AIDS Research and Human Retroviruses

DOI: 10.1089/AID.2021.0162

Title: Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV Infection, Aging, and Immune Function Long-Term Observational Study (HAILO)

Running Head: Regional Variation and Falls in People with HIV

Authors: Mona Abdo[1], Xingye Wu[2], Anjali Sharma[3], Katherine K. Tassiopoulos[4], Todd T. Brown[5], Susan L. Koletar[6], Michael T. Yin[7], Kristine M. Erlandson[8], for the ACTG A5322 Study Team.

[1]Department of Epidemiology, Colorado School of Public Health, Aurora, CO, USA.

[2]Center for Biostatistics in AIDS Research, Harvard T.H. Chan School of Public Health, Boston, MA, USA.

[3]Department of Medicine, Albert Einstein College of Medicine, Bronx, NY, USA.

[4]Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston MA, USA.

[5]Division of Endocrinology, Diabetes, & Metabolism, Johns Hopkins University, Baltimore, MD, USA.

[6]Department of Medicine, Division of Infectious Diseases, Ohio State University, Columbus, Ohio, USA.

[7]Division of Infectious Diseases, Vagelos College of Physicians and Surgeons, Columbia University Irving Medical Center, New York, NY, USA.

[8]Division of Infectious Diseases, School of Medicine, University of Colorado-Anschutz Medical Center, Aurora, CO, USA.

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

Corresponding Author:

Kristine Erlandson, MD

12700 E. 19th Avenue, Mail Stop B168

Aurora, CO 80045

Kristine.Erlandson@cuanschutz.edu Phone: 303-724-4941; Fax: 303-724-4926

Word Count: Abstract: 269 Manuscript: 2524

AIDS Research and Human Retroviruses

Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

Abstract:

Background: Geographic location was a strong predictor of falls among women with and without HIV in the Women's Interagency HIV Study. We examined regional variation in falls in a more geographically diverse cohort of older people with HIV (PWH), and explored whether physical activity, sex, or BMI modified these associations.

Setting: PWH enrolled in A5322 HAILO (HIV Infection, Aging and Immune Function Long-Term Observational Study).

Methods: Participants who reported falls in the 6 months prior to each semiannual visit, and had ≥1 consecutive pair of falls assessments were included. We examined associations between geographic region [Northeast, Midwest, South and West] with recurrent falls (≥2) over each 12-month period using repeated measures multinomial logistic regression models, and assessed effect modification by adding an interaction term between geographic region and each potential effect modifier.

Results: A total of 788 men and 192 women with median age at study entry of 51 years contributed up to 240 weeks of data. U.S. region included Northeast (22%), Midwest (29%), South (20%), and West (28%). In multivariable analyses, compared to Western region, greater risk was seen among Midwestern region (OR=2.35[95% CI=1.29,4.28]) and Southern region (2.09[1.09,4.01]). Among those with higher physical activity, Midwestern region had higher odds of recurrent falls than Western region. Among obese individuals, Southern region had higher odds of recurrent falls than Western region. Sex did not modify the association between region and recurrent falls.

Conclusion: Among older PWH, fall risk varied by geographic region. Associations between geographic region and recurrent falls appeared to be modified by physical activity and obesity. This may help identify subgroups of older PWH for targeted falls screening/interventions.

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

Introduction

Antiretroviral therapy (ART) has been effective in extending survival and narrowing the gap in life expectancy between people with HIV (PWH) and HIV-uninfected individuals [1-3]. With increasing age, however, many PWH experience an increased burden of some comorbidities and impairments including difficulties with balance, slow gait, weakness, and cognitive impairment [4-6]. The increased burden of comorbidities, combined with physical and cognitive impairments has contributed to a higher prevalence of falls in PWH compared to demographically similar HIV-uninfected adults [7-9].

Falls are a major cause of mortality and morbidity globally, with fall-related injuries increasing with age. Every year in the U.S., one in four older adults (65+) has a fall, resulting in over 800,000 fall-related hospitalizations and more than 27,000 fall-related deaths [10]. Risk factors for falls among older adults include age, medications and comorbidities, gait and balance disorders, functional impairment, and cognitive impairment [11,12]. Among PWH, HIV-related risk factors including ART, toxicity of prior ART, and HIV-1 replication may further contribute [13,14]. Two separate studies among PWH have also suggested that geographic location might be a risk factor for falls [13,15]. In the Women's Interagency HIV Study (WIHS), a study of risk factors for falls in women with and without HIV, significant differences in fall occurrences were seen between study sites, with a higher prevalence of falls in the San Francisco site compared to the New York City site [15]. Investigators hypothesized that the differences observed might have been due to reasons such as mode of transportation, weather conditions, seasonality, or physical activity [15]. Similarly, in the Multicenter AIDS Cohort Study (MACS), the odds of a fall were twice as high in the Chicago and Pittsburgh sites compared to the Baltimore site, and lowest in the Los Angeles site [13].

These geographic differences may highlight important structural or environmental factors to consider in fall prevention strategies. However, the MACS and WIHS studies were limited to one city within each region and did not include participants from Southern states. To further investigate geographic differences in fall risk among both men and women with HIV from a variety of geographic locations, we investigated the geographic distribution of falls for participants across the 32 sites of the AIDS Clinical Trials Group

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

(ACTG) study A5322, also known as HAILO (HIV Infection, Aging and Immune Function Long-term Observational Study). We sought to identify factors that could influence the association between geographic region and falls with the goal of identifying subgroups of older PWH at highest risk for falls.

Methods

Participants

HAILO is a longitudinal study of long-term health outcomes among older (≥40 years at enrollment) men and women with HIV. All participants received their initial ART regimen through an ACTG clinical trial and were previously followed long-term after their trial participation in another ACTG observational study, A5001 [16]. HAILO participants were enrolled at one of 32 clinical sites between 2013 and 2014. Data collected at each semiannual visit includes medical chart abstraction, targeted physical examination, fasting laboratory tests, and falls assessment, while frailty and neurocognitive function are assessed annually. All HAILO participants with at least one pair of consecutive falls assessments from study entry though study week 240 (Year 5) were included in this analysis.

Outcome

Falls are self-reported at every visit, starting at week 24, using interview-administered questionnaires. A fall is defined as an unexpected event in which the individual lost their balance and landed on the floor, ground, or a lower level, or hit an object. Participants are asked about the frequency of falls in the past 6 months and whether a fall necessitated medical attention or resulted in a fracture. In this analysis, the number of falls in the pair of consecutive assessments were combined to create the outcome in non-overlapping 12-month windows, for up to five observations per participant. If there were three consecutive assessments, only the first two were used to create the outcome. The outcome measure in this analysis was the number of falls over a 12-month period, categorized as: no falls, single fall, or recurrent falls (≥2).

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

Exposure

The U.S. region of the clinical research site was the main exposure of interest categorized as: Northeast [Massachusetts (MA), Maryland (MD), New Jersey (NJ), New York (NY), Pennsylvania (PA), Rhode Island (RI)]; Midwest [(Illinois (IL), Missouri (MO), Ohio (OH)]; South [(Alabama (AL), Georgia (GA), North Carolina (NC), Puerto Rico (PR), Tennessee (TN), Texas (TX)]; and West [California (CA), Colorado (CO), Washington (WA)].

Confounders

All potential confounders were assessed at study entry. Potential confounders included: age, race/ethnicity, education level, sex at birth, health insurance, smoking status, current (within the past month) alcohol use, other current substance use, prescription use of opioids, benzodiazepine/other sedatives, antidepressants, antihypertensives, or steroids, body mass index (BMI) category (underweight <18.5, normal 18.5-<25, overweight 25-30 or obese >30 kg/m^2), waist circumference above 102 cm for men, 88 cm for women, weight loss ≥10 pounds in past year, weak grip (yes or no with cutoffs for weak grip based on sex and BMI), slow gait (>4 seconds/4 meters), days of vigorous/moderate activities per week (<3 days or ≥3 days)[17], comorbidities established via chart abstraction (diabetes mellitus, hypertension, history of cancer within 5 years, history of osteoporosis, prior fracture, history of chronic hepatitis C virus infection, and history of eGFR <60), peripheral neuropathy (hypoactive ankle reflexes bilaterally or mild, moderate, or severe loss in vibration perception bilaterally)[18], CD4 absolute count (cells/mm^3), nadir CD4 (cells/mm^3), HIV RNA (>50 copies/mL), proportion of time with HIV RNA < 200 copies/ml before baseline, HIV RNA < 200 copies/mL ≥ 75% of the time before baseline, ever use of didanosine/stavudine (DDI/D4T), duration of ART and duration of tenofovir disoproxil fumarate (TDF), history of AIDS-defining condition, average neuropsychological score, and neurocognitive impairment. Neurocognitive performance in HAILO is assessed with four neuropsychological tests: Trail Making Tests A and B, the Wechsler Adult Intelligence Scale-Revised Digit Symbol subtest, and the Hopkins Verbal Learning Test-Revised. The raw score for each test was standardized using demographic-adjusted normative means and individual z-scores were combined in a summary z-score (NPZ-4).

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

Neurocognitive impairment was defined as at least one z-score 2 SD below the mean or at least two z-scores 1 SD below the mean on two separate tests.

Effect Modifiers

A subset of the above covariates were also evaluated as potential effect modifiers: physical activity, BMI (underweight not included due to small numbers), and sex.

Statistical Analysis

The number and proportion of individuals with single and recurrent falls overall and by geographic location were calculated. Associations between geographic region and recurrent falls over the 12-month period were assessed using repeated measures multinomial logistic regression models. The outcome was considered as nominal rather than ordinal for ease of interpretation of the results, and because of the specific interest in evaluating the association between geographic region and recurrent falls, which have greater clinical implications on health. It was decided in advance to include age in all models. Potential confounding variables were evaluated by entering each into the age-adjusted model individually; any variable that changed the age-adjusted effect estimate for geographic region and either category of falls (1 vs no falls or 2+ vs no falls) by ≥10% was retained in the final, multivariable model (Supplemental Table). Odds ratios and corresponding 95% CI were generated from the multinomial logistic regression models; when presenting the results from these models, we focus on the association between geographic region and recurrent falls, with no falls as the reference group. Effect modification was assessed by adding an interaction term between geographic region and each potential effect modifier into the multivariable model, to test for effect modification on the multiplicative scale. All analyses were conducted in SAS v9.4 (Carey, NC).

Results

A total of 788 men and 192 women with median age of 51 years contributed up to 240 weeks (5 years) of data. Baseline (study entry) characteristics are reported in Table 1. U.S. geographic region included 22% Northeast, 29% Midwest, 20% South, and 29% West. Western region had a higher proportion of participants of Hispanic ethnicity, never smokers, overweight participants, and participants with no or unknown insurance whereas

the Midwestern region had a higher proportion of participants with private insurance and with more than high school education. Southern region had a higher proportion of participants with <3 days of vigorous/moderate physical activity and obese participants compared to Western region. Western region had a lower proportion of participants with fall(s) throughout all the time periods whereas Midwestern region had the highest proportion in the first two time periods and Southern region had the highest proportion in the last three time periods (Figure 1a).

Canes were the most common assistive device (reported by 6% of participants at least once during the follow-up period), while only 6 (0.6%) participants used a wheelchair and 3 (0.3%) used a scooter (data not shown). Falls requiring medical attention, including those resulting in a fracture, are summarized in Figure 1b, by region and study time period.

Education level, health insurance, smoking status, current substance use, physical activity, average NPZ-4, neurocognitive impairment, and prescription opioid use changed the age-adjusted model effect estimate by more than 10% and were included in the multivariable model, with one exception; due to collinearity, NPZ-4 but not neurocognitive impairment was included in the multivariable model.

In the multivariable model, Midwestern and Southern regions had a higher occurrence of recurrent falls compared to Western region: the odds of recurrent falls was 2.35 [95% CI=1.29,4.28; p=0.005] times greater for Midwestern region and 2.09 [95% CI=1.09,4.01; p=0.026] times greater for Southern region compared to Western region. There was no difference in the odds of recurrent falls between Northern and Western region (OR=1.37[95% CI=0.73, 2.57; p=0.33]) (Table 2).

The associations between geographic region and recurrent falls by potential effect modifiers are shown in Table 3. There was a strong association between Southern vs. Western region on the risk of recurrent falls among obese participants (OR=3.95 [95% CI= 1.61, 9.69]) but not among either normal weight participants (OR=1.14 [95% CI=0.25, 5.16]) or overweight participants (OR=1.36 [95% CI=0.44, 4.19]). Among participants with higher physical activity, those in the Midwest region had higher odds of recurrent falls (OR=3.55 [95% CI=1.51, 8.34]) than those in the Western region, while there was no

association among those with <3 days of physical activity (OR=1.47 [95% CI=0.70, 3.07]). There was no evidence of effect modification by sex (Table 3).

Discussion

We found significant differences in the risk of recurrent falls across U.S. geographic regions among older PWH, despite accounting for numerous fall risk factors, with higher odds of recurrent falls among PWH in the Midwestern and Southern region compared to those in the Western region.

Physically active individuals in the Midwestern region had a greater odds of recurrent falls compared to active individuals in the Western region. There are a number of possible explanations for these relationships, including differences in weather patterns between the regions: for example, those in the Midwest may be more likely to encounter snowy or rainy conditions while exercising outdoors. The Midwestern region had higher proportions of current smokers, obese participants, and participants with a history of hypertension, compared to the Western region, suggesting that despite being physically active, overall poorer health among HAILO participants in the Midwestern region compared to those in the Western region may have contributed to higher risk of falls. Different reasons may underlie falls, with younger active participants falling in association with exercise and activities opposed to neuromuscular decline due to aging. Active participants might also be provided with more opportunities for falls due to their physical activity compared to participants who are less physically active [19]. Our finding of a greater odds of falls among physically active older adults in the Midwest compared to the South is consistent with prior studies [19,20]. Our results suggest that a greater understanding of factors contributing to falls may aid in better design of fall interventions that are specifically tailored to the population at risk: interventions to decrease weather-related falls among more active older adults will be much different than interventions to decrease indoor falls among sedentary older adults.

We found a higher odds of recurrent falls among obese individuals in the Southern region compared to obese individuals in the Western region. It could be that obese individuals in the Southern region have a greater prevalence of other comorbid health

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

conditions than those in the Western region. Indeed, HAILO sites in the South have a higher proportion of PWH with a history of hypertension, as well as a higher proportion of current smokers. There may also be other, unmeasured health factors that could have contributed to a higher risk of recurrent falls as compared to the West [21,22]. The relatively small number of women may have limited our ability to detect effect modification by sex. Previous studies have observed gender differences in falls that are associated with the type and amount of physical activity. Older men tend to have higher amount of moderate-to-vigorous physical activity and higher proportion of outdoor activity compared to women[23], which we observed as well. A higher proportion of men in this analysis had 3 or more days of moderate-to- vigorous activities/week (55%) compared to women (44%).

This study has several strengths. First, HAILO is a longitudinal cohort that includes a large number of individuals from multiple geographically diverse study sites, which allowed for the examination of numerous risk factors for falls in combination. A second strength is that the study included both men and women, allowing us to explore whether sex modified the association between region and falls. Thirdly, we were able to examine the effect of physical activity on the association between geographic location and falls, which was excluded from analysis in other studies including the WIHS and MACS. Limitations of the study include unmeasured confounding by environmental factors, walkability/transportation of the region, circumstances of the falls (slip on ice, etc), and seasonality (winter/summer), all of which could influence the association between geographic region and falls. There could also be other unmeasured behavior or health characteristics that vary among study participants across different regions. Comorbidities were confirmed by medical record review, but comorbidities may have been undiagnosed in participants not regularly engaged in care. We had few individuals over age 60, thus our ability to detect differences in fall risk by age group was limited. This study was likely underpowered to detect effect modification, which could explain the lack of statistically significant differences in the interactions we examined. Additionally, falls were self-reported and therefore subject to recall bias, although the 6-month period over which participants were asked to recall falls is relatively short.

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

In conclusion, among men and women with HIV, there were differences observed between geographic region and risk of recurrent falls. While falls occurred in all age groups, factors modifying falls suggest that younger participants may experience physical activity-related falls, while factors among older adults may be more traditional fall-related risk factors. While additional research is needed to better understand the characteristics of individuals, and the environments in which they live, that may explain the associations we observed, our findings that obesity and physical activity modify the regional association with falls can inform interventions to minimize risk factors for falls.

Funding:

This work was supported by the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health under Award Number UM1 AI068634, UM1 AI068636, UM1 AI106701, UM1 AI069494; the National Institute of Aging (NIA) R01 AG0504366 (to KME); NIAID K24 120834 (to TTB). Integrative Physiology of Aging Training Grant T32 AG000279-18 (to MA)

Acknowledgments: We thank the study volunteers who participated in A5322, all the ACTG clinical units who enroll and follow participants, and the ACTG.

Conflict of Interest: No relevant conflict of interest

AIDS Research and Human Retroviruses

Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

References

1. van Sighem AI, Gras LA, Reiss P, Brinkman K, de Wolf F, study Anoc. Life expectancy of recently diagnosed asymptomatic HIV-infected patients approaches that of uninfected individuals. *AIDS.* 2010;24(10):1527-1535.
2. Nakagawa F, Lodwick RK, Smith CJ, et al. Projected life expectancy of people with HIV according to timing of diagnosis. *AIDS.* 2012;26(3):335-343.
3. Marcus JL, Leyden WA, Alexeeff SE, et al. Comparison of Overall and Comorbidity-Free Life Expectancy Between Insured Adults With and Without HIV Infection, 2000-2016. *JAMA Netw Open.* 2020;3(6):e207954.
4. Greene M, Covinsky KE, Valcour V, et al. Geriatric Syndromes in Older HIV-Infected Adults. *J Acquir Immune Defic Syndr.* 2015;69(2):161-167.
5. Erlandson KM, Karris MY. HIV and Aging: Reconsidering the Approach to Management of Comorbidities. *Infect Dis Clin North Am.* 2019;33(3):769-786.
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(11):1279-1286.
7. 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.
8. 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. *Clin Infect Dis.* 2008;47(4):542-553.
9. Tassiopoulos K, Abdo M, Wu K, et al. Frailty is strongly associated with increased risk of recurrent falls among older HIV-infected adults. *AIDS.* 2017;31(16):2287-2294.
10. Aging NCo. Falls Prevention Facts https://www.ncoa.org/news/resources-for-reporters/get-the-facts/falls-prevention-facts/. Accessed October 1 2020.
11. Gama ZA, Gomez-Conesa A. [Risk factors for falls in the elderly: systematic review]. *Rev Saude Publica.* 2008;42(5):946-956.

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

12. Deandrea S, Lucenteforte E, Bravi F, Foschi R, La Vecchia C, Negri E. Risk factors for falls in community-dwelling older people: a systematic review and meta-analysis. *Epidemiology.* 2010;21(5):658-668.

13. Erlandson KM, Zhang L, Ng DK, et al. Risk Factors for Falls, Falls With Injury, and Falls With Fracture Among Older Men With or at Risk of HIV Infection. *J Acquir Immune Defic Syndr.* 2019;81(4):e117-e126.

14. 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 Med.* 2016;17(10):740-748.

15. Sharma A, Hoover DR, Shi Q, et al. Falls among middle-aged women in the Women's Interagency HIV Study. *Antivir Ther.* 2016;21(8):697-706.

16. Smurzynski M, Collier AC, Koletar SL, et al. AIDS clinical trials group longitudinal linked randomized trials (ALLRT): rationale, design, and baseline characteristics. *HIV Clin Trials.* 2008;9(4):269-282.

17. Craig CL, Marshall AL, Sjostrom M, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc.* 2003;35(8):1381-1395.

18. Evans SR, Ellis RJ, Chen H, et al. Peripheral neuropathy in HIV: prevalence and risk factors. *AIDS.* 2011;25(7):919-928.

19. Lu Z, Lam FMH, Leung JCS, Kwok TCY. The U-Shaped Relationship Between Levels of Bouted Activity and Fall Incidence in Community-Dwelling Older Adults: A Prospective Cohort Study. *J Gerontol A Biol Sci Med Sci.* 2020;75(10):e145-e151.

20. Chan BK, Marshall LM, Winters KM, Faulkner KA, Schwartz AV, Orwoll ES. Incident fall risk and physical activity and physical performance among older men: the Osteoporotic Fractures in Men Study. *Am J Epidemiol.* 2007;165(6):696-703.

21. Fjeldstad C, Fjeldstad AS, Acree LS, Nickel KJ, Gardner AW. The influence of obesity on falls and quality of life. *Dyn Med.* 2008;7:4.

22. Mukamal KJ, Mittleman MA, Longstreth WT, Jr., Newman AB, Fried LP, Siscovick DS. Self-reported alcohol consumption and falls in older adults: cross-sectional and longitudinal analyses of the cardiovascular health study. *J Am Geriatr Soc.* 2004;52(7):1174-1179.

23. Li W, Procter-Gray E, Churchill L, et al. Gender and Age Differences in Levels, Types and Locations of Physical Activity among Older Adults Living in Car-Dependent Neighborhoods. *J Frailty Aging.* 2017;6(3):129-135.

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

Table 1: Baseline Characteristics Overall and by Geographic Region

Variable		Overall (N=980)	U.S. Region of Entry: Site: Northeast (N=218)	South (N=195)	Midwest (N=285)	West (N=282)	P-value
Age	<50	430 (44%)	84 (39%)	127 (45%)	98 (50%)	121 (43%)	0.059*
	50-90	401 (41%)	98 (45%)	104 (37%)	75 (39%)	124 (44%)	
	≥60	149 (15%)	36 (17%)	54 (19%)	22 (11%)	37 (13%)	
Sex	Male	788 (80%)	162 (74%)	242 (85%)	149 (76%)	235 (83%)	0.006*
	Female	192 (20%)	56 (26%)	43 (15%)	46 (24%)	47 (17%)	
Race/ethnicity	White non-Hispanic	463 (47%)	90 (41%)	186 (65%)	81 (42%)	106 (38%)	<0.001*
	Black non-Hispanic	292 (30%)	94 (43%)	89 (31%)	75 (39%)	34 (12%)	
	Hispanic/Other	225 (23%)	34 (16%)	10 (4%)	39 (20%)	142 (50%)	
Education Level	< High school	156	36	26	13	81	<0.001*

	Highschool	(16%)	(17%)	(9%)	(7%)	(29%)	
	>High school	208 (21%)	54 (25%)	61 (21%)	57 (29%)	36 (13%)	
		616 (63%)	128 (59%)	198 (70%)	125 (64%)	165 (59%)	
Health Insurance	None/unknown	198 (20%)	26 (12%)	33 (12%)	29 (15%)	110 (39%)	<0.001*
	Public	252 (26%)	81 (37%)	60 (21%)	54 (28%)	57 (20%)	
	Private	414 (42%)	83 (38%)	148 (52%)	85 (44%)	98 (35%)	
	Medicare	116 (12%)	28 (13%)	44 (15%)	27 (14%)	17 (6%)	
Smoking Status	Never	401 (41%)	76 (35%)	116 (41%)	71 (36%)	138 (49%)	<0.001*
	Prior	325 (33%)	69 (32%)	83 (29%)	73 (37%)	100 (36%)	
	Current	247 (25%)	73 (34%)	79 (28%)	51 (26%)	44 (16%)	
Current Alcohol Use	Abstainer	373 (38%)	82 (38%)	105 (37%)	76 (39%)	110 (39%)	0.80*
	Light Drinker	354 (36%)	75 (34%)	102 (36%)	77 (40%)	100 (36%)	
	Moderate Drinker	62 (6%)	14 (6%)	22 (8%)	10 (5%)	16 (6%)	
	Heavy Drinker	164	43	52	27	42	

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

		(17%)	(20%)	(18%)	(14%)	(15%)	
History of Hypertension		554 (57%)	136 (62%)	153 (54%)	129 (66%)	136 (48%)	<0.001*
History of Diabetes		124 (13%)	32 (15%)	30 (11%)	25 (13%)	37 (13%)	0.57*
Current Substance use (Tobacco Excluded)		201 (21%)	56 (26%)	57 (20%)	30 (15%)	58 (21%)	0.081*
Prescription opioid use		72 (7%)	26 (12%)	21 (7%)	12 (6%)	13 (5%)	0.017*
Days of vigorous/moderate activities per week	<3 days	438 (45%)	96 (44%)	134 (47%)	106 (54%)	102 (36%)	0.004*
	≥3 days	489 (50%)	111 (51%)	143 (50%)	80 (41%)	155 (55%)	
BMI	Underweight	6 (1%)	1 (1%)	4 (1%)	1 (1%)	0 (0%)	0.022*
	Normal	312 (32%)	66 (30%)	93 (33%)	65 (33%)	88 (31%)	
	Overweight	384 (39%)	82 (38%)	105 (37%)	64 (33%)	133 (47%)	
	Obese	278 (28%)	69 (32%)	83 (29%)	65 (33%)	61 (22%)	
Slowness (>4sec/4 meters)		393 (40%)	99 (45%)	109 (38%)	66 (34%)	119 (42%)	0.068*

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

Weak Grip		220 (22%)	46 (21%)	52 (18%)	49 (25%)	73 (26%)	0.129*
Average Neuropsychological Score (NPZ4)* **	Median (Q1, Q3)	0.2 (-0.5,0.8)	0.0 (-0.7,0.7)	0.4 (-0.2,1.1)	0.1 (-0.5,0.7)	0.0 (-0.8,0.8)	<0.001**
Nadir CD4(cells/mm^3)	Median (Q1-Q3)	193.5 (65.5-301.0)	217 (109-305)	189 (45-284)	173 (58-264)	190 (74-321)	0.024**
CD4 absolute count (cells/mm^3)	Median (Q1-Q3)	621 (452-822)	657 (481-877)	643 (455-819)	640 (474-800)	579.5 (417.0-784)	0.046**
HIV RNA >50 copies/mL		70 (7%)	18 (8%)	21 (7%)	12 (6%)	19 (7%)	0.838*
Duration of ART (year)	Median (Q1-Q3)	7.7 (4.3-11.4)	7.7 (4.0-11.4)	7.9 (4.8-12.0)	7.6 (4.4-10.6)	7.1 (4.1-10.6)	0.008**
Duration of TDF (year)	Median (Q1-Q3)	4.3 (3.1-7.0)	4.5 (3.3-7.0)	4.3 (2.7-7.1)	4.0 (2.6-6.3)	4.2 (3.3-7.1)	0.172**
Ever use of DDI/D4T		143 (15%)	26 (12%)	47 (17%)	25 (13%)	45 (16%)	0.395*

*Chi-Square Test. **Kruskal-Wallis Test. *** with learning effects adjusted
Cutoffs for weak grip strength are based on sex and BMI

Table 2: Age-adjusted Models and Multivariable Models for the Association between Geographic Region and Recurrent Falls

Region	Age-adjusted OR (95% CI)	P-value	Multivariable aOR (95% CI)	P-value
Northeast	1.77 (1.01, 3.10)	0.05	1.37 (0.73, 2.57)	0.33
Midwest	1.97 (1.17, 3.29)	0.01	2.35 (1.29, 4.28)	0.005
South	2.20 (1.25, 3.85)	0.006	2.09 (1.09, 4.01)	0.026

Age, Education level, Health insurance, Smoking status, Current substance use, Physical activity status, Prescription opioid use, and Average Neuropsychological Score were adjusted in the multivariable model.
Reference level for geographic location is West.

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

Table 3: Effect Modification by BMI, Sex, and Physical Activity, on the Association between Geographic Region and Recurrent Falls.

Variable	Northeast vs. West OR (95% CI)	Midwest vs. West OR (95% CI)	South vs. West OR (95% CI)
BMI Category			
Normal	1.51 (0.39, 5.90)	2.18 (0.52, 9.20)	1.14 (0.25, 5.16)
Overweight	1.00 (0.40, 2.49)	2.23 (1.05, 4.71)	1.36 (0.44, 4.19)
Obese	1.78 (0.67, 4.75)	3.42 (1.36, 8.64)	3.95 (1.61, 9.69)
Sex			
Male	1.19 (0.55, 2.59)	2.21 (1.11, 4.40)	2.12 (0.99, 4.55)
Female	1.16 (0.45, 2.97)	2.22 (0.82, 5.97)	1.45 (0.52, 4.07)
Physical Activity Status			
<3 days	1.40 (0.66, 2.96)	1.47 (0.70, 3.07)	1.89 (0.92, 3.86)
≥3 days	1.21 (0.47, 3.14)	3.55 (1.51, 8.34)	2.20 (0.77, 6.31)

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

AIDS Research and Human Retroviruses
Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

Interaction P-values:

Categories	Northeast vs. West	Midwest vs. West	South vs. West
BMI			
Normal vs. Overweight	0.60	0.98	0.85
Normal vs. Obese	0.84	0.60	0.16
Overweight vs. Obese	0.39	0.47	0.13
Sex			
Male vs. Female	0.97	>0.99	0.55
Physical Activity Status			
<3 days vs. ≥3 days	0.80	0.11	0.81

Age, Education level, Health insurance, Smoking status, Current substance use, Physical activity status, Prescription opioid use, and Average Neuropsychological Score were adjusted in the multivariable models.
Reference level for geographic region is West for all models.

Figure Legend

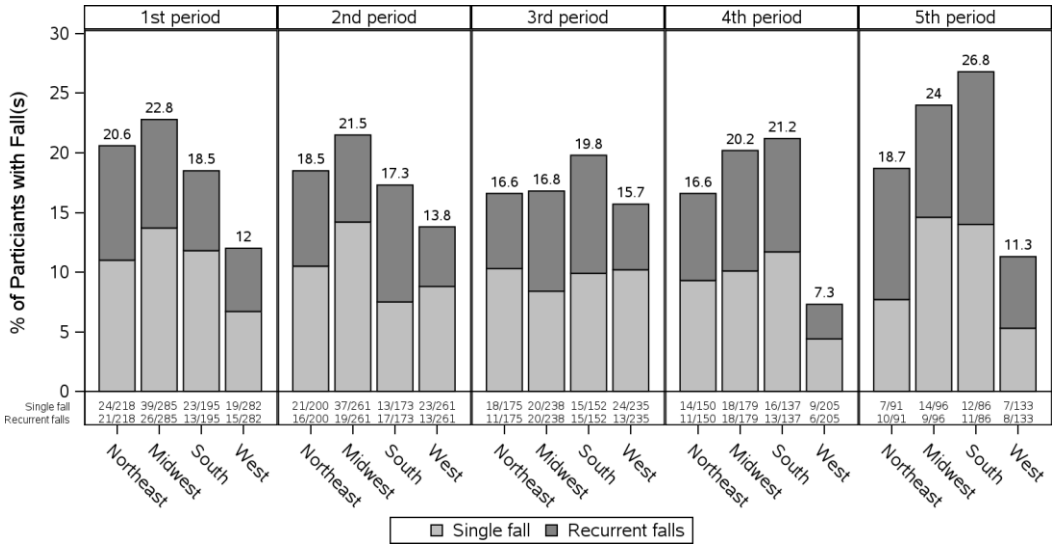

Figure 1a: Regional distribution of falls in each 12-month period

AIDS Research and Human Retroviruses

Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

AIDS Research and Human Retroviruses

Regional Differences in Risk of Recurrent Falls Among Older U.S. Women and Men with HIV in the HIV infection, Aging, and Immune Function Long-Term Observational Study (HAILO) (DOI: 10.1089/AID.2021.0162)

This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

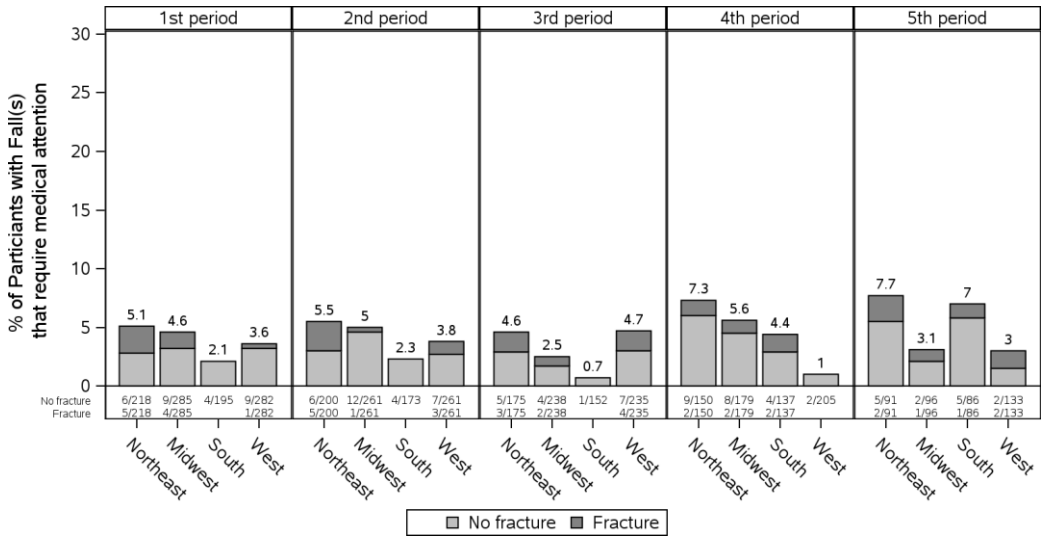

Figure 1b: Regional Distribution of Falls with injury requiring medical attention in each 12-month period