

Geriatric Syndromes in HIV

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Talk outline

- ▶ Geriatric syndromes / function
- ▶ Frailty
- ▶ Falls
- ▶ Fragility fractures / osteoporosis

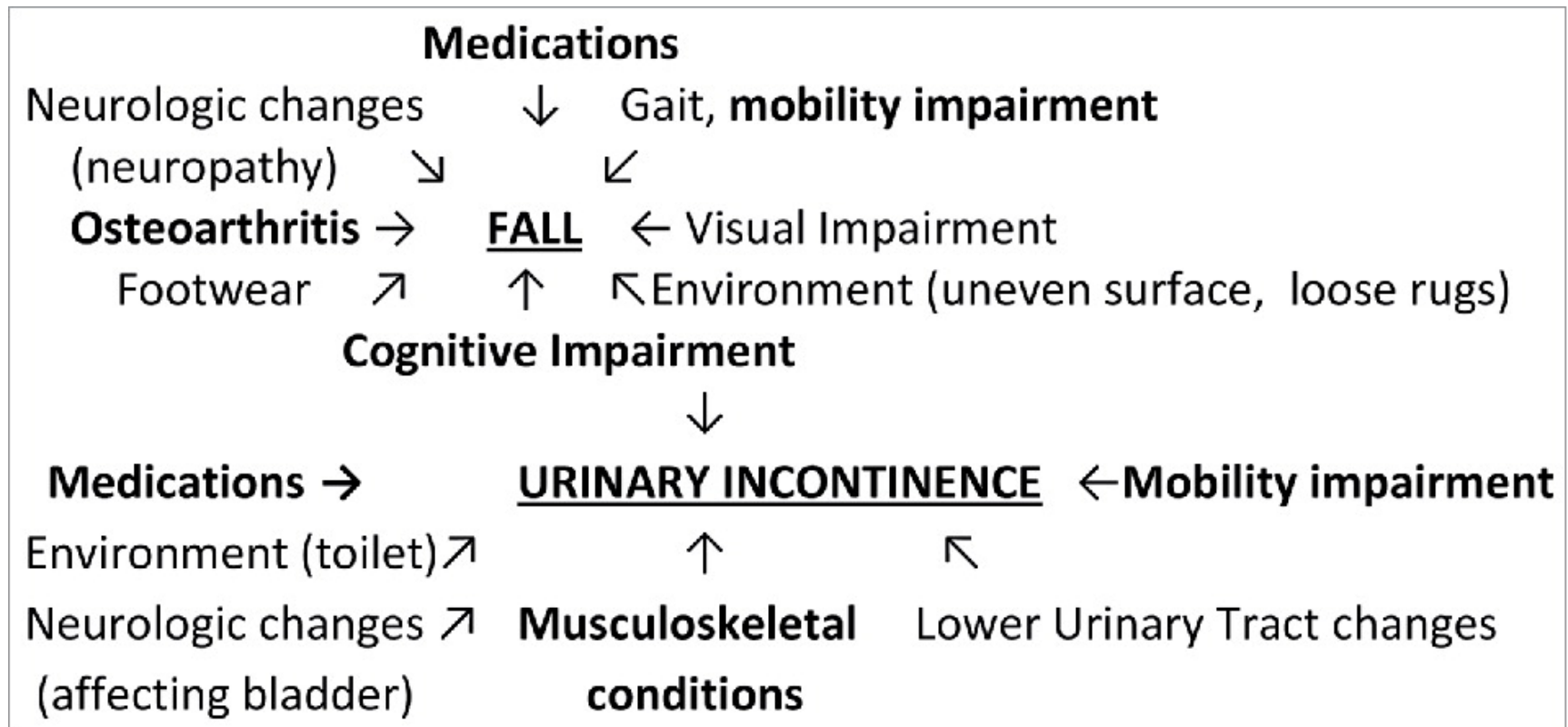
Geriatric Syndromes

“Multifactorial conditions that result from deficits in multiple domains including clinical, psychosocial and environmental vulnerabilities. They provide ‘evidence’ of aging”

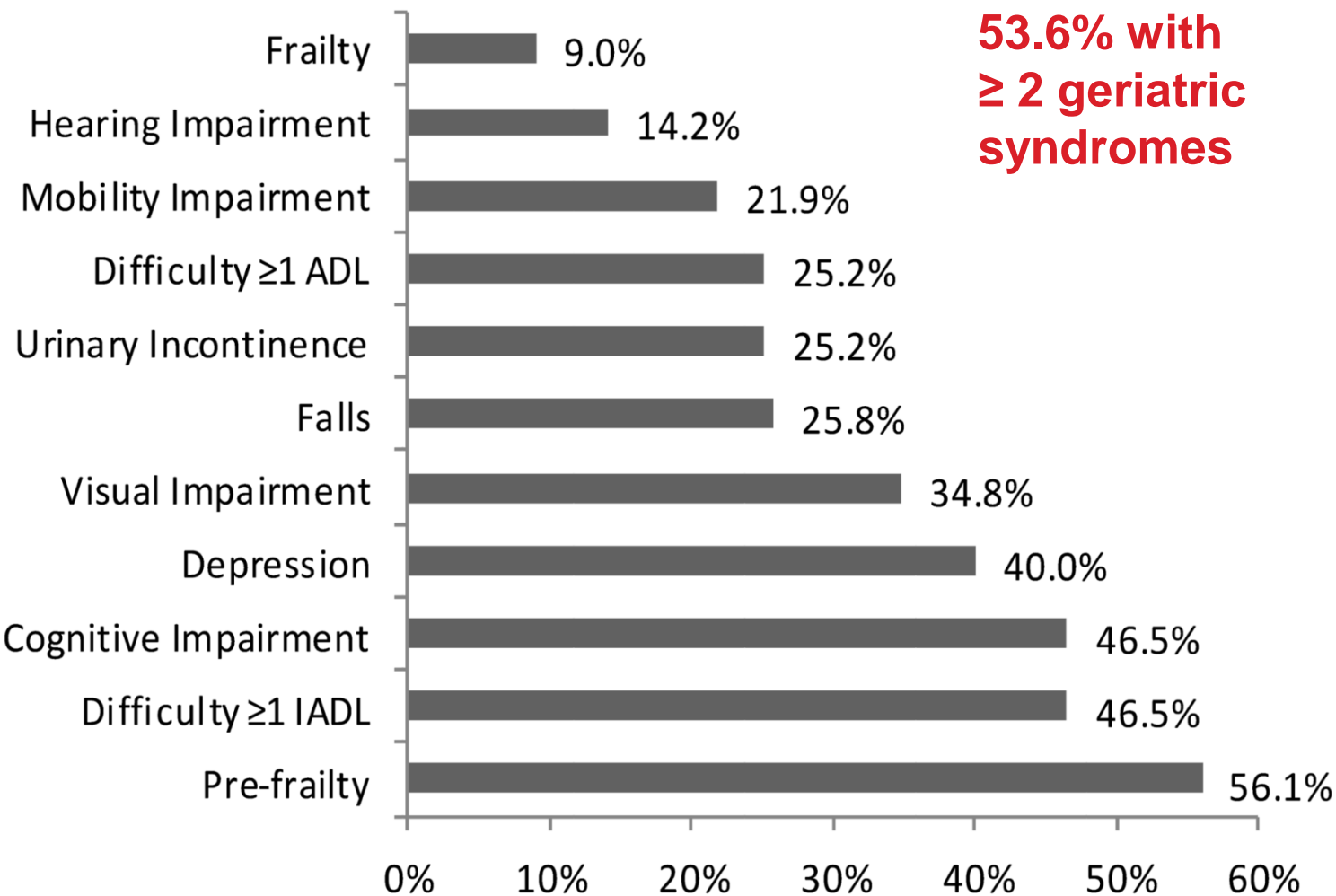
- ▶ Frailty
- ▶ Gait Instability/Falls
- ▶ Cognitive impairment
- ▶ Urinary incontinence
- ▶ Pressure ulcers
- ▶ Delirium

Greene M, Covinsky K, Valcour V et al. Geriatric Syndromes in Older HIV-Infected Adults. JAIDS. 2015; 69: 161-167.

Geriatric syndromes share risk factors



Geriatric Syndromes in an older HIV-infected San Francisco cohort



N=155
 Median:
 Age 57
 CD4 577
 HIV < 400
 (100%)
 CD4 nadir 172
 HIV + 22 years

Age in quartiles

50-54	25.8%
55-59	39.4%
60-64	15.5%
65+	19.4%

Functional Assessment

Basic and Instrumental Activities of Daily Living (ADLs)

ADL

Ambulation (Transferring)

Bathing

Eating

Dressing

Grooming

Toilet



IADL

Finances

Food Preparation

Housekeeping

Laundry

Medication

Shopping

Telephone

Transportation



Rated as independent > needs assistance > dependent

Why do we care about function?

- ▶ In older adults (HIV-) ADL impairment predicts
 - Falls
 - Depression
 - Perioperative outcomes
 - Institutionalization (dependence ≥ 2 ADLs)
 - Death
 - ADL dependence = 27% two/yr mortality
 - Institutionalized > 40% two/yr mortality
- ▶ A functional assessment allows for focusing on potentially fixable problem areas

Frailty

“You know it when you see it”

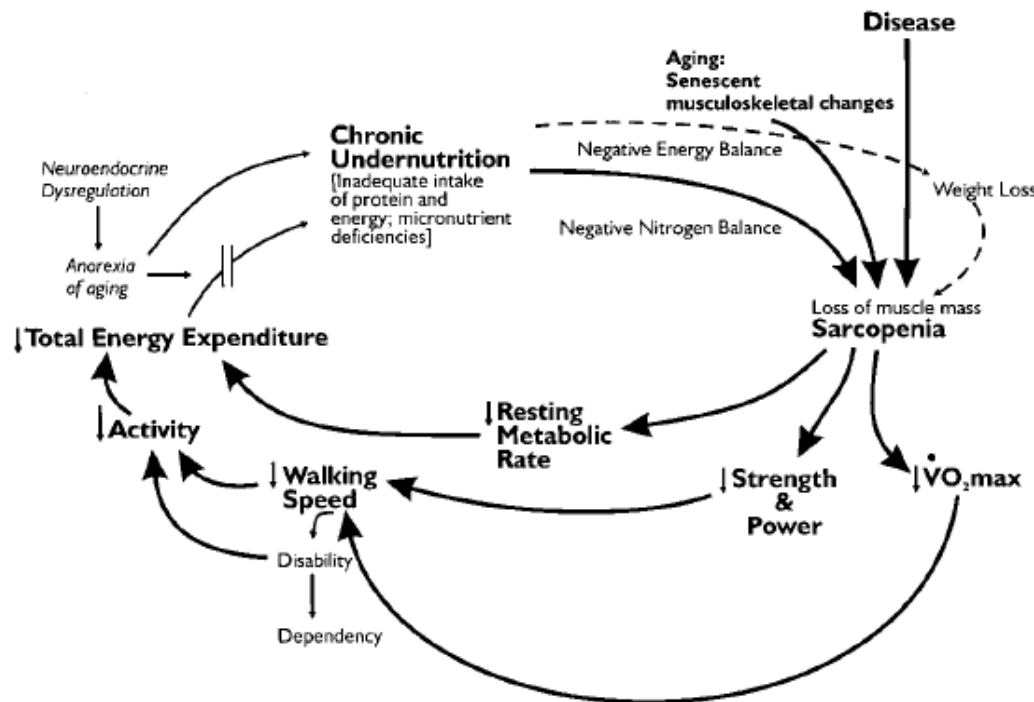
Frailty

- ▶ Consensus definition: “A medical syndrome with multiple causes and contributors that is characterized by diminished strength; endurance and reduced physiological function that increases an individual’s vulnerability for developing increased dependency or death”

Demonstration of the Frailty Phenotype

▶ Data taken from Cardiovascular Health Study

- prospective
- 70-year-old
- Four clinical
- Exclusion
- Baseline
- Outcome
- mortality
- ▶ Hypothesis
- frailty
- strength
- activity
- Multiple components must be present clinically to constitute frailty



community
assessants
sability;
mass,
d low

Demonstration of the Frailty Phenotype (Definition)

Presence of 3 or more of the following:

1. Shrinking

- unintentional ≥ 10 lbs weight loss in past year
- $\geq 5\%$ weight loss at a one year f/u visit

2. Weakness

- Lowest quartile of grip strength (stratified by gender and BMI)

3. Slowness

- Walking 15 feet in ≥ 6 or 7 seconds (stratified by gender and height)

Demonstration of the Frailty Phenotype (Definition)

Presence of 3 or more of the following

4. Poor endurance and energy

- Self-reported exhaustion (CES-D scale)
- “How often in the last week did you feel that....
..everything you did was an effort?”
..you could not get going?”

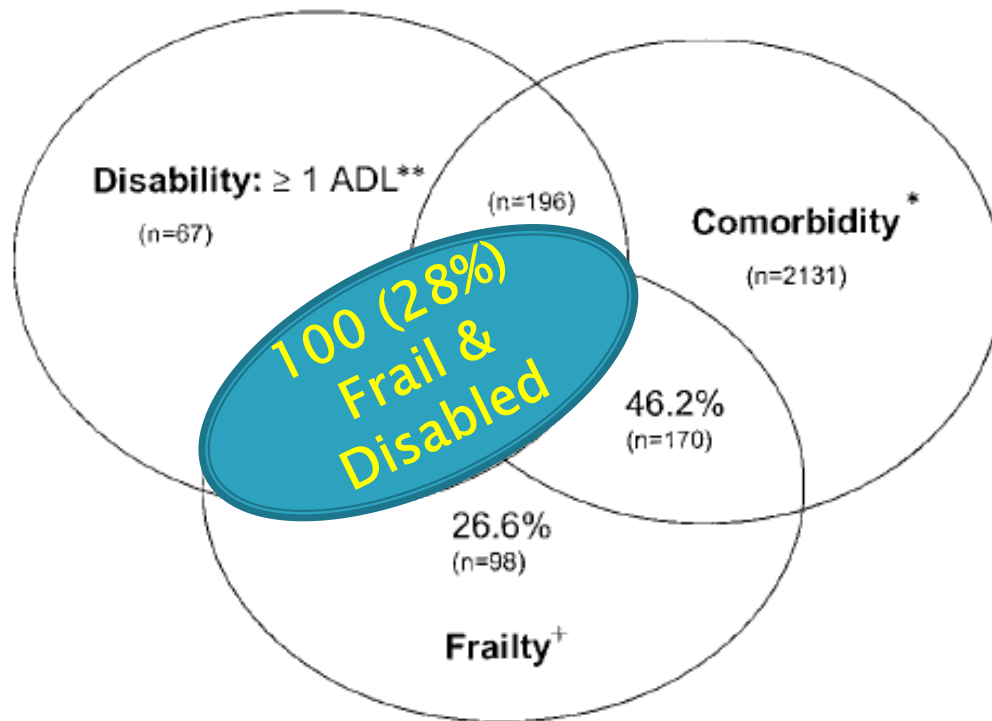
5. Low physical activity

- Self report of activity/kilocalories expended per week (MN Leisure Time Activities Questionnaire)
- Lowest quintile identified for each gender

Demonstration of the Frailty Phenotype (Results)

- ▶ N=5317; 58% F; 15% AA; 65 – 101 yrs
- ▶ Baseline frailty 7% (46% not frail)
- ▶ Frailty more frequently seen with
 - Increase in age (5-year age groups)
 - Women vs men (2-fold)
 - African Americans
 - Depression
 - Cognitive impairment
 - Lower income
 - Higher rates of comorbidities
 - Higher rates of disability (Stepwise increase in disability with increasing frailty status, $p < .001$)

Frailty and Disability: *Overlapping but not Equivalent Concepts*



N = 2762

+ Frail, n=368

* Comorbidity (≥ 2 disease)
n=2576

** Disabled, n=363

*Comorbidity: ≥ 2 of MI, angina, CHF, claudication, arthritis, cancer, DM, HTN, COPD.

Demonstration of the Frailty Phenotype (Results)

- ▶ Frailty independently predicted
 - At 3 years:
 - Worsening mobility (HR 1.50; $p < .0001$)
 - Worsening ADL disability (HR 1.98; $p < .0001$)
 - Incident falls (HR 1.29; $p = 0.54$)
 - Incident hospitalizations (HR 1.29; $p = .004$)
 - Death (HR 2.24; $p = .0001$)
 - At 7 years:
 - HR for all outcomes ranged 1.92–4.46 ($p < .05$; except falls $p = .064$)
- ▶ Odds of becoming “Frail” from “Pre-frail” (1 or 2 components) over 3 years is 2.63.

Using a Frailty-related phenotype (FRP) in HIV-infected MSM during the pre-HAART era (MACS)

Frailty components and corresponding Items collected

1. Physical shrinking

- “Since your last visit, have you had unintentional weight loss of at least 10 pounds?”

2. Exhaustion (SF-36)

- “During the past 4 weeks, as a result of your physical health, have you had difficulty performing your work or other activities (for example, it took extra effort)?”

3. Slowness (SF-36)

- “Does your health now limit you in walking?”

4. Low physical activity level (SF-36)

- “Does your health now limit you in vigorous activities, such as running, lifting heavy objects, participating in strenuous sports?”

5. Weakness (not included in the MACS questionnaire)

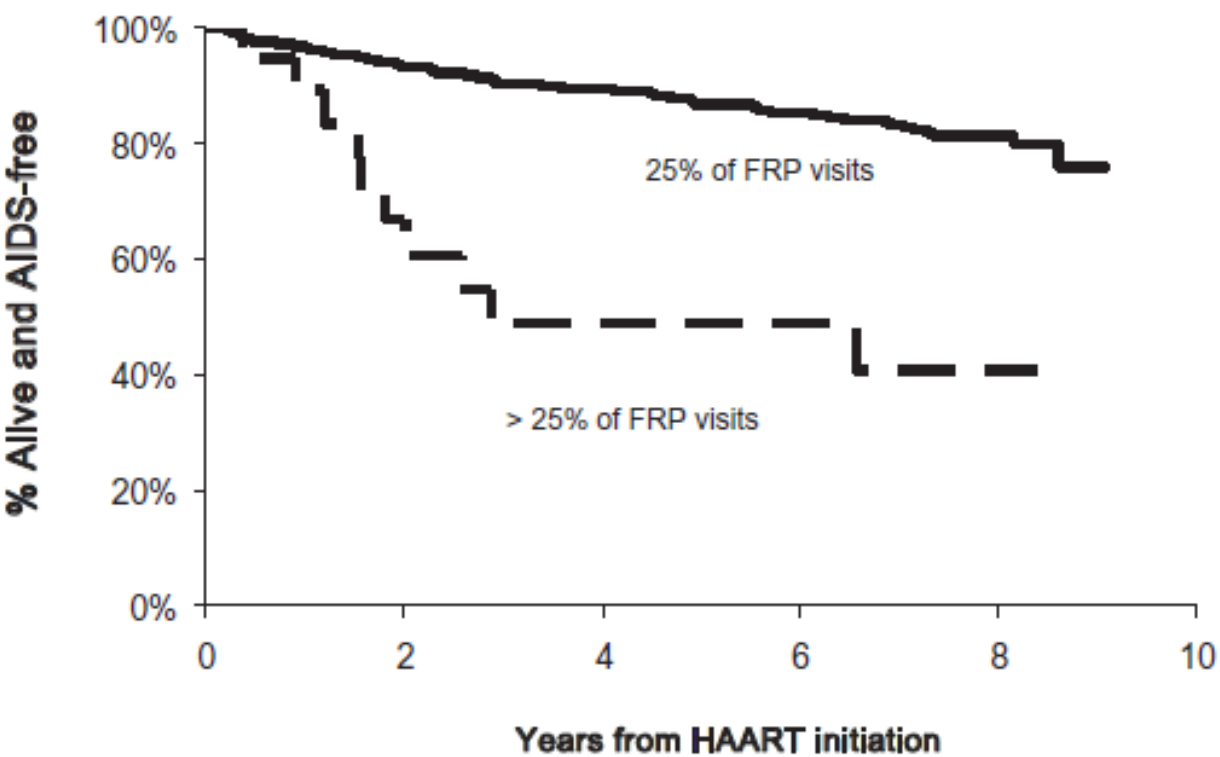
Frailty-related
phenotype (FRP) =
3 or 4 components

Frailty-related phenotype (FRP) in HIV-infected MSM during the pre-HAART era (MACS)

- ▶ **FRP prevalence examined at baseline and at follow up visits**
 - HIV negative (04/01/94–11/1/2004)
 - HIV positive (04/01/94–01/01/96)
- ▶ **FRP occurred 10 years earlier in HIV infected men versus uninfected**
 - FRP of 3.4% occurred at ≥ 55 years for HIV+ and ≥ 65 years for HIV-
- ▶ **Adjusted odds ratio (aOR) 10.97 of expressing FRP (HIV + vs HIV -)**
- ▶ **The longer the duration of HIV infection, the higher odds of FRP**
 - ≤ 4 yrs aOR 3.38
 - 4.01 – 8 yrs aOR 12.95
 - 8.01 – 12 yrs aOR 14.68
- ▶ **Predictors expressing FRP in HIV infected**
 - CD4 < 350
 - VL > 50,000 copies/ml
 - Clinical AIDS **(although 68% of men with AIDS did NOT express FRP)**

Frailty-related phenotype (FRP) as a predictor of AIDS/death in HIV-infected MSM on HAART (MACS)

b



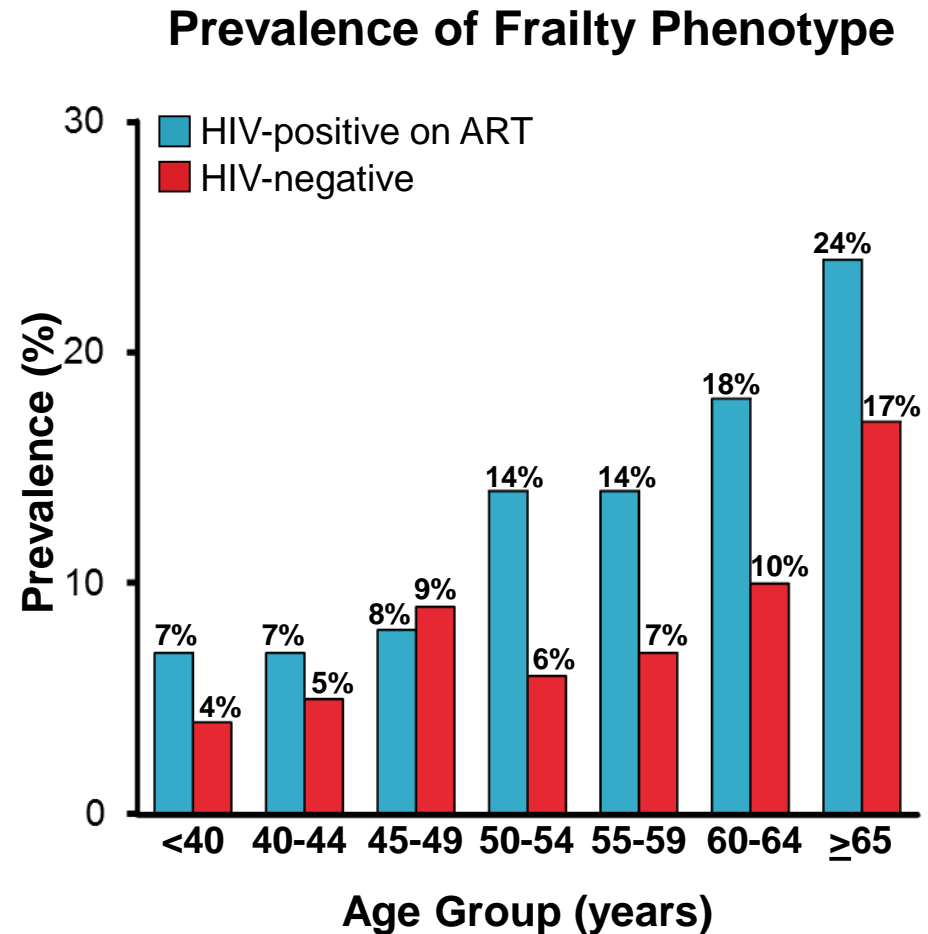
25% of FRP visits pre-HAART predicted AIDS or death

aHR 3.8
p < .01

Kaplan–Meier limit estimates of progression to AIDS-defining illness or death after HAART initiation among 472 men in the MACS who were AIDS-free at HAART initiation, stratified by the percentage of FRP visits in the 3 years before HAART (>25% vs ≤25%).

Frailty phenotype (Fried) in HIV-infected MSM during the HAART era (MACS)

- ▶ Prospective cohort of MSM (2007–2011)
 - 10,571 person-visits
 - HIV positive on ART (n=1946)
 - HIV negative (n=1048)
- ▶ Ages 50 to 64 years
 - Frailty phenotype more common in HIV-positive men versus HIV-negative men
 - May be effect of HIV infection, ART, or both
- ▶ Further longitudinal studies are needed



Other Frailty Instruments Validated in HIV

Frailty Index (Rockwood)

Frail ≥ 0.25

Pre-frail 0.08-0.24

Robust < 0.08

Calculates the proportion of age-related health deficits

Prospective cohort of Italian HIV patients on cART (n=2720)

Independent predictor of

- Survival (HR

1.63)

- Incident multi-morbidity(1.98)

No.	Variable	Deficit description
37-item frailty index		
1	Lipoatrophy	Multicenter AIDS Cohort Study (MACS) criteria [39]
2	Lipohypertrophy	MACS criteria [40]
3	Nonalcoholic fatty liver disease	Liver/spleen ratio < 1.1
4	Menopause or male hypogonadism	If female: FSH > 30 IU/l and LH < 30 IU/l and/or absence of menstruation > 1 year If male: testosterone < 300 ng/dl
5	High or low BMI	< 18 or > 25 kg/m ²
6	High waist circumference	If female: > 88 cm If male: > 102 cm
7	High visceral adipose tissue	VAT > 130 cm ² or VAT/TAT ratio > 0.5
8	Sarcopenia or presarcopenia	Fat-free mass index < -1 SD
9	Insulin resistance	Homeostasis Model Assessment – Insulin Resistance [41] > 2.8
10	High total cholesterol	> 200 mg/dl
11	High low-density lipoprotein	> 100 mg/dl
12	Low high-density lipoprotein	< 40 mg/dl
13	High triglycerides	> 150 mg/dl
14	High homocysteine	If female: > 10 μ mol/l If male: > 15 μ mol/l
15	Abnormal white blood cell counts	< 4000 cells/ μ l
16	Anemia	If female: < 10 g/dl If male: < 12 g/dl
17	Hepatitis C coinfection	Positive
18	Hepatitis B coinfection	Hepatitis B antigen positive
19	Vitamin D insufficiency	< 30 ng/ml
20	Polypharmacy	> 5 drug classes (excluding antiretroviral therapy)
21	Abnormal parathyroid hormone	> 60 pg/ml
22	Elevated D-dimer	$> \text{Sample mean (358)}$
23	Elevated C-reactive protein	> 0.7 mg/l
24	Sedentary lifestyle	< 3 h/week physical activity
25	Atherosclerosis	Coronary artery calcium score > 100 or intima media thickness > 0.85 mm
26	Hyponatremia	< 125 mmol/l
27	Proteinuria or albuminuria	> 5 mg/mmol
28	Elevated aspartate transaminase	> 31 U/l
29	Elevated alanine transaminase	> 31 U/l
30	Abnormal alkaline phosphatase	< 38 or > 126 U/l
31	Elevated γ -glutamyl transphosphatase	> 55 U/l
32	Low platelets	< 150 billion/l
33	Abnormal potassium	< 3.5 or > 5.3 mEq/l
34	Abnormal phosphorus	< 2.5 or > 5.1 mg/dl
35	Abnormal thyroid-stimulating hormone	< 0.27 or > 4.2 mIU/l
36	Elevated total bilirubin	> 1.10 mg/dl
37	Unemployment	Self-report

The Edmonton Frail Scale

Frail ≥ 7

Pre-frail 5-6

Robust 0-4

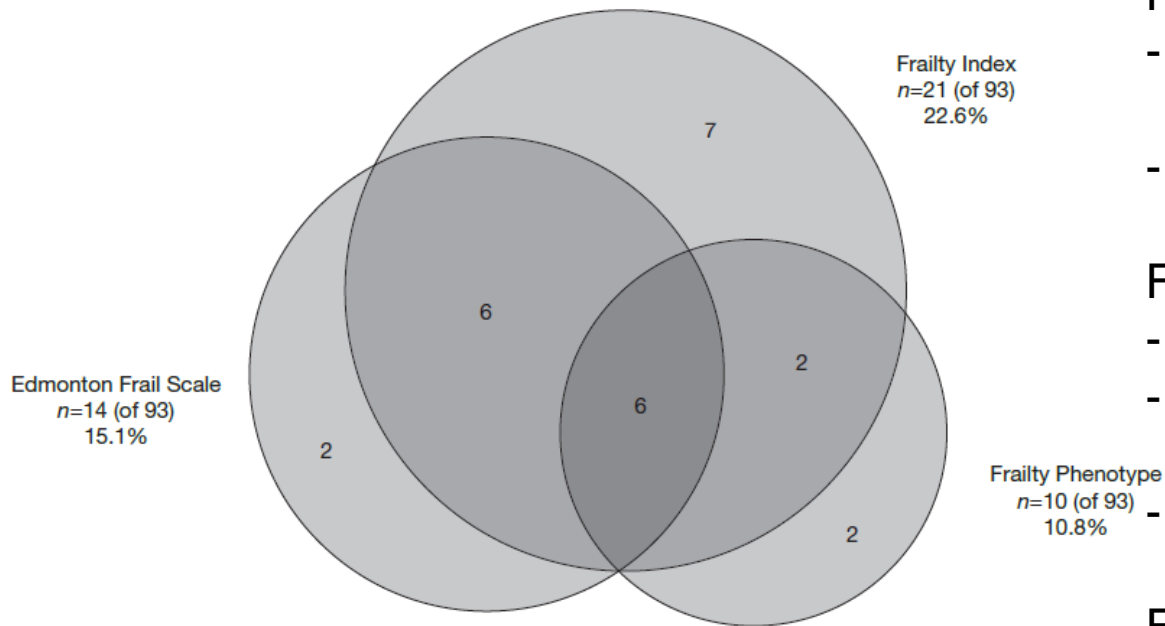
The Edmonton Frail Scale:

Score: ___/17

Frailty domain	Item	0 point	1 point	2 points
Cognition	Please imagine that this pre-drawn circle is a clock. I would like you to place the numbers in the correct positions then place the hands to indicate a time of 'ten after eleven'	No errors	Minor spacing errors	Other errors
General health status	In the past year, how many times have you been admitted to a hospital? In general, how would you describe your health?	0 'Excellent', 'Very good', 'Good'	1-2 'Fair'	≥ 2 'Poor'
Functional independence	With how many of the following activities do you require help? (meal preparation, shopping, transportation, telephone, housekeeping, laundry, managing money, taking medications)	0-1	2-4	5-8
Social support	When you need help, can you count on someone who is willing and able to meet your needs?	Always	Sometimes	Never
Medication use	Do you use five or more different prescription medications on a regular basis? At times, do you forget to take your prescription medications?	No No	Yes Yes	
Nutrition	Have you recently lost weight such that your clothing has become looser?	No	Yes	
Mood	Do you often feel sad or depressed?	No	Yes	
Continence	Do you have a problem with losing control of urine when you don't want to?	No	Yes	
Functional performance	I would like you to sit in this chair with your back and arms resting. Then, when I say 'GO', please stand up and walk at a safe and comfortable pace to the mark on the floor (approximately 3 m away), return to the chair and sit down'	0-10 s	11-20 s	One of >20 s patient unwilling, or requires assistance
Totals	Final score is the sum of column totals			

Comparing three frailty instruments

While significant associations differed according to the instrument used, frailty was associated with poorer quality of life on all three



N = 100

Australian men 50+ with HIV on
cART > 6 months

Frailty phenotype

- pre-1996 ART initiation(OR 3.56)
- Depression (OR 3.74)

Frailty index

- Osteoporosis (OR 4.84)
- Serious non-AIDS events (OR 4.27)
- AIDS (4.62)

Edmonton Frail Scale

- Osteoporosis (OR 7.51)
- Serious non-AIDS events (OR 7.71)
- AIDS (8.53)

Veterans Aging Cohort Study (VACS) Index

- ▶ Clinically feasible measure of frailty validated in veteran and non-veteran populations in N. America and Europe
- ▶ Demonstrated generalizable predictive accuracy
 - ▶ All cause mortality (Justice et al. 2013)
 - ▶ Cause-specific mortality (Tate et al., 2013)
 - ▶ Hospitalization (Akgun et al., 2013)
 - ▶ MICU admits (Akgun et al., 2013)
 - ▶ Fragility fractures (Womack et al., 2013)
- ▶ Associated with:
 - ▶ Cognitive performance (Franklin et al, 2013)
 - ▶ Functional performance (Erlandson et al., 2013)

VACS index

Creates a score by summing pre-assigned points for

- ▶ Age
- ▶ HIV parameters
 - ▶ CD4/HIV VL
- ▶ Hemoglobin
- ▶ End organ damage
 - Kidney disease (eGFR)
 - Advanced liver fibrosis (FIB-4)
- ▶ HCV co-infection (ever)

Table 1. The VACS Index

Component	Level	Points
Age (years)	<50	0
	50 to 64	12
	≥ 65	27
CD4 (cells/mm ³)	≥ 500	0
	350 to 499	6
	200 to 349	6
	100 to 199	10
	50 to 99	28
	< 50	29
HIV-1 RNA (copies/ml)	< 500	0
	500 to 1x10 ⁵	7
	≥ 1x10 ⁵	14
Hemoglobin (g/dL)	≥ 14	0
	12 to 13.9	10
	10 to 11.9	22
	< 10	38
FIB-4	< 1.45	0
	1.45 to 3.25	6
	> 3.25	25
eGFR (mL/min)	≥ 60	0
	45 to 59.9	6
	30 to 44.9	8
	< 30	26
Hepatitis C Co-Infection		5

FIB-4 = age [yr] x AST/platelet x ALT

eGFR = 186.3 x (Cr)^{-1.154} x (age)^{-0.203} x (0.742 for woman) x (1.21 if black)

VACS Index

<https://vacs.med.yale.edu/calculator/IC>

VACS Index Calculator

Age:

Sex:

Race:

CD4:

HIV-1 RNA:

Hemoglobin:

AST (SGOT):

ALT (SGPT):

Platelet count:

FIB-4:

Serum Creatinine:

eGFR:

Hepatitis C:

VACS index: **5 Year Mortality:**

Five year mortality.

On average, if 100 people with HIV infection taking antiretroviral treatment had this VACS Score, 86 of them would be alive 5 years from now and 14 would be dead.

Close

Last comments on Frailty

- ▶ There are 3 main frailty instruments used by HIV aging researchers (Fried's Phenotype; Frailty Index; VACS)
- ▶ No matter what instrument used, the presence of frailty predicts poor outcomes in both HIV infected and uninfected
- ▶ Individual clinicians are left to decide which frailty instrument they want to incorporate in their daily practice, and how it will affect their patient's treatment plan

Falls

Falls in the elderly (> 65)

- ▶ 30 – 40% of community dwelling older adults fall at least once/year
- ▶ 30% of falls leading to fracture occur during transfers (bed to chair/wheelchair to toilet)
- ▶ **People who have fallen before are at higher risk to fall again (OR 1.5 – 6.7)**
- ▶ **Falls are the most common cause of decline and inability to care for oneself (e.g. SNF/LTC care)**

Falls in HIV–infected Older Adults

- ▶ HIV infected older adults are more likely to have conditions associated with falls than HIV uninfected (cognitive impairment, frailty, polypharmacy)
- ▶ Predictors of falls in HIV+ women include depression (2.63), peripheral neuropathy (OR 2.37), number of CNS active agents (3.74 if ≥ 3 agents), illicit drugs (2.70)
- ▶ Slow gait speed and poor physical performance in older HIV+ men suggests increase risk of falls and functional decline

Falls in HIV–infected Older Adults (HAILO)

- ▶ Longitudinal cohort study of 1035 HIV–infected adults 40 years or older at enrollment in ACTG clinical trials (HAILO)
- ▶ Outcomes
 - ▶ Any falls over one year period*

“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.”
 - ▶ Single and recurrent (2+) falls over one year period

**Excluded falls from a major medical event/overwhelming external hazard*

Falls in HIV–infected Older Adults (HAILO)

- ▶ Data collection
 - ▶ Frailty Assessment (Modified Fried's)
 - 4-meter timed walk, grip strength, self reported unintentional weight loss, exhaustion, low activity
 - Frail (3 -5); pre-frail (1 or 2); not frail (0)
 - ▶ Falls questionnaire
 - Any falls in past 6 months? If yes: How many? (1, 2, 3-5, 6+); Required medical attention? Resulted in broken bone(s)?

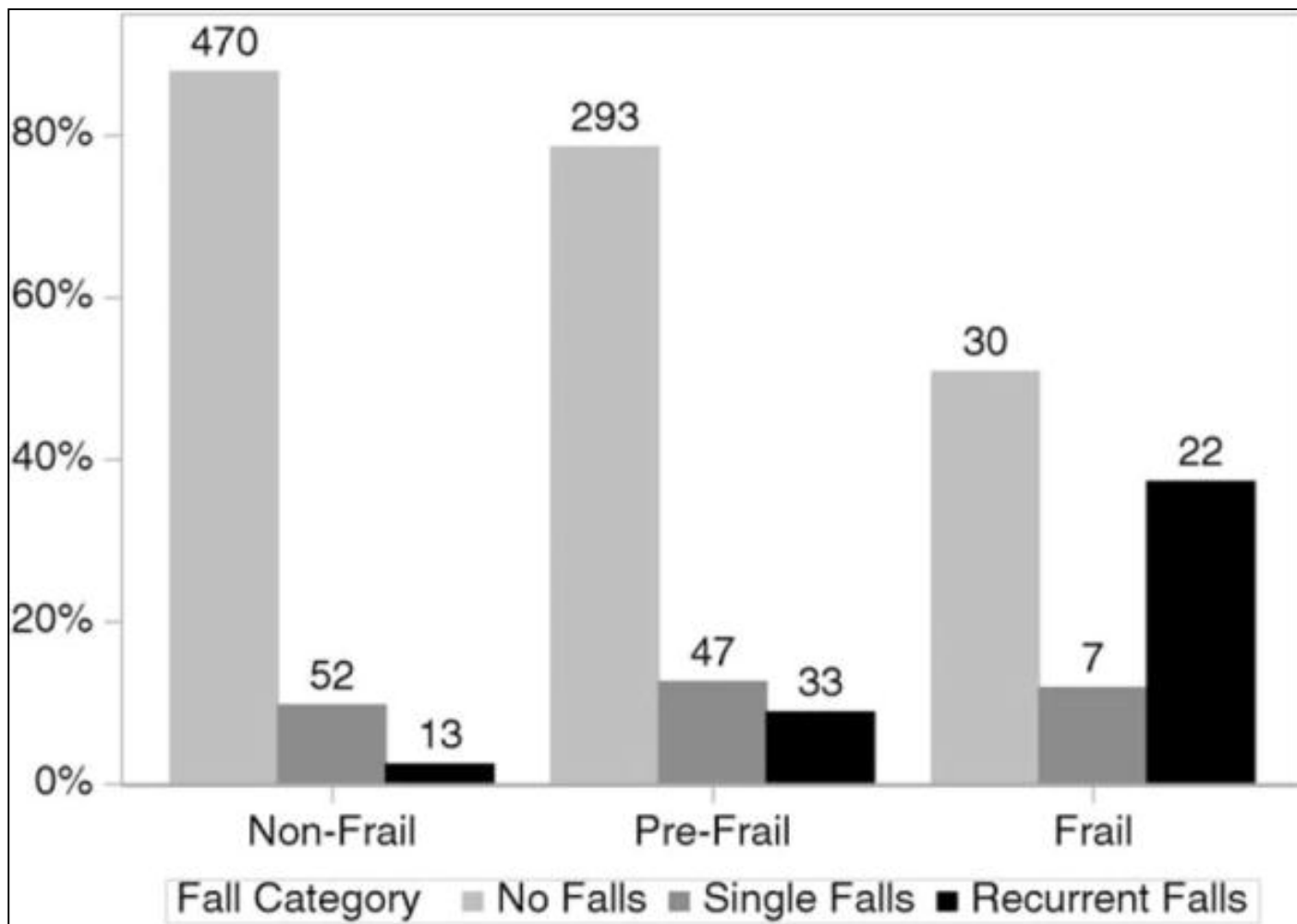
Falls in HIV-Infected Older Adults (HAILO)

93% of HAILO participants completed a frailty assessment at entry visit and a falls interview at 6 and 12 months

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

Median age 51 yrs; 19% F; 48% White; 68% CD4 > 500; 92% VL < 50

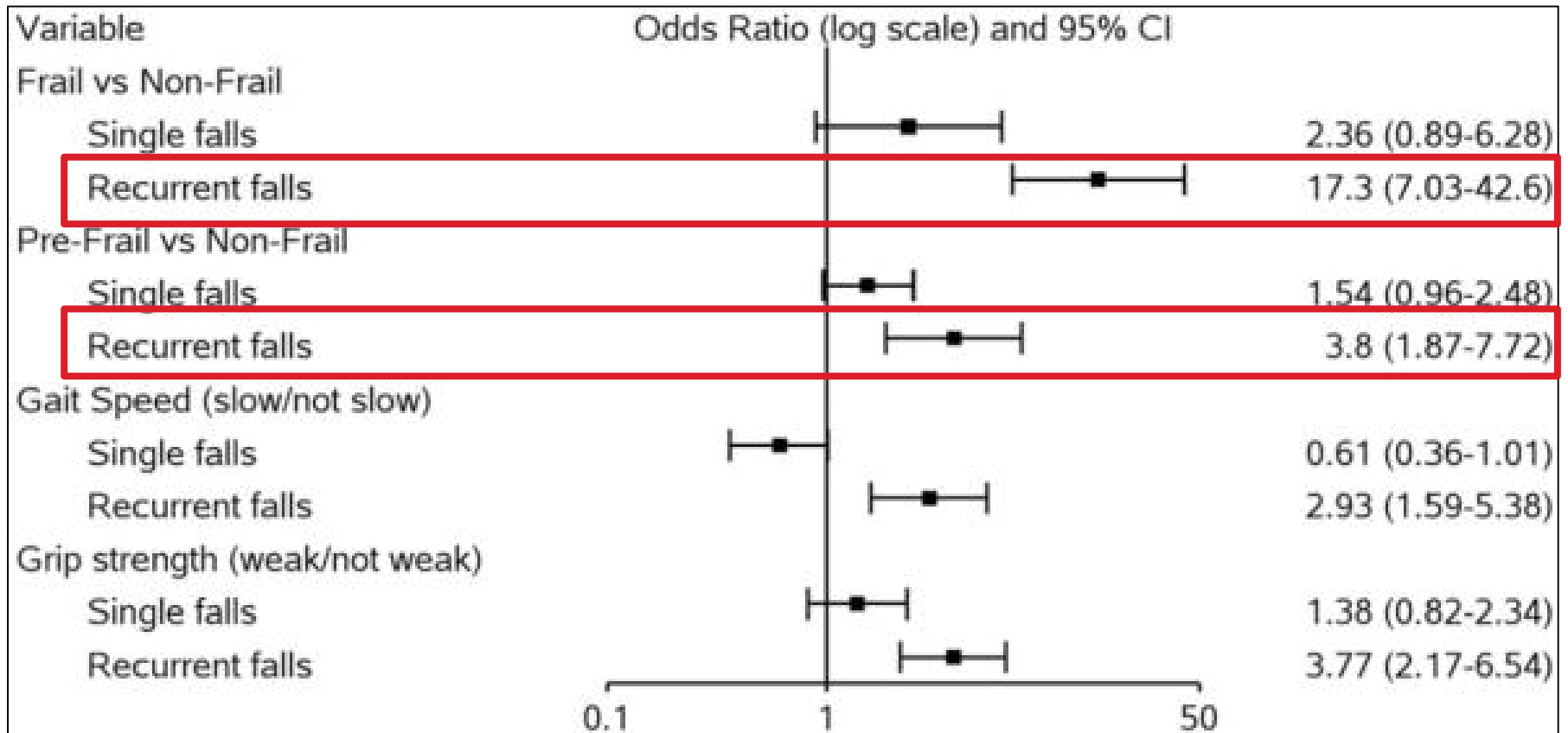
Results (HAILO): Proportion of patients with single and recurrent falls by baseline frailty status.



Frailty is strongly associated with increased risk of recurrent falls among older HIV-infected adults.

Tassiopoulos, Katherine; Abdo, Mona; Wu, Kunling; Koletar, Susan; Palella, Frank; Kalayjian, Robert; Taiwo, Babafemi; Erlandson, Kristine

Results (HAILO): Multivariable Associations between Frailty Measures and Falls



Frailty is strongly associated with increased risk of recurrent falls among older HIV-infected adults.

Tassiopoulos, Katherine; Abdo, Mona; Wu, Kunling; Koletar, Susan; Palella, Frank; Kalayjian, Robert; Taiwo, Babafemi; Erlandson, Kristine

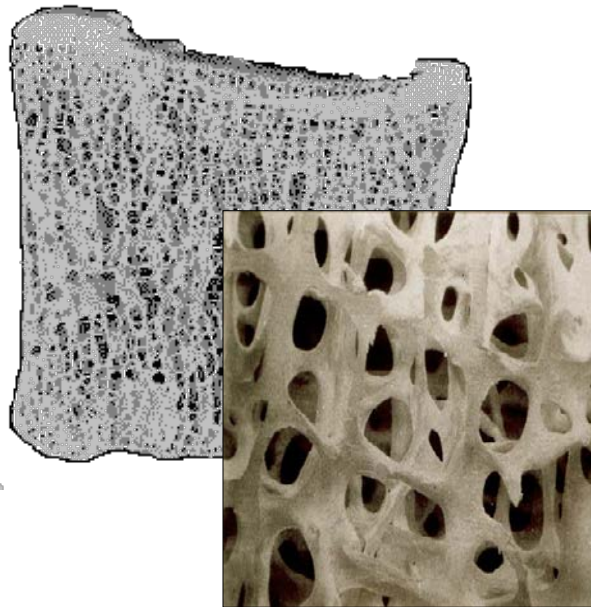
Fragility fractures and Osteoporosis

Fragility fractures

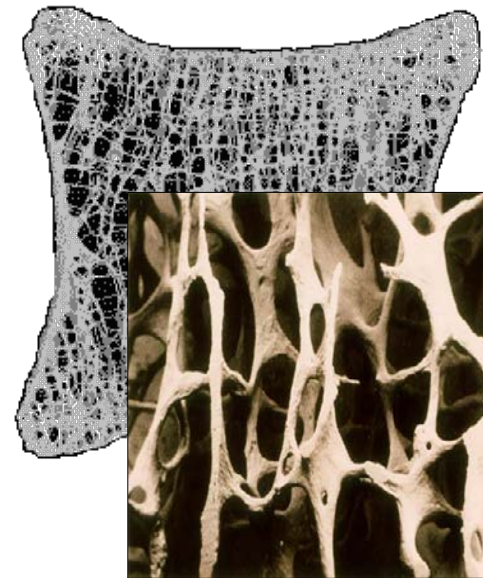
- ▶ A fracture caused by an injury that would be insufficient to fracture normal bone.
 - i.e. A fracture resulting from a fall from a standing height or less, or presenting in the absence of obvious trauma.
- ▶ 20 – 30% of people falling suffer moderate to severe injuries such as hip fractures
- ▶ Elderly sustaining hip fractures
 - 12 month mortality rates ranges from 12 to 37 % (> 90 % if not repaired)
 - 50% of patients are unable to regain their ability to live independently

Osteoporosis

“systemic skeletal disorder characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and fracture.”



Normal vertebral body



Osteoporotic vertebral body

US National Osteoporosis Foundation (NOF) Guidelines for DEXA Screening

- ▶ Those with a fragility fracture after age 50
- ▶ Women \geq 65 yrs, Men \geq 70 yrs
- ▶ Younger postmenopausal women and men 50–69 years with clinical risk factors for fracture
- ▶ Adults with a condition (e.g., rheumatoid arthritis) or taking a medication (e.g., glucocorticoids in a daily dose \geq 5 mg prednisone or equivalent for \geq three months) associated with low bone mass or bone loss

Osteoporosis diagnosis (WHO)

- ▶ DEXA (Dual-energy x-ray absorptiometry)
 - Severe osteoporosis: T-score ≤ -2.5 & fragility fracture
 - Osteoporosis: T-score ≤ -2.5
 - Osteopenia: T-score = -1.0 to -2.5
 - Normal: T-score > -1.0

- ▶ Each 1-SD decrement in bone mineral density (BMD) increases fracture risk by 1.5 – 3.0 fold

- ▶ Caveats:
 - Z-score (≤ -2.0) used in men < 50 years and premenopausal women
 - BMD explains only about 50% of fracture risk

T score = patient's BMD c/w that of a young-adult reference population

FRAX

WHO
developed
from
international
cohorts

FRAX[®] Fracture Risk Assessment Tool

Home Calculation Tool Paper Charts FAQ References English

Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: **US (Caucasian)** Name/ID: [About the risk factors](#)


Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth Age: <input type="text"/> Date of Birth: Y: <input type="text"/> M: <input type="text"/> D: <input type="text"/>	10. Secondary osteoporosis <input checked="" type="radio"/> No <input type="radio"/> Yes
2. Sex <input type="radio"/> Male <input type="radio"/> Female	11. Alcohol 3 or more units/day <input checked="" type="radio"/> No <input type="radio"/> Yes
3. Weight (kg) <input type="text"/>	12. Femoral neck BMD (g/cm ²) Select BMD <input type="text"/>
4. Height (cm) <input type="text"/>	<input type="button" value="Clear"/> <input type="button" value="Calculate"/>
5. Previous Fracture <input checked="" type="radio"/> No <input type="radio"/> Yes	
6. Parent Fractured Hip <input checked="" type="radio"/> No <input type="radio"/> Yes	
7. Current Smoking <input checked="" type="radio"/> No <input type="radio"/> Yes	
8. Glucocorticoids <input checked="" type="radio"/> No <input type="radio"/> Yes	
9. Rheumatoid arthritis <input checked="" type="radio"/> No <input type="radio"/> Yes	


For USA use only

Consider FDA-approved medical therapies in postmenopausal women and men aged 50 years and older, based on the following:


- A hip or vertebral (clinical or morphometric) fracture
- T-score ≤ -2.5 at the femoral neck or spine after appropriate evaluation to exclude secondary causes
- Low bone mass (T-score between -1.0 and -2.5 at the femoral neck or spine) and a 10-year probability of a hip fracture $\geq 3\%$ or a 10-year probability of a major osteoporosis-related fracture $\geq 20\%$ based on the US-adapted WHO algorithm
- Clinicians judgment and/or patient preferences may indicate treatment for people with 10-year fracture probabilities above or below these levels




Weight Conversion

Pounds  kg

Height Conversion

Inches  cm

05598843
Individuals with fracture risk assessed since 1st June 2011

Country : **US(Caucasian)** Name / ID : [About the risk factors](#) 

Questionnaire:

1. Age (between 40-90 years) or Date of birth
 Age: Date of birth: Y: M: D:

2. Sex Male Female

3. Weight (kg)

4. Height (cm)

5. Previous fracture No Yes

6. Parent fractured hip No Yes

7. Current smoking No Yes


8. Glucocorticoids No Yes

9. Rheumatoid arthritis No Yes

10. Secondary osteoporosis No Yes

11. Alcohol 3 more units per day No Yes

12. Femoral neck BMD
 T-score

BMI 21.4 

The ten year probability of fracture (%)

with BMD

Major osteoporotic	18
Hip fracture	4.10

Major osteoporotic fracture – fracture of the spine, forearm, proximal humerus or hip

Risk factors used in the calculation of 10-year risk of fracture

- ▶ Femoral neck T-score
- ▶ Age
- ▶ Previous low trauma fracture
- ▶ Low BMI
- ▶ Ever steroid exposure
- ▶ Family history of hip fracture
- ▶ Rheumatoid Arthritis
- ▶ Current cigarette smoking
- ▶ High alcohol intake (> 3 units/day)*
- ▶ Secondary causes of osteoporosis (Vit D/PTH/TSH/?HIV)

*1 unit = 8 gm alcohol ~ ½ pt. beer ~ glass wine

US National Osteoporosis Foundation (NOF) Guidelines: Who to Treat*

- ▶ Those with hip or vertebral fractures
- ▶ Those with BMD T-scores ≤ -2.5 at the femoral neck, total hip, or spine by DXA
- ▶ Those with osteopenia (T-score -1 – -2.5) AND
 - 10-year hip fracture probability $\geq 3\%$ OR
 - 10-year all major osteoporosis-related fracture $\geq 20\%$ based on FRAX model

*applies to post-menopausal women and men ≥ 50 years

Osteoporosis management

▶ General recommendations

- Calcium/vitamin D supplementation
- Smoking cessation, Alcohol reduction
- Weight-bearing exercise
- Assess fall risk (Are you worried about falling?)
- Strength/Balance Training

▶ Treatment options

- Antiresorptives (Inhibits osteoclast mediated bone resorption) *Bisphosphonates*
- Anabolics (Stimulate osteoblasts to form new bone)
Selective estrogen receptor modulator; Estrogen; PTH analogue; monoclonal AB

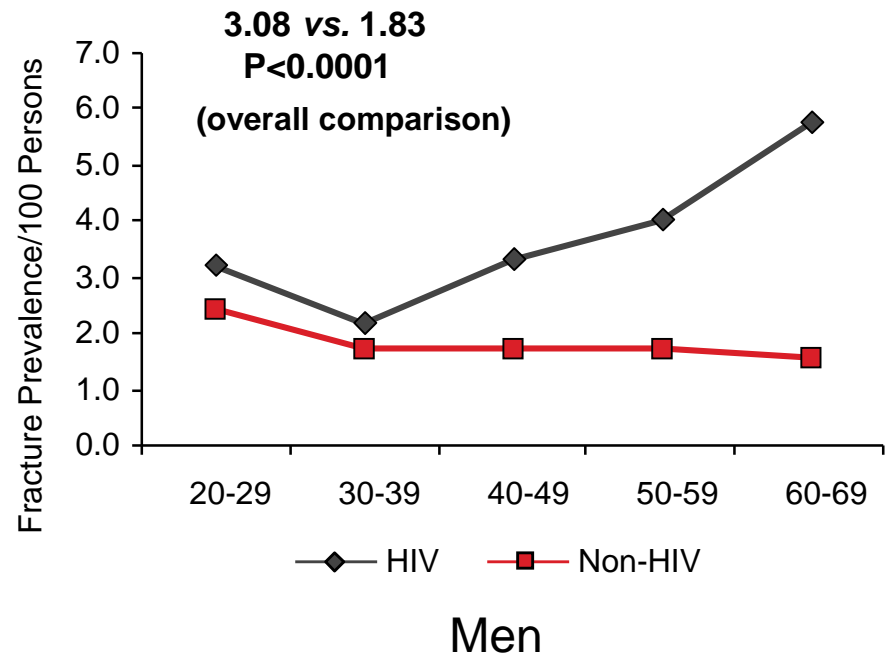
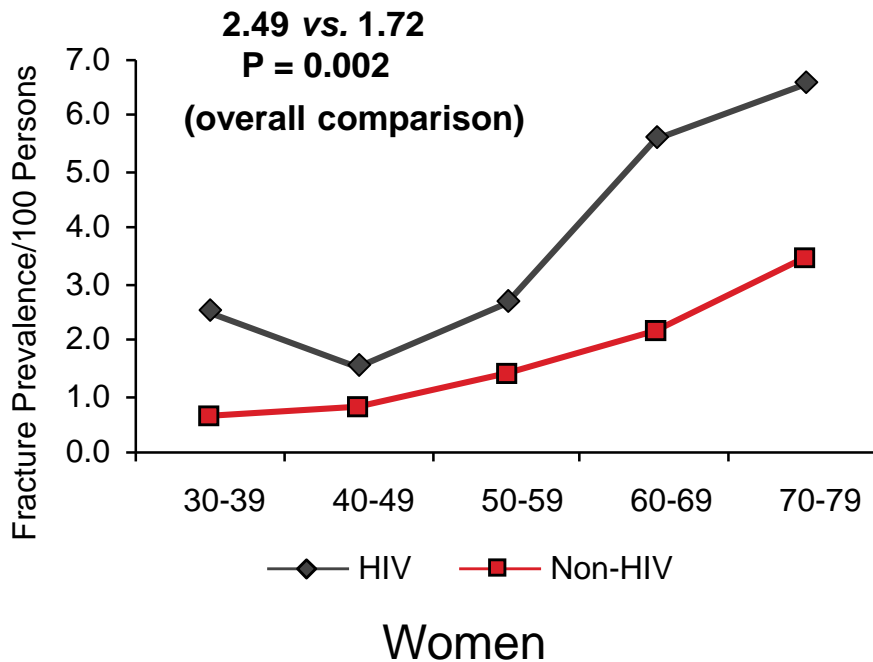
Bisphosphonates

- ▶ Encompass the majority of prescriptions for osteoporosis (alendronate/zolendronic acid)
- ▶ Reduces vertebral & non-vertebral fractures by 25–50% in non-HIV
- ▶ Need to remain sitting up for 30–60 minutes after ingestion (pill esophagitis)
- ▶ Avoid if CrCl <35; clinically significant esophageal disease (achalasia)
- ▶ Severe adverse effects
 - atypical femoral fractures (1 / 100K to 5 / 10K)
 - osteonecrosis of jaw: exposed bone in the maxillofacial region that does not heal within 8 weeks (< 1 / 10K)

Bisphosphonates: Zolendronic Acid

- ▶ Poor adherence to oral bisphosphonates (40% at 1 year)
- ▶ Once yearly infusion of 5 mg (over 15 minutes)
 - 70% reduction of vertebral fractures
 - 41% reduction of hip fractures
 - 25% reduction of non-vertebral fractures
- ▶ Adverse effects
 - 30% of patients with flu like symptoms for up to 3 days after the first infusion (Rare for subsequent infusions)
 - Tylenol reduces incidence by 50% and severity of reactions

Fracture Prevalence in People with and without HIV in MGH/Partners Healthcare System: 1996–2008



8,525 HIV-infected
2,208,792 non HIV-infected patients

Osteoporosis Risk Factors in HIV

▶ Host Factors

- Low Body Weight
- Smoking
- Alcohol Use
- Opiate Use
- Hepatitis C Co-infection
- Physical Inactivity
- Hypogonadism
- Low Vitamin D

▶ HIV Disease Factors

- Inflammation and Viral Proteins causing low BMD
 - ↑ bone resorption
 - ↓ bone formation

▶ Medication Factors

- TDF
- Certain PIs
- ART initiation (↓ BMD by 2–6% over 96 weeks)

Osteoporosis Screening in HIV with DEXA

	Infectious Disease Society of America (IDSA) (2009)	McComsey et al. (2010)	European AIDS Clinical Society (2014)	IDSA/HIV Medicine Association (2014)
DXA indicated	PM women \geq 65	PM women or Men \geq 50	PM women or Men \geq 50	PM women or Men $>$ 50
DXA indicated with following risk factors (partial list)	PM women or Men $>$ 50 with risk factors Fracture Hypogonadal Glucocorticoid CKD Alcohol AED Diabetes		(For age 40–50, perform FRAX)	

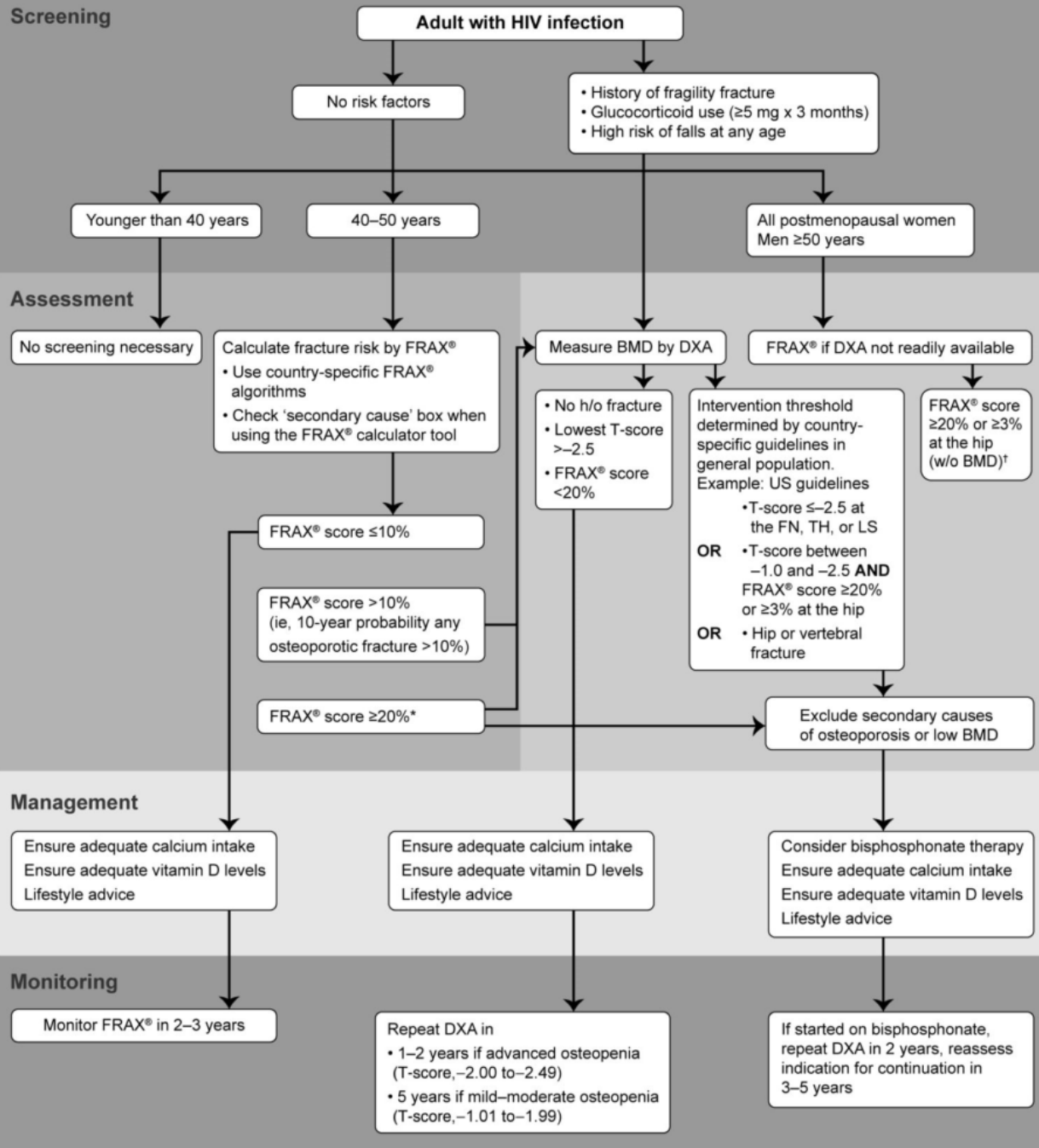
Aberg JA, et al. *Clin Infect Dis.* 2014;58(1):1-10; Aberg JA, et al. *Clin Infect Dis.* 2009;49(5):651-81; Cosman F, et al. *Osteoporos Int.* 2014;25(10):2359-81; European AIDS Clinical Society Guidelines. www.eacsociety.org. Accessed 6/22/16; McComsey GA, et al. *Clin Infect Dis.* 2010;51(8):937-46.

AED = antiepileptic drug; BMD = bone mineral density; CKD = chronic kidney disease; FRAX = fracture risk assessment tool; PM = postmenopausal; PPI = proton pump inhibitors; RA = rheumatoid arthritis

Recommendations for Evaluation and Management of Bone Disease in HIV

Todd T. Brown,¹ Jennifer Hoy,² Marco Borderi,³ Giovanni Guaraldi,⁴ Boris Renjifo,⁵ Fabio Vescini,⁶ Michael T. Yin,⁷ and William G. Powderly⁸

From: Recommendations for Evaluation and Management of Bone Disease in HIV
 Clin Infect Dis. 2015;60(8):1242-1251



^{*}In some countries, persons at high risk of fracture by FRAX® are eligible for further workup/osteoporosis treatment without DXA

[†]Based on US guidelines (National Osteoporosis Foundation). Country-specific intervention thresholds are preferred

Bisphosphonates in HIV

6 RCT in HIV+ subjects in combination with calcium and vitamin D

- ▶ 1st-line treatment to prevent fractures in HIV+ with low BMD or other risk factors for fracture
- ▶ At 2 years
 - Increased lumbar spine BMD by 8%
 - Increased total hip BMD by ~4%
- ▶ No significant drug interactions with ART

Author, year (N)	T-score	Medication (duration)	Spine	Hip
Guaraldi, 2004 (N=41)	< -1.0	Alendronate 70 mg/wk (1 yr)	NS	NS
Mondy, 2005 (N=31)	< -1.0	Alendronate 70 mg/wk (1 yr)	+5.2% vs +1.3%*	NS
McComsey, 2007 (N=82)	< -1.5	Alendronate 70 mg/wk (1 yr)	+3.1% vs +1.1%*	+4.0% vs +1.4% [†]
Rozenberg, 2012 (N=44)	< -2.5	Alendronate 70 mg/wk (2 yrs)	+7.4% vs +4.1%	NS
Bolland, 2007 (N=43)	< -0.5	Zoledronic acid 4 mg/year (2 yrs)	+8.9% vs +2.6% [†]	+3.8% vs -0.8% [†]
Huang, 2009 (N=30)	< -1.5	Zoledronic acid 5 mg/year (1 yr)	+3.7% vs +0.7%*	+3.2% vs -1.8%*

*P < 0.05; [†]P < 0.001; NS = not significant

Guaraldi G, et al. *HIV Clin Trials*. 2004;5(5):269-77; Mondy K, et al. *J Acquir Immune Defic Syndr*. 2005;38(4):426-31; McComsey GA, et al. *AIDS*. 2007;21(18):2473-82; Rozenberg S, et al. *AIDS Res Hum Retroviruses*. 2012;28(9):972-80; Bolland MJ, et al. *J Clin Endocrinol Metab*. 2007;92(4):1283-8; Huang J, et al. *AIDS*. 2009;23(1):51-7.

What to Do to Prevent Bone Loss with ART Initiation?

- ▶ Avoid TDF (instead ABC, TAF, MVC, Nuke-sparing)
- ▶ Avoid PIs (instead, INSTI, EFV, RPV)
- ▶ Start at a higher CD4 cell count
- ▶ Calcium and vitamin D
- ▶ Pre-ART Bisphosphonate (ZOL 57% reduction bone loss at week 48)

What to Do to Prevent Bone Loss during ART?

Switching from TDF To TAF in HIV-Infected Adults With Low BMD: A Pooled Analysis

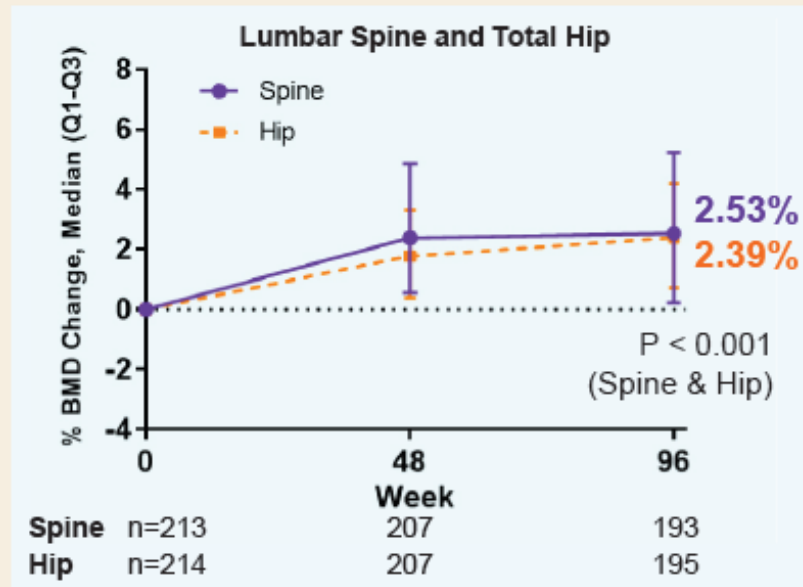
Todd T Brown¹, Michael T Yin², Samir Gupta³, Christine Katlama⁴, Adriano Lazzarin⁵, Kathy Melbourne⁶, Calvin Cohen⁶, YaPei Liu⁶, Thai Nguyen-Cleary⁶, Scott McCallister⁶

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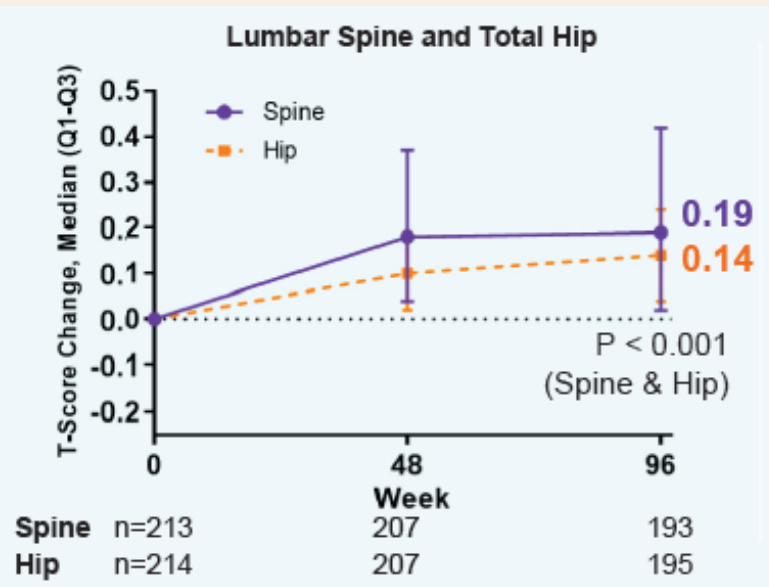
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Figure 2. Changes in BMD (%) and in T-Score Through Week 96

A. Changes in BMD



B. Changes in T-Score



P value for the change from baseline in BMD (%) or T-score at Week 96 (Wilcoxon Signed Ranked Test).

BMD improves by 2–3% over a 2–3-y time frame in HIV-1–infected adults who switch from TDF to tenofovir alafenamide (TAF)



Conclusions

- ▶ As people with HIV are living longer screening for geriatric syndromes such as frailty, gait instability/falls and osteoporosis will become critical in the care of our patients
- ▶ Screening for geriatric syndromes will ideally provide opportunities to decrease risks of functional decline, thus preventing ADL dependence/need for long term care
- ▶ I look forward to more fruitful collaborative efforts between Geriatric and HIV providers on how to allow all of our patients to age gracefully and independently

Resources for HIV providers on Aging



Grand Opening: The Go-To Place On HIV And Aging

Editorial February 5, 2014 3 Comments

In the U.S. the HIV population is aging. By 2015 half of the over 1.4 million people infected with HIV will be age 50 and older. Each day 80 more people become part of this older adult group. And, 1 in every 6 new HIV diagnoses occurs in the age 50 and older population. This graying of... [Continue Reading](#)

Card For Clinicians Caring For HIV-Infected Older Adults

Science Spotlight February 5, 2014

CARD FOR CLINICIANS CARING FOR HIV-INFECTED OLDER ADULTS The Quick Reference Card for Managing Older Adults with HIV was developed out of the New York State Dept. of Health AIDS Institute Office Of The Medical Director. To obtain a copy, access www.hivguidelines.org. The AIDS Institute determined HIV and Aging as a priority over ten years ago. The number... [Continue Reading](#)

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<http://hiv-age.org/>

With special thanks to



- ▶ Dorcas Baker & MAETC
- ▶ Dr Todd Brown
- ▶ Dr Genie Siegler
- ▶ Stephen Karpiak PhD

QUESTIONS.....