 (21.9)	95 (17.1)	
2	295 (22.4)	113 (20.3)	
NCAE medication type			
Anxiolytics	145 (11.0)	57 (10.2)	0.61
Anticholinergics	350 (26.6)	133 (23.8)	0.95
Anticonvulsants	59 (4.5)	26 (4.7)	0.86
Antipsychotics	92 (7.0)	45 (8.1)	0.41
Amphetamines	7 (0.5)	2 (0.4)	0.62
Opioids	160 (12.2)	57 (10.2)	0.23
Beta blockers	40 (3.0)	16 (2.9)	0.84
Gastrointestinal agents	34 (2.6)	12 (2.2)	0.58
Antihistamines	115 (8.7)	45 (8.1)	0.64
Muscle relaxants	53 (4.0)	31 (5.6)	0.14
Antidepressants	283 (21.5)	72 (12.9)	<0.001
Anti-COPD [*]	33 (2.5)	18 (3.2)	0.38

[*] Chronic Obstructive Pulmonary Disease

Table 3.

Associations Between Polypharmacy and Risk of Falls Among Women with and Without HIV

Number of non-antiretroviral medications (ref: 0–4)	Single Fall Vs. No Fall aOR (95%CI)	Multiple Falls Vs. No Fall aOR (95%CI)	Falls with Injury aOR (95% CI)
Model A: adjusted for HIV status and study site			
5–9	1.67 (1.36, 2.06) p <0.001	2.31 (1.83, 2.93) p <0.001	2.26 (1.74,2.92) p=<0.0001
10+	2.74 (2.18, 3.44) p <0.001	4.83 (3.69, 6.33) p <0.001	4.14 (3.09,5.55) p=<0.0001
Model B: adjusted for Model A + demographics [*]			
5–9	1.57 (1.27, 1.95) p <0.001	2.13 (1.68, 2.70) p <0.001	2.08 (1.60,2.72) p=<0.0001
10+	2.34 (1.83, 2.98) p <0.001	4.31 (3.24, 5.72) p <0.001	3.54 (2.60,4.83) p=<0.0001
Model C: adjusted for Model B + comorbidities [†]			
5–9	1.53 (1.23, 1.92) p <0.001	1.80 (1.41, 2.30) p <0.001	1.89 (1.43,2.50) p=<0.0001
10+	2.09 (1.60, 2.71) p <0.001	2.78 (2.06, 3.76) p <0.001	2.56 (1.84,3.55) p=<0.0001
Model D: adjusted for Model C + substance use [‡]			
5–9	1.52 (1.22, 1.90) p <0.001	1.71 (1.34, 2.19) p <0.001	1.85 (1.39,2.45) p=<0.0001
10+	2.08 (1.60, 2.69) p < 0.001	2.69 (2.00, 3.62) p <0.001	2.43 (1.74,3.37) p=<0.0001
Model E: adjusted for Model D + NCAE medication use			
5–9	1.39 (1.10,1.76) p=0.0053	1.43 (1.10,1.86) p=0.0070	1.72 (1.27,2.31) p=0.0004
10+	1.81 (1.36, 2.41) p <0.001	1.94 (1.40,2.70) p <0.001	2.09 (1.45,3.01) p <0.0001

[*] 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); depression (CESD 16); diabetes mellitus; renal dysfunction (eGFR <60 ml/min); hypertension; HCV infection; and cognitive complaints.

[‡] Substance Use: tobacco use; cocaine, crack, and/or heroin use; marijuana use; and alcohol use (heavy, moderate, light, or none)

Table 4.

Associations Between NCAE Medication Use and Risk of Falls Among Women with and Without HIV

Number of NCAE medications (ref: 0)	Single Fall Vs. No Fall aOR (95% CI)	Multiple Falls Vs. No Fall aOR (95% CI)	Falls with Injury aOR (95% CI)
Model A: adjusted for HIV status and study site			
1	1.70 (1.36, 2.11) p<0.001	2.13 (1.64, 2.77) p<0.001	1.70 (1.28, 2.26) p=0.0003
2+	2.25 (1.80, 2.81) p<0.001	4.38 (3.41, 5.62) p<0.001	2.96 (2.26, 3.88) p=<0.0001
Model B: adjusted for Model A + demographics [*]			
1	1.61 (1.29, 2.02) p<0.001	1.97 (1.51, 2.58) p<0.001	1.54 (1.15, 2.07) p=0.0035
2+	2.04 (1.62, 2.56) p<0.001	3.82 (2.94, 4.96) p<0.001	2.53 (1.90, 3.36) p=<0.0001
Model C: adjusted for Model B + comorbidities [†]			
1	1.49 (1.19, 1.88) p<0.001	1.65 (1.26, 2.17) p<0.001	1.31 (0.97, 1.77) p=0.0823
2+	1.73 (1.36, 2.19) p<0.001	2.52 (1.92, 3.31) p<0.001	1.84 (1.37, 2.48) p=<0.0001
Model D: adjusted for Model C + substance use [‡]			
1	1.46 (1.16, 1.83) p=0.0013	1.60 (1.23, 2.10) p<0.001	1.29 (0.95, 1.75) p=0.11
2+	1.66 (1.30, 2.11) p<0.001	2.37 (1.81, 3.11) p<0.001	1.79 (1.32, 2.42) p=0.0002
Model E: adjusted for Model D + polypharmacy			
1	1.29 (1.02, 1.63) p=0.03	1.41 (1.06, 1.88) p=0.02	1.08 (0.78, 1.49) p=0.64
2+	1.29 (0.99, 1.68) p=0.06	1.79 (1.33, 2.41) p<0.001	1.31 (0.94, 1.82) p=0.11

[*] 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; diabetes mellitus; renal dysfunction (eGFR <60 ml/min); hypertension; HCV infection; and cognitive complaints.

[‡] Substance Use: tobacco use; cocaine, crack, and/or heroin use; marijuana use; and alcohol use (heavy, moderate, light, or none)