Assessing Frailty in Older People with HIV

Kristine M. Erlandson, MD, MS
Associate Professor of Medicine and Epidemiology
University of Colorado Denver
Denver, Colorado

Learning Objectives

After attending this presentation, learners will be able to:

- Describe the clinical relevance of physical function and frailty measures
- Select appropriate tools for physical function and frailty in the clinical or research setting
- Conduct (or find resources to conduct) these assessments in the clinical or research setting

Slide 3 of 30



80 years vs 80 years



Slide 4 of 30

How Can We Describe These Differences?

IMPAIRMENT in body function
- Arthritis, hearing impairment

LIMITATIONS in activity
- Slow gait speed, balance impairment

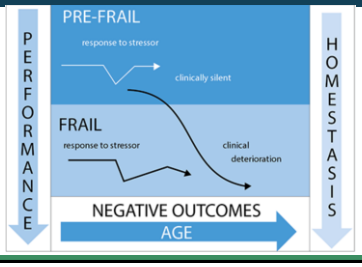
DISABILITY in participation
- Unable to use public transportation or work

FRAILTY
- Vulnerability

Slide 5 of 30

Erlandson et al. Curr HIV/AIDS Rep 2014

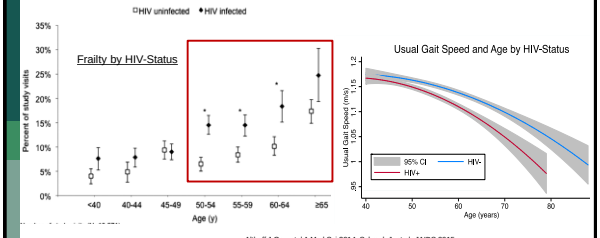
Frailty: A Measure of Vulnerability



Slide 6 of 30

L de Villiers
CMEJ.org.za

Frailty and Functional Limitations Appear to Occur More Frequently, and Perhaps Early with HIV



Slide 7 of 30

Althoff J Gerontol A Med Sci 2014; Schrack J, et al. JAIDS 2015

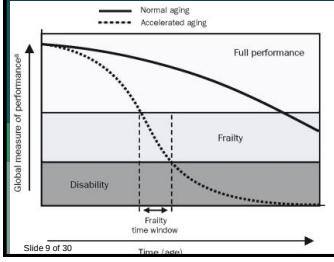
Which Tool(s) Should I Choose: What is the Question?

Tool	Implication	Intervention
Function (gait, grip, chair rise)	• High risk for disability/frailty • Identify earlier impairments	• Greatest potential to reverse with prevention/ intervention • Rehabilitation • Exercise, weight loss, nutrition
Frailty	• Vulnerability to stressors	• Minimize risk for progression- avoid unnecessary procedures • Treat underlying conditions • Exercise, nutrition • High-priority for referral to geriatric consultation • Address fall risk
Disability	• Decreased access to healthcare/ resource support	• Rehabilitative services • Community/social support • Minimize risk for social isolation

Slide 8 of 30

Fried LP, et al. J Gerontol Med Sci 2004

Where/When Can We Intervene to *Slow or Reverse Limitations*?



Frailty = highest risk for poor outcomes but difficult to reverse

***Early* interventions are more likely to shift function back to the "normal" trajectory**

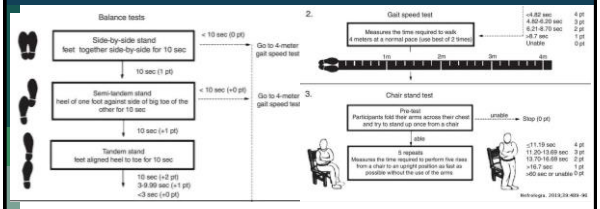
Slide 9 of 30

What Tool(s) Should I Choose for Assessing Functional Limitations?

Test	Pros	Cons
Short Physical Performance Battery	Well-validated in geriatric literature, objective outcomes, only requires chair and 4-m space	Takes 5-10 min, ceiling effects as the standard 12-scale exam, prospective
4-m walk	Well-validated in older populations, quick, no equipment, continuous outcome	Requires some training to standardize across sites; space, prospective
Chair rise time	Easy/fast, only requires chair, continuous outcome, less ceiling effect with more stands, greatest impairment in HIV, change with intervention	Patients with severe knee problems may be unable to complete, prospective; focused on lower extremity strength
Timed-up-and-go	Associated with increased falls, easy to do in the clinic, requires minimal equipment, multi-factorial assessment	Not as standardized for use in clinical trials More subjective interpretation into performance
400-mw/6 min walk	Higher level, less ceiling, continuous outcome, identify more subtle impairments	Takes more time, requires more space

Slide 10 of 30

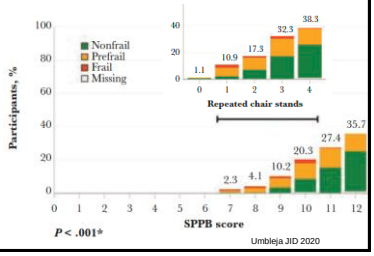
Short Physical Performance Battery



*Gait speed at usual pace
*Chair rise as fast as possible

More Subtle Physical Function Findings Might Better Detect Differences in PWH

- Frailty in 6%
- Impairments on other measures may identify more subtle impairments
- Almost 40% with SPPB score ≤10
- 62% with at least some difficulty rising from a chair



Umbleja JID 2020

Tandem Stand from SPPB

[redacted]

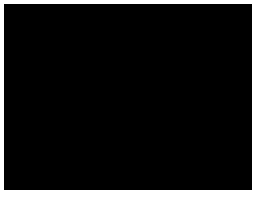
Tips:
- Read the script
- Demonstrate the procedure first
- Stand near enough to help balance the participant
- Test becomes progressively more difficult
- Don't talk to the participant during the 10 (or 30 second) interval
- No "re-do"

Gait Speed

- 4- METER walking test (short distance)
- Unobstructed finish line
- Don't pace the participant (walk behind, or wait at finish line if high-functioning)
- Usual pace

Slide 14 of 30

5 Times Sit-to-Stand (Chair Rise)



Tips:
- Read the script
- Demonstrate the procedure first
- Use a chair pushed against the wall (ideally without cushion and without arms)
- Participant crosses arms across chest
- Start the timer when you say go
- Position yourself where you could steady the participant
- Count aloud as the participant stands completely (don't pace them)
- Keep the timer going if the participant needs a break

Slide 15 of 30

Short Physical Performance Battery

- Free, downloadable training materials available on the NIA website to standardize
- Separate video on tips and tricks
- https://www.nia.nih.gov/research/labs/leps/short-physical-performance-battery-sppb

Slide 16 of 30

MODIFIED Short Physical Performance Battery

- Less ceiling effect in higher functioning persons
- 30 seconds for each balance test + one leg
- Gait speed test same
- 10 chair rises instead of 5, with split time at 5



Slide 17 of 30

Simonsick et al. J Gerontol 2001

Is it Feasible?

- Study evaluating the feasibility of administering the Short Physical Performance Battery across 3 HIV clinics
  - 2 clinics before/after a routine clinic visit
  - 3rd site administered at separate visit
- Training for staff was ~ 1 hour
- Mean assessment time was 7 minutes
- Feasible to implement without 'serious disruptions' or injuries

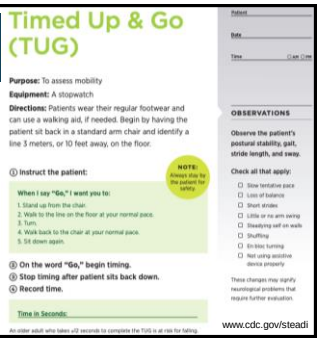
Crane et al. OFID 2019

Slide 18 of 30

100s of Options!

- 400-m walk
  - 8 laps on 50m course
  - Continuous, better discrimination at higher function
- TUG (Timed-up-and-Go)
  - Predictive of falls
  - Easy to do in the clinic

https://geriatrictoolkit.missouri.edu/


Timed Up & Go (TUG)

Purpose: To assess mobility

Equipment: A stopwatch

Directions: Patients wear their regular footwear and can use a walking aid, if needed. Begin by having the patient sit back in a standard arm chair and identify a line 3 meters, or 10 feet away, on the floor.

ⓘ Instruct the patient:

NOTE: Always stay by the patient for safety.

When I say "Go," I want you to:
1. Stand up from the chair.
2. Walk to the line on the floor at your normal pace.
3. Turn.
4. Walk back to the chair at your normal pace.
5. Sit down again.

ⓐ On the word "Go," begin timing.
ⓑ Stop timing after patient sits back down.
ⓒ Record time.

Time in Seconds:

An older adult who takes ≥12 seconds to complete the TUG is at risk for falling.

Patient
Date
Time

OBSERVATIONS

Observe the patient's postural stability, gait, stride length, and sway.

Check all that apply:

- ☐ Slow tentative pace
- ☐ Loss of balance
- ☐ Short strides
- ☐ Little or no arm swing
- ☐ Steadying self on walls
- ☐ Shuffling
- ☐ En-bloc turning
- ☐ Not using assistive device properly

These changes may signify neurological problems that require further evaluation.

www.cdc.gov/steadi

Slide 19 of 30

What Tool(s) Should I Choose for Assessing Frailty?

Test	Pros	Cons
Frailty Phenotype	Well-validated in geriatric literature and HIV literature	Requires dynamometer; categorical; subjective components; prospective only; 10 min to complete; cognition or depression may confound results; ceiling effect
Frail Scale	Very fast, correlates relatively well with the Frailty Phenotype and Frailty Index, requires no equipment	Subjective, very limited data in HIV; unclear how amenable this is to change
Frailty or VACS Index	Easy to derive from labs, can collect retrospectively, continuous outcome	No measure of physical function; takes effort up front to develop; measure of comorbidity burden rather than a unique phenotype of aging
Questionnaires	Easy to standardize, can be done in waiting room or by mail, might be more appropriate as a brief screen	Subjective; may not be amenable to interventions

Slide 20 of 30

The Frailty Phenotype

Reflects a *vulnerability* as result of multiple impairments:

- Slow gait
- Weak grip
- Low activity
- Exhaustion
- Unintentional weight loss (≥10 lbs in prior year)



0= Robust
1-2 = Pre-frail
3+ = Frail

Fried, J Gerontol A Biol Sci Med Sci 2001

Slide 21 of 30

The Frailty Phenotype

- **Walk Time**, stratified by gender and height (gender-specific cutoff a medium height).

Men	*Cutoff for Time to Walk 15 feet criterion for frailty*
Height ≤ 173 cm	≥7 seconds
Height > 173 cm	≥6 seconds
Women	
Height ≤ 159 cm	≥7 seconds
Height > 159 cm	≥6 seconds

= 4.57 meters (vs 4 meters in the SPPB)

- **Grip Strength**, stratified by gender and body mass index (BMI) quartiles:

Men	*Cutoff for grip strength (Kg) criterion for frailty*
BMI ≤ 24	≤29
BMI 24.1–26	≤30
BMI 26.1–28	≤30
BMI > 28	≤32
Women	
BMI ≤ 23	≤17
BMI 23.1–26	≤17.3
BMI 26.1–29	≤18
BMI > 29	≤21

Cut-points based on the upper 20% of performance in a larger geriatric cohort

Fried, J Gerontol A Biol Sci Med Sci 2001

Slide 22 of 30

Frailty Phenotype Components/Definitions

- Exhaustion based on CES-D Depression Scale, how often did you feel this way (3-4 days/week or more = frailty criteria):
  - "I felt that everything I did was an effort" or
  - "I could not get going"
- Physical Activity: Short version of Minnesota Leisure Time Activity questionnaire (Kcals <383/week for men and <270 for women)
  - Replaced by SF-36 question on limitations in vigorous activity for many HIV studies

Slide 23 of 30 Fried, J Gerontol A Biol Sci Med Sci 2001

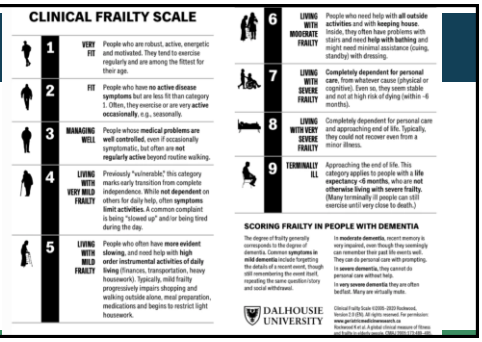
Frailty Differs in Prevalence (Sampling of Studies)

Authors	Site	Study Population	Prevalence of Frailty
Wulunggono	Indonesia	164 HIV, age 30+, all on ART	4%
Onen	US	Median age 47; 95% on ART	5%
Erlandson	US	Aged 40+, 99% on ART	6%
Umbleja	US	Age 40+, substudy of REPRIEVE	6%
Erlandson	US	359 HIV, 45-65 years; 100% ART	8%
Kooij	Amsterdam	Age 45+, 94% on ART	11%
Allavena	France	Age 70+	13.5%
Piggott	US	≥18 years; IVDU; 54% ART	15%
Pathai	Capetown	≥30 years; 87% on ART	18% ART; 28% no ART
Rees	US	CD4<200, weight loss, poor adherence	19%

Differing components, cut-points, and control populations may contribute to varying prevalence of frailty

Slide 24 of 30 Onen, J Frailty Aging 2014; Erlandson, HIV Clin Trials 2012; Onen, J Infect 2009; Piggott, PLOS One 2013; Pathai, JAIDS 2013; Rees, J Vis Exp 2013; Sandkovsky HIV Clin Trials 2013; Erlandson JID 2017; Althoff 2014; Kooij AIDS 2016

Simpler Version



Slide 25 of 30

Frailty: By Index

- *Accumulation of deficits*
- Variables that increase with age but are not ubiquitous with age (ie, presbyopia) and are associated with health status
- Generally a minimum of 50 variables is recommended
- Can be derived from chart review and developed for a specific health system/study/cohort
- # of variables impaired/ # variables assessed

Searle, et al. A standard procedure for creating a frailty index. BMC Geriatr 2008
Jones, et al. Operationalizing a frailty index from a standardized comprehensive geriatric assessment. JAGS 2004.

Slide 26 of 30

Appendix 1: List of variables used by the Canadian Study of Health and Aging to construct the 70-item CSHA Frailty Index

Activities of daily living, physical function, falls

- Changes in everyday activities
- Head and neck problems
- Poor muscle tone in neck
- Bradykinesia, facial
- Problems getting dressed
- Problems with bathing
- Problems carrying out personal grooming
- Urinary incontinence
- Toileting problems
- Bulk difficulties
- Rectal problems
- Gastrointestinal problems
- Problems cooking
- Sucking problems
- Problems going out alone
- Impaired mobility
- Musculoskeletal problems
- Bradykinesia of the limbs
- Poor muscle tone in limbs
- Poor limb coordination
- Poor coordination, trunk
- Poor standing posture
- Irregular gait pattern
- Falls

Mood, cognition, neurologic

- Mood problems
- Feeling sad, blue, depressed
- History of depressed mood
- Tiredness all the time
- Depression (clinical impression)
- Sleep changes
- Restlessness
- Memory changes
- Short-term memory impairment
- Long-term memory impairment
- Changes in general mental functioning
- Onset of cognitive symptoms
- Clouding or delirium
- Paranoid features
- History relevant to cognitive impairment or loss
- Family history relevant to cognitive impairment or loss
- Impaired vibration
- Tremor at rest
- Postural tremor
- Intention tremor
- History of Parkinson's disease
- Family history of degenerative disease

More neurologic + cardiovascular, endocrinology & respiratory

- Seizures, partial complex
- Seizures, generalized
- Syncope or blackouts
- Headache
- Cerebrovascular problems
- History of stroke
- History of diabetes mellitus
- Arterial hypertension
- Peripheral pulses
- Cardiac problems
- Myocardial infarction
- Arrhythmia
- Congestive heart failure
- Lung problems
- Respiratory problems
- History of thyroid disease
- Thyroid problems
- Skin problems
- Malignant disease
- Breast problems
- Abdominal problems
- Presence of snout reflex
- Presence of the palmomental reflex
- Other medical history

Rockwood, CMAJ 2005

Slide 27 of 30

Slide 28 of 30

A Frailty Index for HIV Using 50 Variables

Guaraldi, et al. AIDS 2015

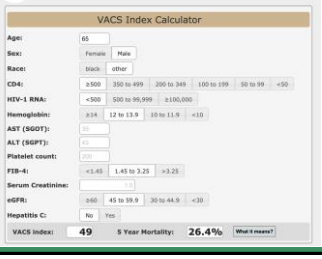
Variable	Deficit description
Lipoatrophy	Multicenter AIDS Cohort Study (MACS) criteria [39]
Lipohypertrophy	MACS criteria [40]
Nonalcoholic fatty liver disease	Liver/spleen ratio < 1.1
Menopause or male hypogonadism	If female: FSH > 30 IU/l and LH < 30 IU/l and/or absence of menstruation > 1 year If male: testosterone < 300 ng/dl
High or low BMI	<18 or >25 kg/m²
High waist circumference	If female: > 88 cm If male: > 102 cm
High visceral adipose tissue	VAT > 130 cm² or VAT/FAT ratio >0.5
Sarcopenia or pseudosarcopenia	Fat-free mass index < −1 SD
High total cholesterol	>200 mg/dl
High low-density lipoprotein	>100 mg/dl
Low high-density lipoprotein	<40 mg/dl
High triglycerides	>150 mg/dl
High homocysteine	If female: >10 μmol/l If male: >15 μmol/l
Abnormal white blood cell counts	<4000 cells/μl
Anemia	If female: <10 g/dl If male: <12 g/dl
Hepatitis C coinfection	Positive
Hepatitis B coinfection	Hepatitis B antigen positive
Vitamin D insufficiency	<30 ng/ml
Polypharmacy	≥5 drug classes (excluding antiretroviral therapy)
Abnormal parathyroid hormone	>68 pg/ml
Elevated D-dimer	>Sample mean (358)
Elevated C-reactive protein	>0.7 mg/l
Sedentary lifestyle	<3 hours/week physical activity
Atherosclerosis	Coronary artery calcium score > 100 or intima media thickness > 0.85 mm

Variable	Deficit description
Hyponatremia	<125 mmol/l
Proteinuria or albuminuria	≥5 mg/mmol
Elevated aspartate transaminase	>31 U/l
Elevated alanine transaminase	>31 U/l
Abnormal alkaline phosphatase	<38 or >126 U/l
Elevated γ-glutamyl transphosphatase	>55 U/l
Low platelets	<150 billion/l
Abnormal potassium	<3.5 or >5.3 mEq/l
Abnormal phosphorus	<2.5 or >5.1 mg/dl
Abnormal thyroid-stimulating hormone	<0.27 or >4.2 mU/l
Elevated total bilirubin	>1-10 mg/dl
Unemployment	Self-report
Cardiovascular disease	Clinical diagnosis
Hypertension	Measured blood pressure or on treatment
Diabetes mellitus type II	Fasting glucose >125 mg/dl or on treatment
Chronic kidney disease	Two estimated glomerular filtration rate measurements <60 ml/min/1.73 m²
Cirrhosis	FIB-4 score >3.25
Chronic obstructive pulmonary disease	Spirometry: FEV1/FVC ratio <0.7
Osteoporosis	Dual-energy X-ray absorptiometry T or Z score < −2.5 or fragility fracture
Any cancer	Clinical diagnosis with biopsy confirmation
Current CD4⁺ cell count	<500 cells/μl
Nadir CD4⁺ cell count	<200 cells/μl
HIV viral load	>40 copies/ml
CD4⁺/CD8⁺ cell ratio	<1.0
Duration of HIV infection	>10 years
Pre-HAART start	Start of antiretroviral therapy before 1 January 1997
History of AIDS	History of CDC category C HIV disease [42]
ART failure	History of viral load > 1000 copies/ml while on ART

Frailty: By Index

- Veterans Aging Cohort Study Index is a similar concept of laboratory-derived variables
- Used to identify those at high risk of mortality with (or without) HIV

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



Slide 29 of 30

Summary

- Functional limitations and frailty occur earlier and more often in people with HIV
- Assessment of function and frailty can identify at risk patients to prioritize for early interventions
- Many different tools are available, depending on the goal(s) of assessment, setting, equipment, and personnel

Slide 30 of 30

Question-and-Answer Session