

Longitudinal Study of Falls among HIV-infected and Uninfected Women: Results from the Women's Interagency HIV Study

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Falls in Older Persons in the U.S.

- One-third of community dwelling adults aged ≥ 65 fall annually in the U.S.
- >\$30 billion yearly direct medical costs
- Many adverse health outcomes: fracture, traumatic brain injury, disability, and death

Risk Factors for Falls Among HIV+

- HIV+ more likely to have conditions associated with both aging and falls: cognitive impairment, frailty syndrome, and polypharmacy vs. HIV-
- Slow gait and poor physical performance reported in older HIV+ men

Falls and Fractures in HIV

- Low bone mineral density is prevalent in HIV+
- Occurrence of falls in HIV+ older adults may confer a greater risk of osteoporotic fracture
- Middle aged HIV+ women had higher fracture rates than HIV- women in in the Women's Interagency HIV Study (WIHS)

Prevalence of Falls in the WIHS Cohort

- At least one fall was reported in 263 HIV+ (19%) vs. 119 HIV- (18%) women with median age 48 years
- ≥ 2 falls reported in 133 HIV+ (9%) vs. 65 HIV- (10%) women
- Falls were associated with factors affecting cognition, but not HIV status
- Factors independently associated with any fall:
 - Age, current marijuana use, depressive symptoms, subjective cognitive complaints, obesity, number of CNS active agents, and WIHS site

OBJECTIVES

- To determine the rate of falls among middle-aged HIV+ and HIV- women in the Women's Interagency HIV Study (WIHS)
- To evaluate the relationship between cognition and falls among HIV+ and HIV- women



METHODS

WIHS Study Population

- Ongoing, multicenter prospective cohort study of the natural and treated history of HIV infection in women
- Enrolled in 1994-95, 2001-02, 2011-12 in U.S. 6 sites
 - Bronx/Manhattan NY, Brooklyn NY, Chicago IL, Washington DC, San Francisco CA, and Los Angeles, CA
- 2014-15: LA site closed and 4 Southern U.S. sites added:
 - Atlanta GA, Chapel Hill NC, Miami FL, Birmingham AL/Jackson MI
- HIV- women were recruited from high risk groups
- Semiannual visits: physical examinations, biological specimens, and assessment of clinical, behavioral, and demographic characteristics via face to-face interviews

Ascertainment of Falls

- In 2014 (semiannual visit 40), all WIHS participants were asked to report any history of fall within the prior 6 months
- Participants reporting any fall were asked:
 - If they had either “1” or “2 or more”
 - Whether any of these falls resulted in injury for which they sought medical attention
 - Whether any of these falls resulted in fracture

Definition of Falls

“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”

- Participants instructed to exclude
 - ***“Falls that result from a major medical event***
 - ***OR from an overwhelming external hazard***

Primary Predictor: Subjective Cognitive Impairment

- Defined by self-report
- EITHER: major problems with memory or concentration that interfered with normal everyday activities and lasted >2 weeks
- OR: confusion, getting lost in a familiar place or inability to perform routine mental tasks

Statistical Analysis

- Hierarchical models evaluated associations between subjective cognitive complaints (and HIV status) and having at least one any fall (vs. none) during the prior 6 months
- Sequentially adjusted for:
 1. Demographics,
 2. Co-morbid conditions,
 3. Substance abuse / CNS active agents
 4. HIV-specific factors for HIV+ women
- Covariates were measured at the closest study visit prior to first falls assessment.

Statistical Analysis

- Logistic regression models for prediction of falls were fit
 - covariates associated with any fall in univariate analysis ($p < 0.1$) included in multivariable models
- Because associations with falls did not vary across visits, all three visits were pooled
- Generalized estimating equations (GEE) with logit link adjusted for within-person correlation due to use of repeated measures



RESULTS

Participant Characteristics: Demographics

Characteristic	HIV+ (N=1289)	HIV- (N=587)	P value
Age, median (IQR)	49 (43-55)	47 (39-54)	0.0002
Race/Ethnicity, N (%)			0.26
Black (ref)	929 (72%)	438 (75 %)	
White	200 (16%)	74 (13%)	
Other	154 (12%)	72 (12%)	
Education ≥ high school	840 (66%)	401 (69%)	0.17
Income ≥ \$12,000	612 (48%)	295 (52%)	0.16
WIHS enrollment year			0.0013
94-95 (ref)	477 (38%)	173 (30%)	
01-02	318 (25%)	184 (32%)	
11-14	472 (37%)	218 (38%)	

Participant Characteristics: Comorbidities

Characteristic	HIV+ (N=1289)	HIV- (N=587)	P value
Subjective cognitive complaints, N (%)	148 (11%)	63 (11%)	0.63
Neuropathy, N (%)	261 (20%)	91 (16%)	0.02
Obesity (BMI \geq 30 kg/m ²), N (%)	604 (48%)	335 (58%)	<0.0001
Quality of life (range 1-10), median, (IQR)	8 (7-9)	8 (6-9)	0.001
CESD score \geq 16, N (%)	370 (29%)	177 (30%)	0.52
Diabetes Mellitus, N (%)	261 (20%)	130 (22%)	0.36
Renal dysfunction (eGFR<60), N (%)	121 (9%)	35 (6%)	0.01
Cancer, N (%)	19 (1%)	6 (1%)	0.43
Hypertension, N (%)	648 (50%)	291 (50%)	0.73
Hepatitis C virus infection, N (%)	157 (12%)	46 (8%)	0.005

Participant Characteristics: Substance Use

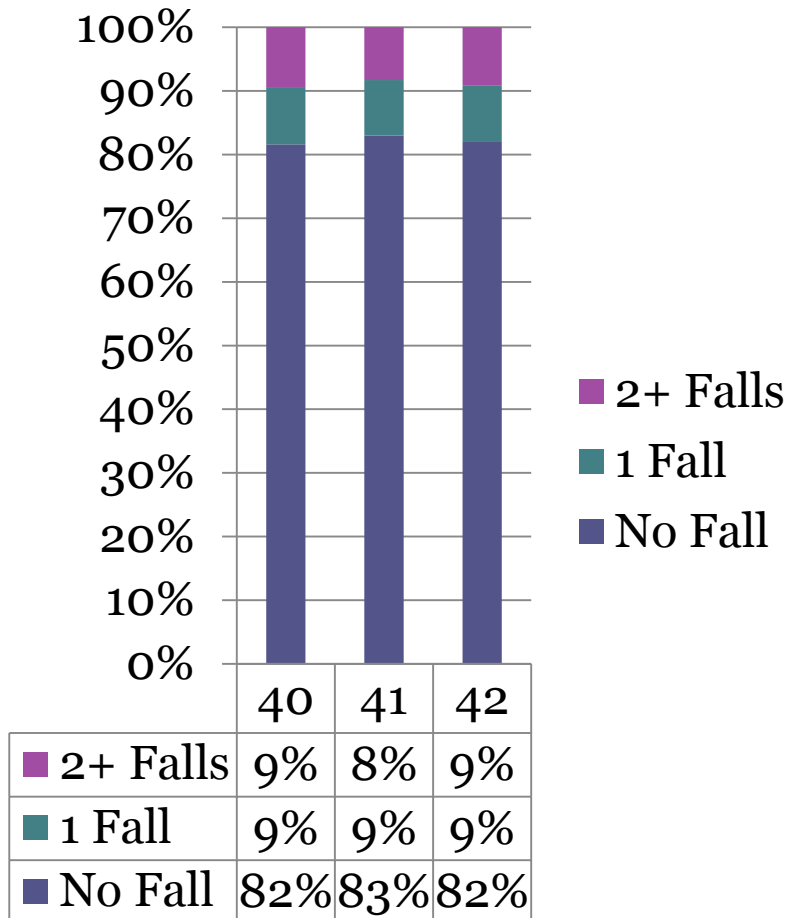
Characteristic	HIV+ (N=1289)	HIV- (N=587)	P value
Smoking			0.0001
Never	424 (33%)	163 (28%)	
Former	379 (29%)	142 (24%)	
Current	486 (38%)	282 (48%)	
Crack/Cocaine/Heroin use			0.004
Never	669 (52%)	277 (47%)	
Former	514 (40%)	236 (40%)	
Current	102 (8%)	74 (13%)	
Marijuana use			0.03
Never	200 (34%)	496 (39%)	
Former	245 (42%)	543 (42%)	
Current	142 (24%)	246 (19%)	
Alcohol use			<0.0001
None	712 (56%)	249 (43%)	
Light (<3 drinks/wk)	427 (33%)	209 (36%)	
Moderate (3-13 drinks/wk)	53 (4%)	48 (8%)	
Heavy (≥14 drinks/wk)	90 (7%)	78 (13%)	

Characteristics of HIV+ Participants

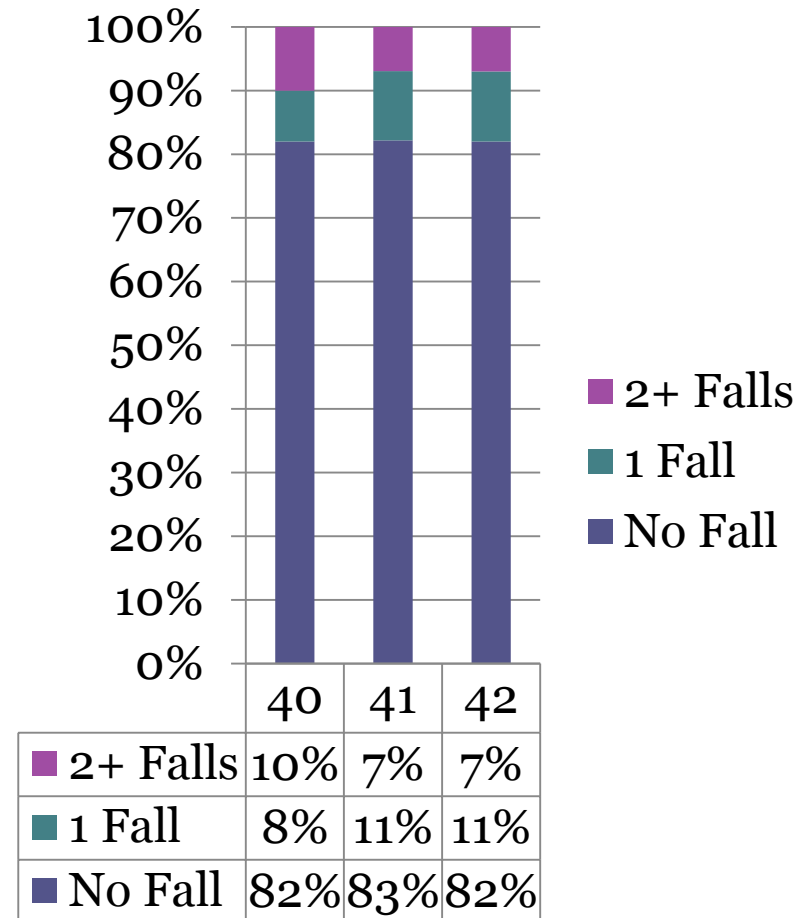
Nadir CD4+ count, median (IQR)	279 (161-409)
Current CD4+ count, median (IQR)	586 (382-777)
Current antiretroviral therapy use	1131 (88%)
Undetectable (<20c/mL) HIV RNA VL, N (%)	798 (63%)
History of AIDS defining illness	439 (34 %)

Falls Status at Each Study Visit

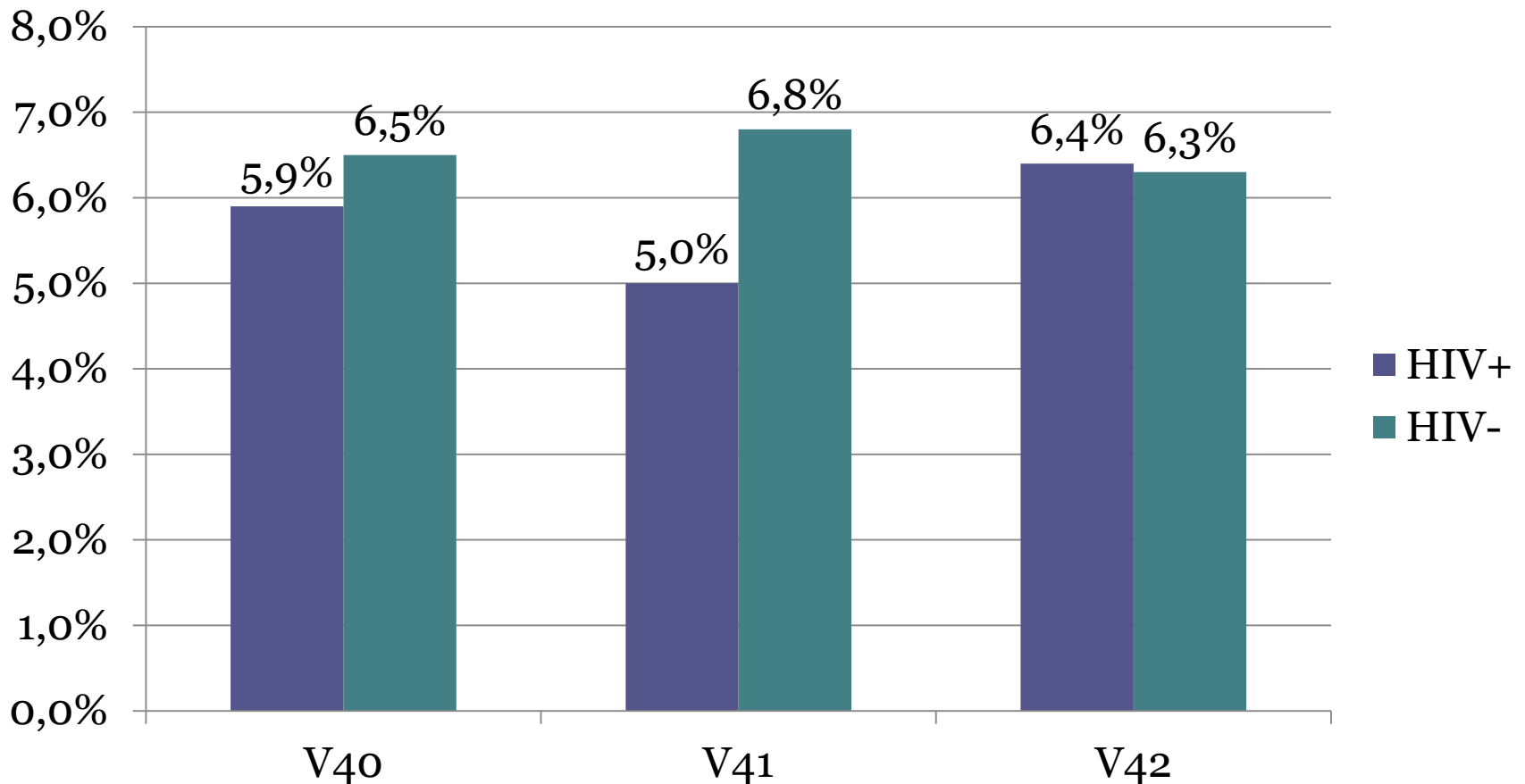
HIV+ Women



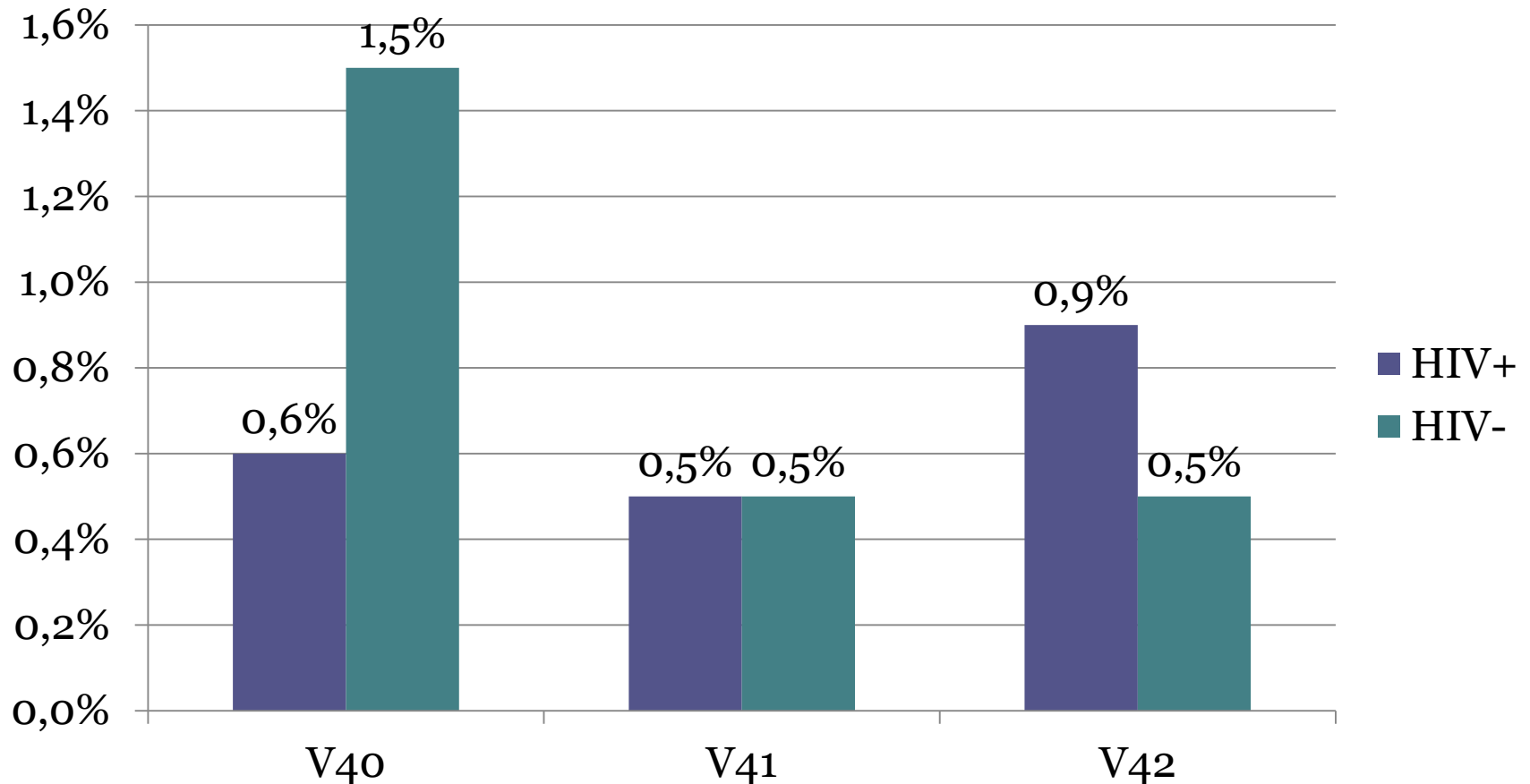
HIV- Women



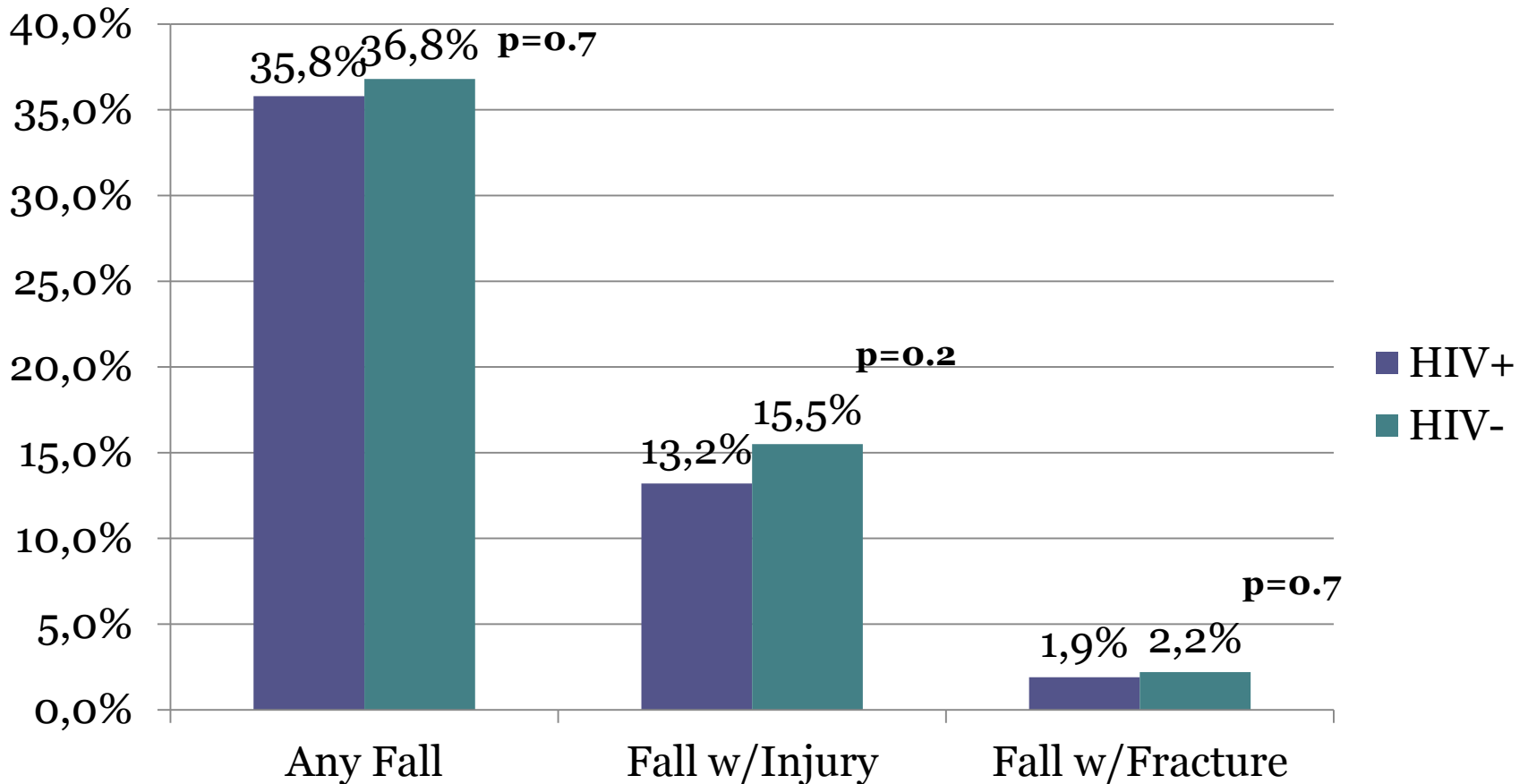
Fall with Injury at Each Study Visit



Fall with Fracture at Each Study Visit



Overall Falling Status: HIV+ and HIV- Women



Factors Associated with Any Fall

Demographics	Odd Ratio (95% CI)	P value
Age (per 10-year)	1.34 (1.22, 1.47)	<0.001
Race (ref: Black)		
White	1.22 (0.97, 1.53)	0.08
Other vs. Black	0.90 (0.69, 1.16)	0.41
Income ≥\$12,000	0.69 (0.58, 0.82)	<0.001
Enrollment year (ref: 1994-95)		
2001-02	0.58 (0.46, 0.73)	<0.001
2011-14	0.97 (0.80, 1.17)	0.72
WIHS site (Ref: Bronx)		
Brooklyn	0.56 (0.39, 0.79)	0.001
Washington DC	1.40 (1.04, 1.89)	0.03
San Francisco	2.54 (1.90, 3.39)	<0.001
Chicago	1.81 (1.33, 2.45)	<0.001
Southern Sites	1.47 (1.12, 1.92)	0.006
Transmission Risk Category (ref: IDU)		
Heterosexual	0.68 (0.54, 0.86)	0.001
Other	0.45 (0.35, 0.56)	<0.001

Factors Associated with Any Fall

Comorbidities	Odds Ratio (95%CI)	P value
HIV-infection	1.00 (0.83, 1.20)	0.98
Subjective Cognitive Complaints	2.60 (2.06, 3.28)	<0.001
Quality of life	0.83 (0.79, 0.87)	<0.001
Neuropathy	2.37 (1.96, 2.88)	<0.001
Obesity	1.17 (0.99, 1.39)	0.07
CES-D score ≥ 16	2.63 (2.21, 3.13)	<0.001
Diabetes	1.32 (1.08, 1.62)	0.006
eGFR CAT < 60	1.73 (1.34, 2.24)	<0.001
Cancer	1.82 (0.92, 3.60)	0.09
Hypertension	1.73 (1.46, 2.05)	<0.001
HCV Status	1.69 (1.33, 2.15)	<0.001

Factors Associated with Any Fall

Substance Use/CNS Active Medications	Odds Ratio (95%CI)	P value
Smoking (ref: never)		
Former	1.58 (1.25, 2.00)	<0.001
Current	1.70 (1.37, 2.11)	<0.001
Use of crack/cocaine/heroin (ref: never)		
Former	1.58 (1.31, 1.89)	<0.001
Current	2.70 (2.07, 3.54)	<0.001
Injection drug use (ref: never)		
Former	1.97 (1.60, 2.42)	<0.001
Current	2.67 (1.21, 5.86)	0.02
Marijuana use (ref: never)		
Former	1.44 (1.18, 1.76)	<0.001
Current	2.19 (1.74, 2.76)	<0.001
Alcohol use (re: none)		
Light (<3 drinks/wk)	1.00 (0.83, 1.21)	0.10
Moderate (3-13 drinks/wk)	1.13 (0.77, 1.67)	0.52
Heavy (≥ 14 drinks/wk)	1.54 (1.15, 2.05)	0.003
CNS Active medications (ref: 0)		
1	1.97 (1.59, 2.43)	<0.001
2	2.27 (1.78, 2.90)	<0.001
≥3	3.74 (2.77, 5.05)	<0.001

Subjective Cognitive Complaints and Odds of Any Fall in WIHS

	HIV+ and HIV- women*		HIV+ women only	
	AOR (95% CI)	P value	AOR (95% CI)	P value
Model 1: Subjective Cognitive Complaints	2.60 (2.06, 3.28)	<0.0001	2.30 (1.73, 3.07)	<0.0001
Model 2: Adjusted for Model 1 + Demographics	2.30 (1.78, 2.96)	<0.0001	2.03 (1.49, 2.76)	<0.0001
Model 3: Adjusted for Model 2 + Comorbidities	1.46 (1.12, 1.91)	0.006	1.23 (0.89, 1.71)	0.20
Model 4: Adjusted for Model 3 + Substance Abuse & CNS active agents	1.42 (1.08, 1.86)	0.01	1.18 (0.85, 1.64)	0.33
Model 5: Adjusted for Model 4 + Prior AIDS	N/a	N/a	1.09 (0.83, 1.42)	0.55

*Analyses of HIV+ and HIV- women are all adjusted for HIV status

Summary

- Falls were common among middle-aged HIV+ and HIV- women in the WIHS
- Overall occurrence of falls, injury resulting from falls, and fractures did not differ by HIV status
- Cognitive complaints were associated with over twice the odds of falling in unadjusted analyses
- Risk was reduced by 45% with full adjustment of covariates

Conclusions

- Among HIV+ women, the association between cognitive complaints and falls appears to be mediated by comorbid medical illness
- Additional studies are needed to understand which comorbid illnesses are most influential and whether management of those conditions can prevent falls among aging HIV+ women

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