

# Frailty and the Risk of Falls in HIV-Infected Older Adults in the ACTG A5322 Study

Katherine Tassiopoulos, Mona Abdo, Susan L. Koletar, Frank Palella, Babafemi Taiwo, and Kristine M. Erlandson for the A5322 Team

# Background/Rationale

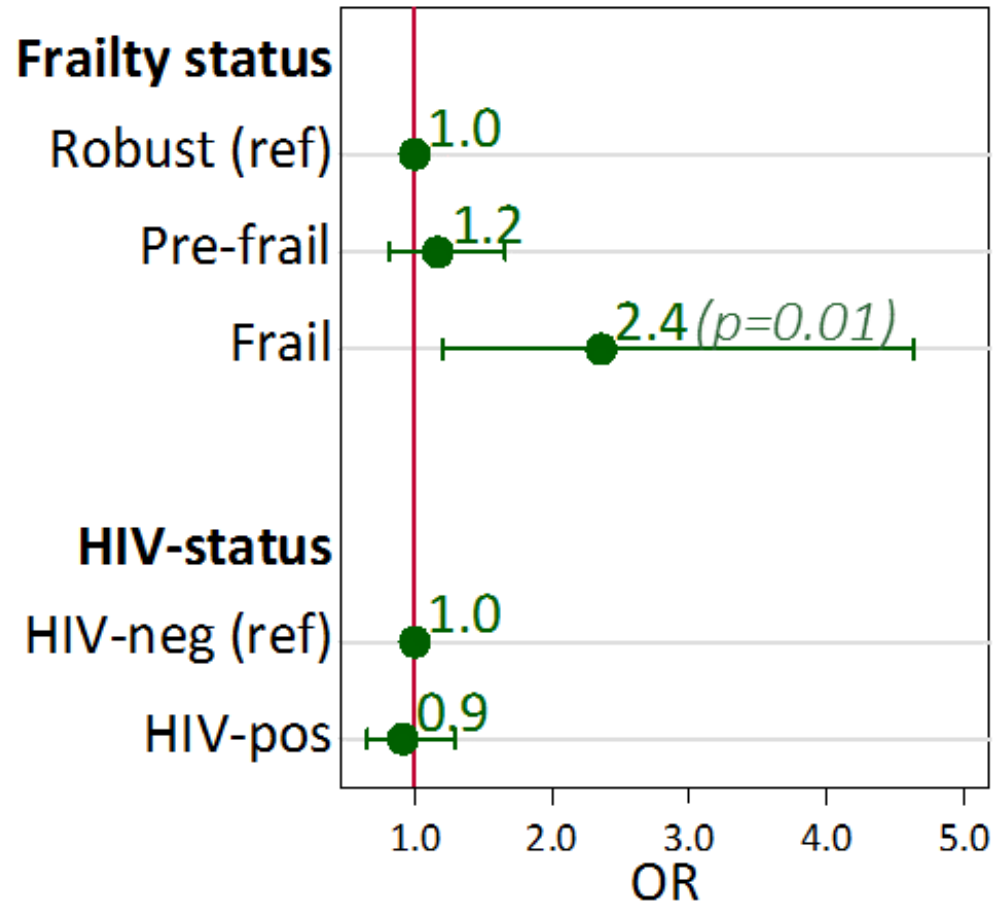
- Falls are a significant risk factor for health-related complications and mortality in the general population (*Rubenstein et al, Age and Ageing 2006*)
- Falls may occur at younger ages among HIV-infected individuals compared to the general population (*Erlandson et al, JAIDS 2012*)
- Falls are common in HIV-infected adults; recent studies show  $\geq 20\%$  with  $\geq 1$  fall in 12-month period (*Erlandson, JAIDS 2012; Erlandson, HIV Med 2016; WIHS presentation*)

# Background/Rationale

- As HIV-infected adults age, frailty will also become a more prevalent problem (*Brothers et al, JID 2014*)
- Studies of the association between frailty (particularly pre-frailty) and falls in the context of HIV infection are limited
- **N=359 HIV+ men and women:** For frail vs non-frail individuals, the OR for recurrent falls was 9.5 (95% CI=3.6, 25.1) (*Erlandson, 2012*)

# Background/Rationale

AGEHIV Cohort Study:  
Frailty but not pre-frailty  
predicted  $\geq 1$  fall over  
one year follow-up



(Kooij et al, EACS [European AIDS Clinical Society] Conference 2015)

# A5322/HAILO

- The AIDS Clinical Trials Group (ACTG) protocol A5322 (HAILO) is a longitudinal cohort study of 1035 HIV-infected adults
  - 40 years or older at enrollment
  - Received their initial ART regimen through an ACTG clinical trial
  - Subsequently followed long-term in ACTG observational study A5001

# A5322/HAILO

## Research visits take place every 6 months

Every 6 months	Yearly
Medical chart abstraction	Body measurements
Medication review	Laboratory tests
<b>Falls interview</b>	<b>Frailty assessment</b>
	Questionnaires (Cigarettes/drugs/alcohol, sexual behavior, insurance, instrumental activities of daily living)
	Neurocognitive evaluation
	Repository specimens (plasma/serum every 6 mos, PBMC every 2 yrs)

# Frailty Assessment

- ▣ Fried's Frailty assessment - 5 components:
  1. **4-meter walk speed**
  2. **Grip strength**
  3. Self-reported **unintentional weight loss** ( $\geq 10$  lbs) in past year
  4. Self-reported **exhaustion**
    - ▣ Experiencing  $\geq 3$ -4 times/week that "everything I do is an effort" or "sometimes I just cannot get going"
  5. Self-reported **low physical activity levels**
    - ▣ "Limited a lot" in response to Short Form (SF)-36 question, "does your health limit you in vigorous activities such as running, lifting heavy objects, or participating in strenuous sports?"



# Falls Assessment

- ▣ Falls questionnaire administered every 6 months
- ▣ Any falls in past 6 months? If yes:
  - ▣ How many? (1, 2, 3-5, 6+)
  - ▣ Required medical attention?
  - ▣ Resulted in broken bone(s)?



# Objectives

1. Identify number of HALO participants with any falls (1+) and recurrent falls (2+) over 12 month period, and proportion of falls resulting in medical treatment or fracture
2. Examine association between frailty status and incidence of single and recurrent falls

# Methods: Study Population

- All HAILO participants who completed frailty assessment at entry visit and  $\geq 1$  falls interview over the next year

# Methods

## Exposure

- Primary exposure: 3-category frailty variable
  - Frail =  $\geq 3$  of 5 components
  - Pre-frail = 1-2 components
  - Non-frail = 0 components
- Individual frailty components also examined
  - Slow 4-m walk speed (>4 seconds)
  - Weak grip strength (sex-specific cutoffs)

## Outcome

- Any falls over one year period
- Single and recurrent (2+) falls over one year period



# Methods: Potential Confounders

<b>Demographic</b>	<b>Behavioral</b>
Age	Physical activity
Sex	Alcohol use
Race/ethnicity	Substance use
Education	Cigarette smoking
<b>Clinical/Medical</b>	<b>HIV-Disease Specific</b>
Health insurance	Peripheral neuropathy
BMI	Didanosine/stavudine use
Waist circumference	AIDS-defining condition
Hypertension medication	
Depression/anxiety medication	
Co-morbidities (diabetes, hypertension, HCV, CVD, kidney or liver disease, cancer)	

# Methods: Statistical Analyses

- ▣ Multinomial logistic regression to assess the association between frailty (and weak grip, slow walk speed) and falls (single and recurrent falls)
- ▣ Each potential confounder added one at a time to univariable model
- ▣ Variables that changed effect estimate by  $\geq 15\%$  kept in final, multivariable model

# Results: Study Population Characteristics

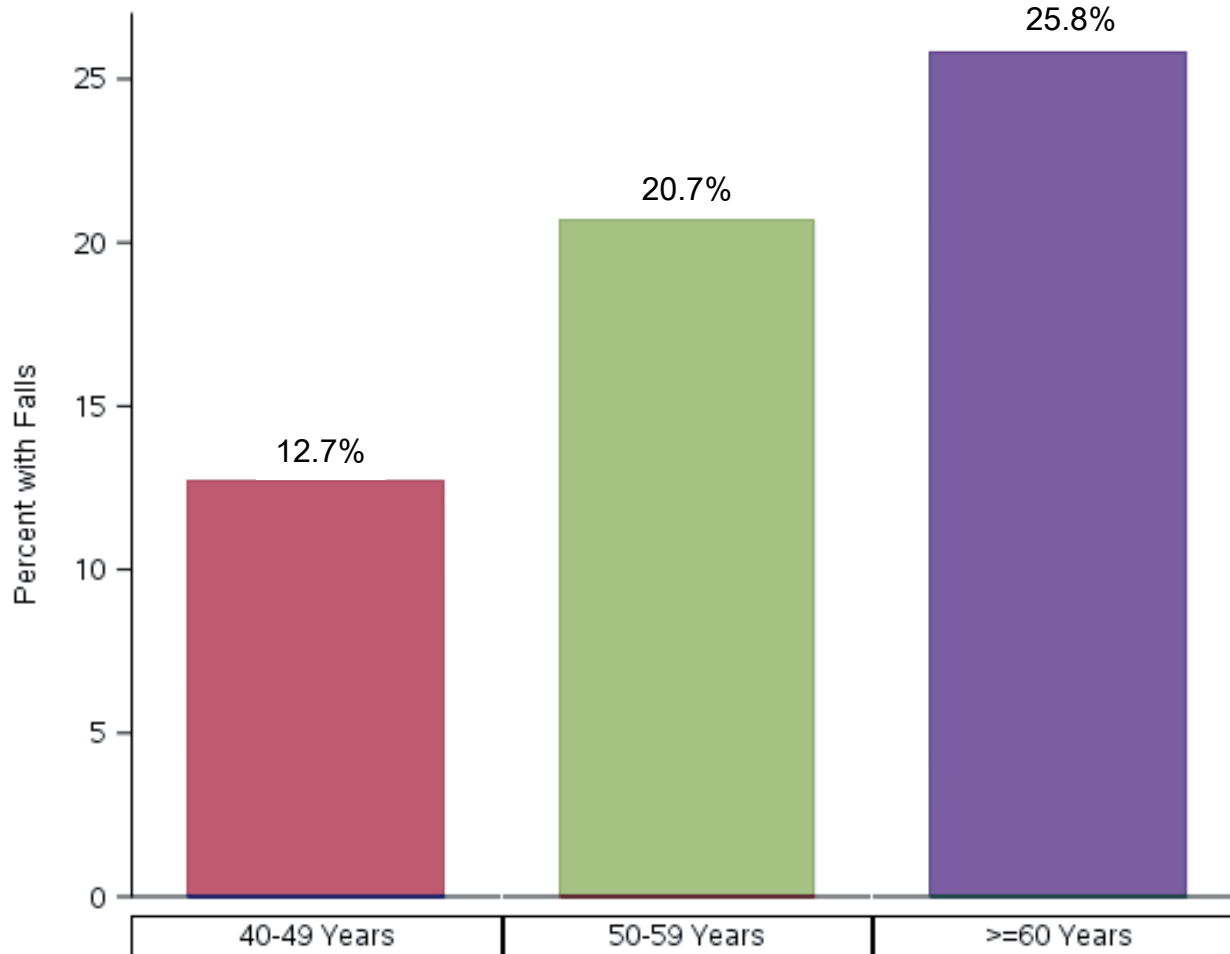
Entry Characteristics	N=967
Median (Q1, Q3) age, years	51 (46-56)
Female	19%
White, non-Hispanic	48%
HIV-1 RNA <50 copies/ml	92%
CD4 count (cells/mm <sup>3</sup> )	
≤ 500	32%
501-700	28%
> 700	40%

# Results: Occurrence of Falls

<b>All Participants</b>	<b>N=967</b>
Participants with any (1+) falls over 12 months	174 (18.0%)
Participants with recurrent (2+) falls	68 (7.0%)
<b>Participants with 1+ Falls</b>	<b>N=174</b>
Sought medical attention for fall	36 (20.7%)
Fall resulted in fracture	9 (5.2%)

# Results: Falls by Age

## Percent of Participants with Any Fall through Week 48 by Age

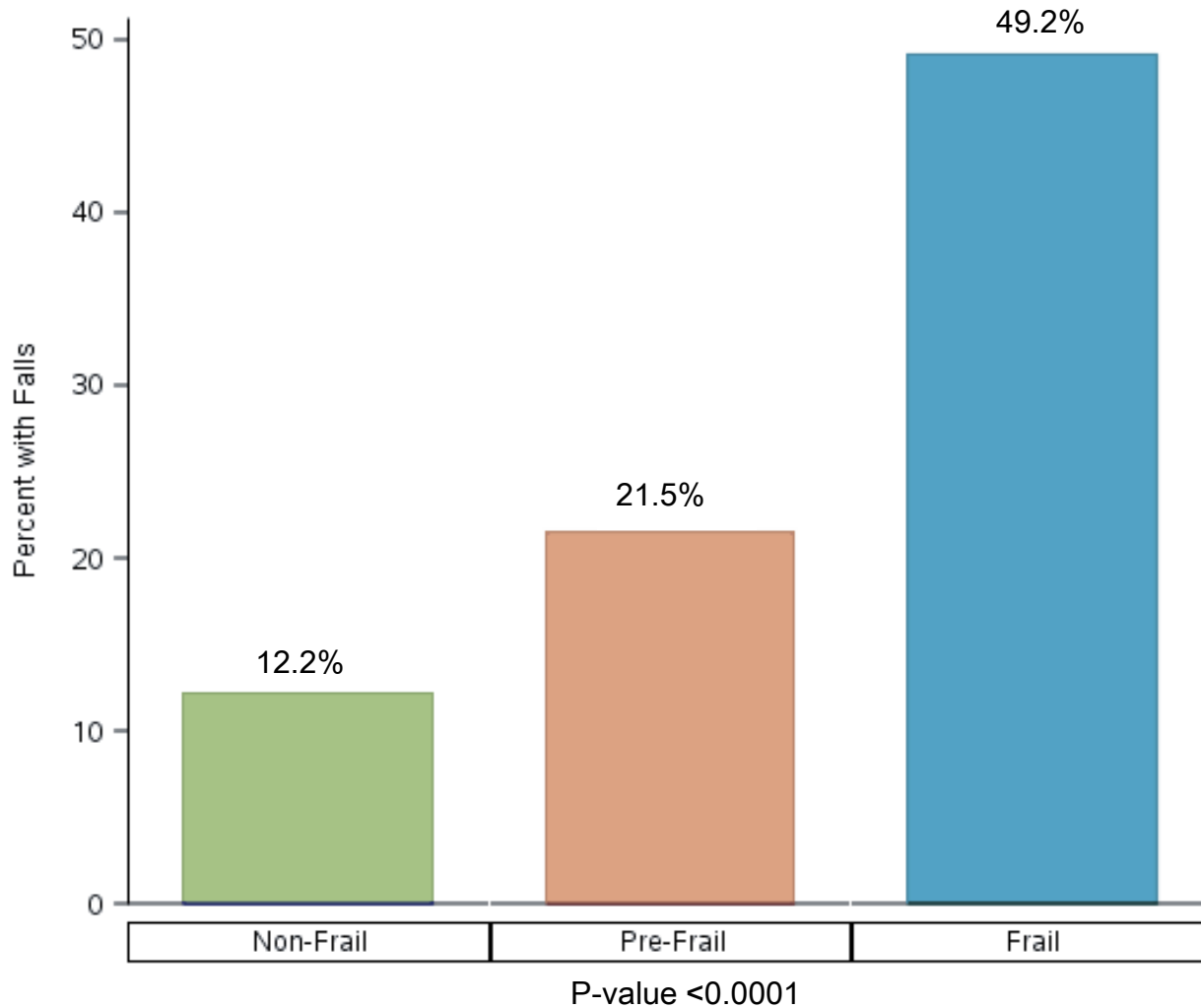


P-value = 0.0003

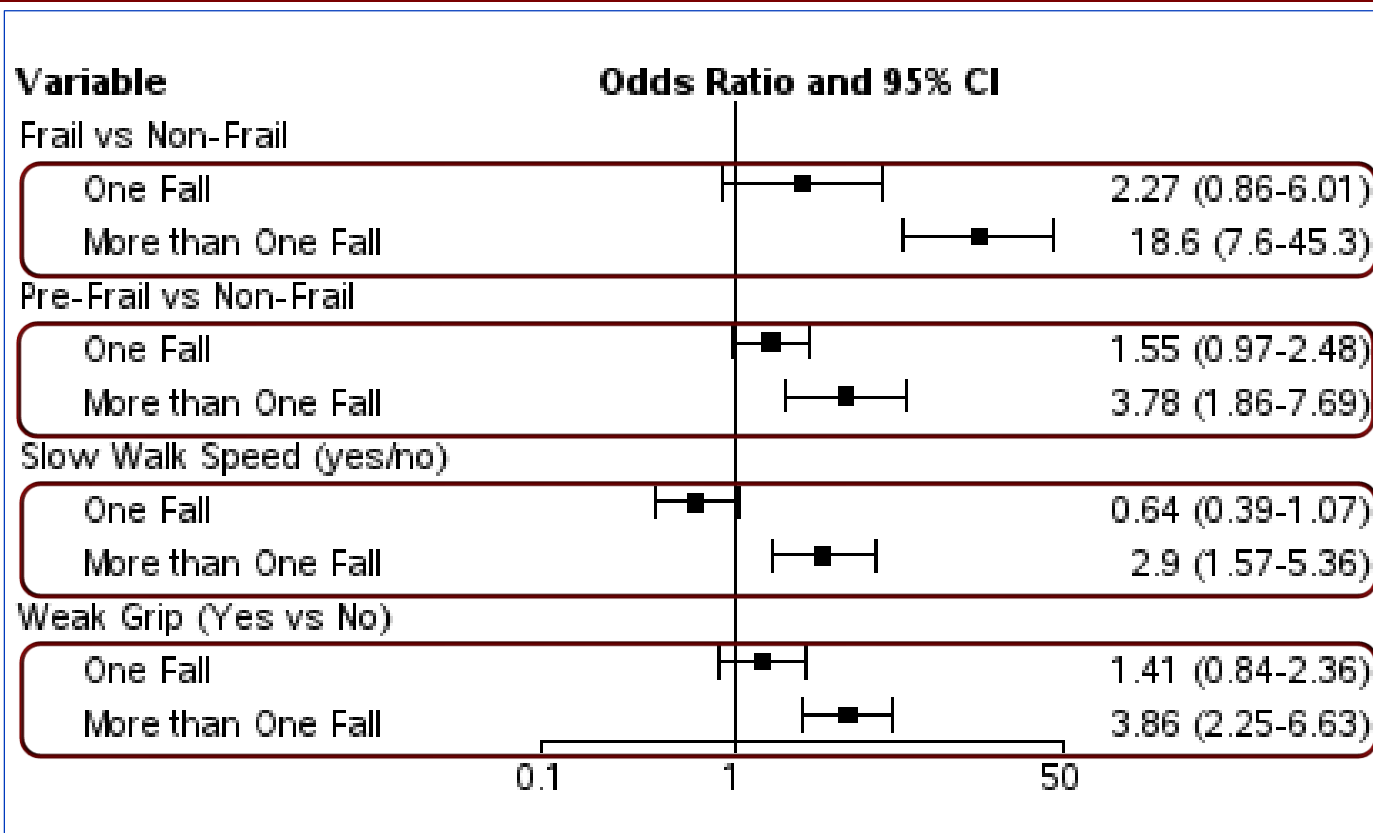


# Results: Falls by Frailty Status

## Percent of Participants with Any Fall through Week 48 by Frailty Status



# Results: Multivariable Associations between Frailty Measures and Falls



Frailty and pre-frailty associated with both single and recurrent falls

Slow walk speed and weak grip associated with recurrent falls only

**Frailty-Falls** models adjusted for: age, race/ethnicity, alcohol use, neuroscreen score

**Walk-Falls** models adjusted for: age, race/ethnicity, alcohol use, neuroscreen score, health insurance, education

**Grip-walk** models adjusted for: age, race/ethnicity, alcohol use, substance use, physical activity, diabetes, and health insurance

# Summary

- ▣ Aging HIV-infected pre-frail and frail individuals are at significantly increased risk of falls
- ▣ Individual components of frailty assessment may be useful predictors of recurrent falls
- ▣ Incorporation of frailty assessments or simple assessments of 4-m walk or grip strength in the clinical setting may help identify older HIV-infected individuals at increased risk for falls and persons who would benefit from falls prevention interventions

# Acknowledgements

**The A5322 / HAILO Participants, Sites and Study Team**

**The AIDS Clinical Trials Network**

**NIAID AI 036219 and U01AI068636**